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INVITED REVIEW

Influence of food-derived bioactives on gut microbiota compositions and their metabolites by focusing on neurotransmitters

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Abstract
The behavior of gut microbiota is closely involved in sustaining balanced immune and metabolic homeostasis, and the dysbiosis of gut microbiota can lead to severe disease. Foods and dietary patterns are the primary drivers in shaping/designing gut microbiota compositions and their metabolites across the lifetime. This indicates the importance of functional molecules present in the food matrix in the life of gut microbiota and their influence on the host's biological system. In this contribution, the effects of different dietary choices and bioactive compounds (i.e., phenolics, vitamins, carotenoids) on gut microbiome compositions and their metabolites are comprehensively discussed by focusing on neurotransmitters. This study may provide useful information that fills a gap in understanding the role of the gut microbiota and its alterations as affected by foods and food-derived bioactives.

Keywords Gut microbiota · Gut-Brain-Axis · Bioactive compound · Gut microbiota-derived metabolite · Neurotransmitter

Gut microbiota

The collection of microorganisms including bacteria, archaea and eukaryotes inhabiting the gut is referred to as the 'gut microbiota' (Foster and Neufeld, 2013). The gut microbiota is engaged in sustaining balanced metabolism by contributing to the successful degradation of macromolecules ingested such as carbohydrates, proteins, and lipids (Chait et al., 2020). Recent findings show that gut microbiota plays a crucial role in the functions of the central nervous system (CNS) (Heijtz et al., 2011). Residential and commensal bacteria colonize the gut of human beings after birth and throughout life; 10^{14}–10^{15} of bacteria along with 1000 distinct bacterial species live in the gut, contributing to the immune function, nutrient processing, and other aspects of the host's physiology (Foster and Neufeld, 2013; Macpherson and Uhr, 2004; Tlaskalová-Hogenová et al., 2004).

Recent advanced techniques such as molecular and metagenomic approaches have enabled the characterization of the composition of the gut microbiota, revealing that the diverse microbiomes in the gut form a complex ecology and community (Foster and Neufeld, 2013). There are two predominant bacterial phyla in the gut: *Firmicutes* and *Bacteroides*, which account for more than 70% of the microbiome in the gut (Eckburg et al., 2005; Lay et al., 2005). Moreover, *Proteobacteria*, *Fusobacteria*, *Actinobacteria*, and *Verrucomicrobia* also reside in the gut in a lower number compared to *Firmicutes* and *Bacteroides*. A variety of environmental factors (i.e., genetics, diet, age, metabolism, geography, stress, and antibiotic treatment) affect the gut microbiota composition and behavior, which in turn influence its metabolic functions. In this review, we mainly focus on how food-derived bioactives affect gut microbiota profiles and their metabolites.

Diseases related to the dysbiosis of gut microbiota

The human gut possesses trillions of symbiotic microorganisms (bacteria, archaea, fungi, etc.) that play a crucial role in regulating the host's unique physiology in health and disease (Foster and Neufeld, 2013). Gut dysbiosis is referred to as a disruption of gut microbiota homeostasis due to an imbalance in microflora, alterations in their functional profiles and metabolism, or changes in their distribution (Moos et al.,

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2016). A range of factors such as diet, age, genetics, and medications are responsible for gut dysbiosis (Chait et al., 2020; Heiman and Greenway, 2016; Maier et al., 2018; Odamaki et al., 2016).

Recent findings reported that the dysbiosis of gut microbiota is strongly associated with the occurrence of many severe diseases such as inflammatory bowel disease, type 2 diabetes, Crohn's disease, Parkinson's disease, Alzheimer's disease, schizophrenia, and autism as well as mental illnesses such as major depressive disorder and anxiety (Carding et al., 2015; Clarke et al., 2013; Diaz et al., 2011; Gabbay et al., 2017; Nedic et al., 2021), indicating the importance of maintaining a well-balanced gut microbiota.

Gut dysbiosis by psychotropics

Psychotropic medications, such as antidepressants, mood stabilizers, antipsychotics, and anxiolytics, are widely applied in the treatment of many psychiatric disorders in which they exert their bioactivity by contributing to CNS reactions (Kaye et al., 2018). According to recent research, the alteration of gut microbiota diversity can be caused by psychotropic medications (Chait et al., 2020). Indeed, much attention has been paid to the alteration of gut microbiota by psychotropic administration in both in vitro and in vivo models. Chait et al. (2020) examined the antimicrobial activity of psychotropics in which the abundance of *Akkermansia muciniphila*, *Bifidobacterium animalis* and *Bacteroides fragilis* were remarkably changed by antidepressant drugs such as phenelzine, desipramine, venlafaxine, bupropion, (S)-citalopram, and aripiprazole. Moreover, olanzapine administration increased the abundance of *Firmicutes* and *Erysipelotrichi*, while it decreased the level of *Bacteroidetes*, *Proteobacteria*, and *Actinobacteria* in a rat model (Davey et al., 2012; Morgan et al., 2014). In addition to the above evidence, a variety of studies have been carried out to screen the alteration of the gut microbiota profile upon psychotropic administration (Cussotto et al., 2019; Lyte et al., 2019). However, research on how this alteration affects gut microbiota-derived metabolites is limited.

The importance of gut microbiota-derived metabolites

Metabolites secreted by gut microbiota have a significant function in the gut microbiota-brain axis; for instance, gut microbiota secrete diverse metabolites including neurotransmitters and their precursors, and these molecules influence the interaction between the gut and brain via the endocrine, immune, and neurotransmitter systems (Chen et al., 2021). For instance, gut bacteria secrete lipopolysaccharide and other endotoxins responsible for the activation of the peripheral immune system through immune cell activation and cytokine release, leading to the initiation of CNS inflammation (Caspani and Swann, 2019). Moreover, the gut microbiota produces metabolites such as gamma-aminobutyric acid (GABA), acetylcholine, short-chain fatty acid (SCFA), norepinephrine, and dopamine, and these molecules influence brain functions and conditions (Cox and Weiner, 2018; Cryan et al., 2020). Thus, gut microbiota-derived metabolites significantly affect the host's body and brain health, emphasizing the importance of the alteration of gut microbiota diversity upon exposure to psychotropic administration. Until now, despite tremendous scientific efforts to understand the alteration/dysregulation of gut microbiota as affected by psychotropics, critical limitations remain in understanding changes in the metabolites of gut microbiota upon exposure to psychotropics and following the alteration of gut microbiota composition. Today, much progress has been made in mass spectrometry-based metabolomics in the identification and quantification of metabolites in a wide spectrum of biological samples (i.e., plant, microbial and mammalian samples), demonstrating that mass spectrometry-based is a rapid and high throughput approach in the determination of metabolite profiles in target samples. (Fernie et al., 2004; Gieger et al., 2008; Rinschen et al., 2019).

Gut-brain-axis

The gut-brain axis, which refers to the two-way communication between the gut microbiota and the brain, has a crucial role in neuronal development, cognitive regulation, and brain function (Cryan et al., 2020) (Fig. 1). There are two main pathways in transmitting information between two areas: "top-down" and "bottom-up". The top-down pathway is regulated by the hypothalamus–pituitary–adrenal axis in which the cortisol and cytokine secreted by immune cells significantly influence the gut microbiota community locally and systemically, influencing the diversity of gut microbiota and gut permeability (Cryan and Dinan, 2012). Conversely, the gut microbiota can influence alterations in the levels of circulating cytokines, affecting brain functions, and is referred to as the "bottom-up" pathway. In this way, the level of tryptophan and its interaction with the vagus and enteric nerve act as key functions in the gut-microbiota-brain axis. In addition, recent findings indicate that the gut microbiota produces a wide spectrum of metabolites including neurotransmitters and their precursors, which then take part in the bottom-up pathway. For example, spore-forming bacteria produce metabolites that can improve the biosynthesis of serotonin in enterochromaffin cells (Chen et al., 2021). In addition, certain neurotransmitters and their precursors

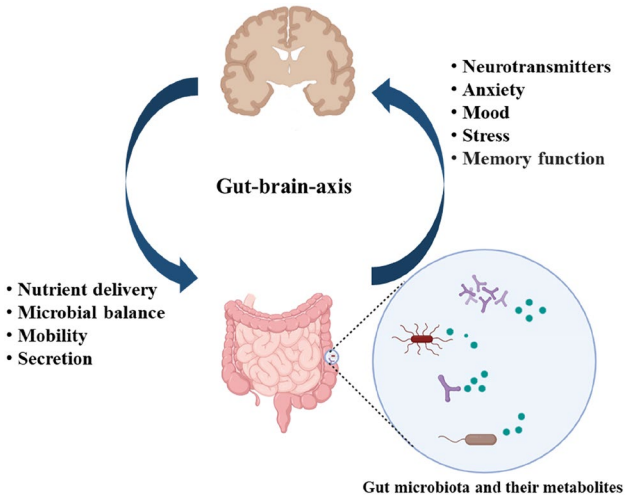

Fig. 1 Gut-brain-axis: The importance of bidirectional communication between the brain and gut microbiota and their metabolite in controlling mental disorders

released by the gut microbiota and enteroendocrine cells enter into the blood circulation and eventually reach the brain. This demonstrates the significance of gut microbiota and their metabolites in the communication between the gut and brain, in particular in the "bottom-up" pathway.

Gut microbiota-derived metabolites with a focus on neurotransmitters

Many recent studies have investigated the biosynthesis of neurotransmitters (GABA, SCFA, dopamine, acetylcholine, norepinephrine, etc.) by gut microbiota as their metabolites as well as their influence on the brain's functions (Cox and Weiner, 2018; Cryan et al., 2020). For example, some research groups reported that interference in producing monoamine due to gut dysbiosis resulted in depressive disorder in the animal system, indicating a strong influence of gut microbiota on the occurrence of mental disorders (Clarke et al., 2013; Diaz et al., 2011; Neufeld et al., 2011). Moreover, patients with depression showed a notable alteration in the level of *Firmicutes, Actinobacteria,* and *Bacteroidetes* compared to a control group (Zheng et al., 2016). Minato et al. (2017) reported that a significantly reduced level of *Prevotellaceae* was found in patients with progressive Parkinson's disease, which led them to suggest that the abundance of *Prevotellaceae* is a biomarker for Parkinson's disease. Moreover, Li et al. (2017) stated that the level of *Faecalibacterium* is strongly related to the development and neuropathology of Parkinson's disease. The above evidence clearly shows the crucial roles of the diversity of gut microbiota and their metabolite profiles in sustaining a healthy brain.

Synthesis and production of neurotransmitters by gut microbiota

Dopamine is a major catecholaminergic neurotransmitter and plays a crucial role in many functions of the brain such as emotion, memory, attention, motivation, and reward (Klein et al., 2019; Kleinridders and Pothos, 2019). Increasing evidence has demonstrated that dysregulation in the production of dopamine is closely related to mental disorders, including depression and anxiety (Belujon and Grace, 2017; Camardese et al., 2014; Carpenter et al., 2012; Gonzalez-Arancibia et al., 2019; Moraga-Amaro et al., 2014). Some *Bacillus* species such as *B. cereus*, *B. subtilis,* and *B. mycoides* can synthesize dopamine (Tsavkelova et al., 2000). In addition, *Hafnia alvei* (NCIMB, 11,999), (NCIMB, 10,466), *Klebsiella pneumoniae* (NCIMB, 673), and *morganii* enable the production of dopamine in the gut (Özoğul, 2004; Shishov et al., 2009). Cryan and Dinan (2012) also demonstrated the production and secretion of dopamine by *Bacillus* and *Escherichia* species. However, the mechanism of dopamine synthesis in the gut microbiota has not yet been fully investigated.

Serotonin is engaged in diverse brain functions including mood, modulating reward, memory, cognition, learning, and other physiological processes (i.e., vasoconstriction and vomiting). Changes in the expression and production of serotonin in the brain lead to the pathogenesis of mental illnesses, including depressive disorders and anxiety (Helton and Lohoff, 2015). The main pathway for the biosynthesis of serotonin is through enterochromaffin cells in the gut, thereby tryptophan hydroxylase 1 (Tph1) is involved in the reaction as the rate-limiting enzyme (Kwon et al., 2019). The synthesis rate of serotonin by enterochromaffin cells is largely affected by the available concentration of tryptophan required for the reaction; therefore, sustaining an adequate amount of tryptophan in the gastrointestinal tract is important to maintaining an adequate level of serotonin.

Many studies have found serotonin-producing bacteria in the gut such as *E. coli* (K-12), *Lactococcus lactis* subsp. *cremoris* (MG 1363), *Lactobacillus plantarum* (FI8595), *Candida* spp., *Streptococcus* spp., *Streptococcus thermophilus* (NCFB2392), *Escherichia* spp., and *Enterococcus* spp. (Cryan and Dinan, 2012; Özoğul et al., 2012; Shishov et al., 2009). Gut microbiota also indirectly engage in the synthesis of serotonin; for example, enterochromaffin cells synthesize serotonin when they receive signals via gut microbiota-derived metabolites, which increase the expression of the gene TPH1. Moreover, SCFAs produced by gut microbiota elevate the production of serotonin in the enterochromaffin cells (Reigstad et al., 2015). However, additional research should be carried out to understand the direct pathways for the synthesis of serotonin in gut microbiota.

Transportation of gut microbiota-derived neurotransmitters to the brain

Gut microbiota-derived GABA is transferred to the brain via different pathways. Much attention has been paid to exploring the transportation mechanisms of GABA to the brain produced by the gut microbiota. GABA absorption in the intestinal system takes place via the transcellular pathway with the assistance of carrier proteins. GABA in plasma can enter the blood–brain barrier (BBB) via GABA transporters, including GABA transporter type 1, 2, 3, and 4, which are also localized in other organs including the kidneys and liver. The plasma membrane GABA transporters in the brain have a significant role in sustaining an adequate level of extracellular GABA around the synapses (Zhou and Danbolt, 2013). The GABA transporters are the active voltage-dependent system through which the inward electrochemical gradient of Na^+ considerably influences the action of GABA transporters (Scimemi, 2014). In addition, the GABA transporter displays a weak micromolecular affinity to GABA, and it demands Cl^- in the extracellular matrix (Scimemi, 2014). Therefore, the mechanism of GABA transportation from the intestinal system to the brain is well understood.

SCFAs produced by the fermentation of fiber by the gut microbiota are absorbed via colonocytes through sodium-coupled monocarboxylate transporters (SMCTs) and monocarboxylate transporters (MCTs), referred to as active transport (Vijay and Morris, 2014). The transportation of SCFAs occurs through MCT1 transporters in an H^+-dependent, while they can also be transported via sodium-dependent and electrogenic SMCTs, which is referred to as SCFA anion transport (Stumpff, 2018). SCFAs present in colonocytes are metabolized through the citric acid cycle in the mitochondria to generate ATP and energy (Schönfeld and Wojtczak, 2016). However, certain portions of SCFAs in colonocytes are not metabolized, leading them to enter circulation for consumption as an essential energy source in hepatocytes, except for acetic acids, which are not metabolized in the liver (Schönfeld and Wojtczak, 2016). This implies that only a certain range of colon-derived SCFAs enter the systemic circulation; for instance, 36%, 9%, and 2% of gut microbiota-derived acetate, propionate, and butyrate, respectively, enter the blood plasma and tissue (Boets et al., 2015). Bloemen et al. (2009) demonstrated that the usual levels of acetate, propionate, and butyrate in portal blood were 260 μM, 30 μM, and 30 μM, respectively. However, the penetration abilities of SCFAs to the BBB have been rarely investigated; thus, further studies are needed for a better understanding of the effects of gut-derived neurotransmitters on the roles of the brain. Meanwhile, the majority of neurotransmitters, including norepinephrine, dopamine, and acetylcholine, in blood circulation cannot get through the BBB due to the absence of proper transporters (Chen et al., 2021). However, the precursor molecules of these neurotransmitters, including tryptophan and tyrosine, can penetrate the BBB. Thus, they can be localized in the relevant cells and utilized for the biosynthesis of neurotransmitters in the brain.

Alteration of gut microbiomes by bioactive compounds

Increasing findings show the remarkable influence of bioactive compounds in shaping the compositional and functional patterns of the gut microbiota. Many studies have shown that bioactive compounds derived from diverse food sources cause substantial alterations in the composition of the gut microbiota (Wen and Duffy 2017; Wu et al. 2011). The alterations of gut microbiota profiles as affected by food bioactives are summarized in Table 1.

Polyphenols also have regulatory effects on gut microbiota composition. Gallic acid significantly reduced the counts of *Bacteroides* spp. and increased the abundance of *Atopobium* spp. (Hidalgo et al., 2012). Catechin improved the growth of the *Clostridium coccoides–Eubacterium rectale* group, *E. coli*, and *Bifidobacterium* spp. and repressed the level of the *Clostridium histolyticum* group in in vitro batch-culture fermentation systems. The exposure of epicatechin to the gut microbiota increased the abundance of the *C. coccoides–E. rectale* group (Tzounis et al., 2011). Clavel et al. (2005) found that the administration of isoflavones at a dose of 100 mg/day for two months in human tests caused an enhancement in the level of the *C. coccoides–E. rectale* cluster, *Faecalibacterium prausnitzii* subgroup, *Lactobacillus-Enterococcus* group, and *B.* spp. The administration of stilbene (resveratrol) dramatically improved the counts of *Bifidobacterium* and *Lactobacillus* during 20 days in rats in in vivo dietary intervention tests (Larrosa et al., 2009). Quercetin elevated the level of *Bacteroides*, *Bifidobacterium*, *Lactobacillus*, and *Clostridia* and reduced those of *Fusobacterium* and *Enterococcus* in a mouse model (Lin et al., 2019).

Research has also been carried out regarding the influence of proanthocyanidin on gut microbiota composition. For instance, Hidalgo et al. (2012) tested the effects of malvidin-3-glucoside on the alteration of gut microbiota in batch-culture fermentation with human fecal bacteria. Malvidin-3-glucoside remarkably improved the level of the beneficial bacteria *B.* spp. and *Lactobacillus* spp. In addition to the above findings, many studies have reported on the alteration of gut microbiota as affected by diverse phenolic

Table 1 Alteration in gut microbiota profiles by bioactive compounds

Bioactive compound	Change in the composition of gut microbiome	Reference
Gallic acid	Reducing the counts of *Bacteroides* spp. and enhancement in the abundance of *Atopobium* spp.	Hidalgo et al. (2012)
Catechin	Simulate the growth of the *C. coccoides–E. rectale* group, *Bifidobacterium* spp. and *E. coli*, and repress the level of *C. histolyticum* group in in vitro batch-culture fermentation system	Tzounis et al. (2011)
Epicatechin	Increase in the counts of the *C. coccoides–E. rectale* group in in vitro batch-culture fermentation system	Tzounis et al. (2011)
Isoflavones	Enhancement in the abundance of *C. coccoides-E. rectale* cluster, *F. prausnitzii* subgroup, *L.-Enterococcus* group, and *Bifidobacterium* spp.	Clavel et al. (2005)
Quercetin	Increase in the abundance of *Bacteroides*, *Bifidobacterium*, *Lactobacillus*, and *Clostridia* and a decrease in *Fusobacterium* and *Enterococcus* in mice	Lin et al. (2019)
Stilbene (resveratrol)	Increase in the counts of *Bifidobacterium* and *Lactobacillus* during 20 days in the rats in vivo dietary intervention tests	Larrosa et al. (2009)
Malvidin-3-glucoside	Increase in the level of beneficial bacteria *Bifidobacterium* spp. and *Lactobacillus* spp.	Hidalgo et al. (2012)
Phloridzin	Elevate the adhesion of *L. rhamnosus* to Caco-2 cells	Parkar et al. (2008)
Astaxanthin	Increase in the abundance of *Proteobacteria* and *Bacteroides* in six-week-old male and female BCO2 knockout mice Increase in the abundance of *Actinobacteria* and *Bifidobacterium* in male genetic background C57BL/6 J mice	Lyu et al. (2018)
Eugenol	Increase in the population of *Clostridales* in mice	Wlodarska et al. (2015)
Curcumin	Increase in the population of *Clostridium* spp., *Bacteroides* spp., *Citrobacter* spp., *Cronobacter* spp., *Enterobacter* spp., *Enterococcus* spp., *Klebsiella* spp., *Parabacteroides* spp., and *Pseudomonas* spp. in human study	Peterson et al. (2018)

compounds. Phloridzin improved the adhesion of *Lactobacillus rhamnosus* to Caco-2 cells (Parkar et al., 2008).

Meanwhile, carotenoids also showed a remarkable influence on the alteration of gut microbiota profiles. For instance, *β*-carotene remarkably reduced the level of *Bacteroidetes* and the *genus Prevotella* and *Blautia*, while it led to an increase in the abundance of phyla Firmicutes, genera p-75-a5, and Parabacteroides (Li et al., 2021). Moreover, a *β*-carotene treatment significantly enhanced the level of *Faecalibacterium* in a rat model system (Zhu et al., 2021).

Recently, accumulating evidence has shown that vitamins from the plant- and animal-based foods lead to alterations in the microbiome profiles in the gut. The changes in gut microbiome composition can result from exposure to certain food-derived bioactives or indirectly due to changes in the physiology of gut and intestinal lumen conditions (Pham et al., 2021). Vitamins have been proven to be microbiome-modulators through several pathways. Some vitamins, including vitamins A, B6, C, and E, cause direct alterations in gut microbiome profiles (Castillo et al., 2016; Miki et al., 2017; Vergalito et al., 2018;). In this section, a wide spectrum of examples regarding the effect of vitamins on changes in gut microbiota composition are summarized.

Liu et al. (2017) reported that giving 200,000 IU of a vitamin A supplement to 64 young children suffering from autism disorders significantly increased the abundance of *Bacteroidetes*, while it reduced the abundance of *Proteobacteria*, *Actinobacteria*, *Enterobacter*, *Escherichia-Shigella*, and *Clostridium*. Lv et al. (2016) studied the alteration of gut microbiota of infants with persistent diarrhea profiles through a vitamin A supplement in which the results showed that the levels of *Enterococcus*, *Enterococcaceae*, and *Lactobacillales* were remarkably increased, while the abundance of *Escherichia-Shigella* was decreased. Meanwhile, another study showed that the administration of vitamin A to 16 adult patients with cystic fibrosis enhanced the level of *Clostridium* and *Gemellales* and significantly decreased *Bacteroidetes/Bacteroidia/Bacteroidales* (Li et al., 2017). Thus, the above examples provide crucial information regarding discrepancies in the alteration of gut microbiota profiles due to the supplementation of vitamin A depending on the health status of patients, the dose, and other environmental differences. Other bioactive molecules such as astaxanthin, eugenol, and curcumin also remarkably affect alterations of the composition of gut microbiota.

Changes in gut microbiota-derived metabolites by bioactives and diets

Recently, increasing research has focused on the influences of food-derived bioactives on alterations in gut microbiota composition and their metabolites, in particular in neurotransmitters. Changes in gut microbiota-derived metabolites as affected by bioactives are summarized in Table 2.

Fogliano et al. (2011) investigated the influence of polyphenols in the water-insoluble cocoa fraction. They found an increase in the abundance of *Bifidobacteria* and *Lactobacilli*

Table 2 Changes in gut microbiota-derived metabolites by bioactives

Diet/food ingredient	Alteration in gut microbiome-derived metabolite	Reference
Polyphenols in the water-insoluble cocoa fraction	Increase in the level of butyrate	Fogliano et al. (2011)
Apple juice extracts and red beet juice extracts	Increase in the contents of acetate and total short-chain fatty acids (propionic acid and butyric acid) in rats	Sembries et al (2006)
Anthocyanin-rich blueberry extract	Increase in the production of kynurenic acid by altering tryptophan metabolism	Marques et al. (2018)
Berberine	Promotion in the production of butyrate in rats	Wang et al. (2018)
Dietary fiber (resistant starch from potatoes)	Increase in the production of short-chain fatty acids including butyrate	Baxter et al. (2019)
Western-style diet (high in fat)	Enhancing the level of *Firmicutes*/*Bacteroidetes* ratio and the abundance of *Proteobacteria* and *Spirochaetes* in mice model Reducing the level of SCFAs including acetic, propionic, and butyric acids in cecal contents along with altered anxiety-like behavior	Ohland et al. (2013)
Carbohydrates (fiber)	A decrease in carbohydrates intake (including fiber) significantly reduced the richness of fiber-degrading bacteria, whereas the abundance of *Eggerrthella, Lactococcus*, and *Streptococcus* was increased, leading to a decrease in the production of SCFAs	Mardinoglu et al. (2018)

followed by the elevation of butyrate production, indicating that bioactives from diets can modulate gut microbiota composition and their metabolites. Sembries et al. (2006) demonstrated that apple juice extracts and red beet juice extracts enhanced the level of neurotransmitters such as acetate, propionic acid, and butyric acid in a rat model. Moreover, Marques et al. (2018) found an increase in the production of kynurenic acid by altering tryptophan metabolism in a rat model. Other studies also demonstrate improvements in the level of SCFAs in rat models upon exposure to food sources; namely, berberine promoted the production of butyrate in rats, and dietary fiber (resistant starch from potatoes) increased the production of SCFAs including butyrate (Baxter et al., 2019; Wang et al., 2018).

In addition, recent research has indicated a strong association between gut microbiota and mental health, and given that diets affect the diversity of gut microbiota to a large extent, the composition of a host's diet may play an important role in their mental health. For example, a western-style diet elevated the *Firmicutes/Bacteroidetes* ratio and the abundance of *Proteobacteria* and *Spirochaetes* in a rat model. This led to a decrease in the level of SCFAs such as acetic and propionic in cecal contents and anxiety-like behavior (Ohland et al., 2013). In a recent human cohort study, a reduced level of carbohydrate intake resulted in a rapid rearrangement in the composition of human gut microbiota within 24 h; for instance, a reduction in carbohydrate intake significantly decreased the abundance of fiber-degrading bacteria, while the level of *Eggerrthella*, *Streptococcus*, and *Lactococcus* was enhanced followed by a decrease in the secretion of SCFAs (Mardinoglu et al., 2018).

In summary, although many studies have been conducted regarding alterations in the diversity of gut microbiota as affected by food ingredients, research on how food ingredients influence the alteration of gut microbiota-derived neurotransmitters is limited. However, based on the above investigations, it is expected that individual food ingredients/components play a significant role in modulating gut microbiota composition and the following changes in their secretion of neurotransmitters.

This review provides comprehensive, in-depth knowledge of the significant functions of gut microbiota in maintaining metabolism and homeostasis as well as the alteration of their profiles as affected by food intake and the consumption of food-derived bioactive compounds. Moreover, this contribution summarizes the significance of food sources and dietary choices in designing gut microbiota profiles and their metabolites. Food sources and bioactive compounds remarkably affect the composition of gut microbiomes and their metabolites, indicating their importance in sustaining balanced-immune and metabolic homeostasis. Despite the increasing research on the influence of food bioactives on gut microbiota-derived metabolites, there is still a lack of information on related fields. Nevertheless, this review provides a valuable summary for understanding the role of foods and food-derived bioactives in controlling the composition of gut microbiota and their metabolites.

Declarations

Conflict of interest The authors declare no conflict of interest.

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