Trends in Food Science & Technology 92 (2019) 194–204

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Dietary plants, gut microbiota, and obesity: Effects and mechanisms

Shi-Yu Cao[a], Cai-Ning Zhao[a], Xiao-Yu Xu[a], Guo-Yi Tang[a], Harold Corke[b], Ren-You Gan[b,c], Hua-Bin Li[a,*]

[a] Guangdong Provincial Key Laboratory of Food, Nutrition and Health, Department of Nutrition, School of Public Health, Sun Yat-Sen University, Guangzhou, 510080, China
[b] Department of Food Science & Technology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, 200240, China
[c] Institute of Urban Agriculture, Chinese Academy of Agricultural Sciences, Chengdu, 610213, China

ARTICLE INFO

Keywords:
Obesity
Anti-Obesity
Gut microbiota
Fruit
Vegetable
Spice

ABSTRACT

Background: Obesity is a leading contributor to numerous diseases, such as diabetes mellitus, cardiovascular diseases, and cancers. Therefore, seeking effective and safe approaches to control obesity is essential. Gut microbiota has been demonstrated to play a critical role in the occurrence of obesity via the regulation of energy metabolism. The composition and abundance of gut microbiota can be altered by the diet. Recently, many dietary plants have been demonstrated to exert anti-obesity effects through bioactive components that modulate gut microbiota, which has drawn increasing research attention.

Scope and approach: In this review, the obesity-associated gut microbiota has been summarized and classified into obesogenic and anti-obesity categories. Subsequently, some anti-obesity dietary plants with gut microbiota-modulating activities and the mechanisms of action of their bioactive components are discussed.

Key findings and conclusions: The effects of gut microbiota on obesity have been found in most animal and some human studies. Certain strains of *Firmicutes*, *Lactobacillus*, and *Bacteroidetes* are positively associated with obesity development, while *Bifidobacterium*, most *Lactobacillus*, and some *Bacteroidetes* show anti-obesity activities. Some dietary plants, such as grapes, berries, apple, turmeric, chili, soy, sorghum, and barley, show anti-obesity efficacy through increasing the diversity of gut microbiota, up-regulating anti-obesity gut microbiota and down-regulating obesogenic gut microbiota.

This review may stimulate further development of functional foods to treat obesity through modulating gut microbiota. Future work will rely on the exploration of more dietary plants and their components with anti-obesity and gut microbiota-modulating effects, and further investigation of related mechanisms as well as clinical trials.

1. Introduction

Obesity is a chronic metabolic disorder, and a rapidly increasing global health problem. According to a report from the World Health Organization (WHO), over 1.9 billion (accounting for 39%) adults were overweight, and 650 million of these were obese in 2016 (https://www.who.int/mediacentre/factsheets/fs311/zh/). Obesity is associated with several diseases, such as diabetes mellitus, cardiovascular diseases, and cancers, posing a heavy economic burden on society (Mokdad et al., 2003). Therefore, managing and reducing obesity has attracted increasing interest and attention from researchers.

The main therapeutic options to treat obesity include diet modification, exercise, surgery, and pharmacotherapy. However, conventional weight loss therapies often do not have satisfactory outcomes, and the prevalence of obesity is predicted to continue to rise (Kazemipoor et al., 2015). Many dietary plants have shown anti-obesity activity by reducing appetite, inhibiting nutrient absorption, reducing adipogenesis, and enhancing energy expenditure (Fu, Jiang, Guo, & Su, 2016). In recent years, the influence of gut microbiota on obesity has become a hot research focus, and is a potentially effective target to treat obesity. The impact of dietary plants on the gut microbiota has become a particular focus of attention.

Gut microbiota can be regarded as a microbial organ residing in the host, which has a significant impact on host physiology (Bäckhed, Ley, Sonnenburg, Peterson, & Gordon, 2005; Zhang et al., 2015a). Studies show that gut microbiota has a tight association with host metabolism

* Corresponding authors. Department of Food Science & Technology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, 200240, China.
E-mail addresses: caoshy3@mail2.sysu.edu.cn (S.-Y. Cao), zhaocn@mail2.sysu.edu.cn (C.-N. Zhao), xuxy53@mail2.sysu.edu.cn (X.-Y. Xu), tanggy5@mail2.sysu.edu.cn (G.-Y. Tang), hcorke@sjtu.edu.cn (H. Corke), ganrenyou@caas.cn (R.-Y. Gan), lihuabin@mail.sysu.edu.cn (H.-B. Li).

https://doi.org/10.1016/j.tifs.2019.08.004
Received 18 January 2019; Received in revised form 5 July 2019; Accepted 12 August 2019
Available online 13 August 2019
0924-2244/

via the production of gut microbiota-derived metabolites, such as short-chain fatty acids (SCFAs) which can supply energy for colonic epithelial cells (Tremaroli & Bäckhed, 2012), trimethylamine-N-oxide (TMAO) which is associated with the formation of white adipose tissue (Schugar et al., 2017), and inosine-5-monophosphate (IMP) which has been found involved in the metabolism of lipids (Whitehead et al., 2004). In addition, gut microbiota can modulate host immune system (Round & Mazmanian, 2009), and regulate bile acid profile which can affect the digestion and metabolism of the host (Sayin et al., 2013). Dysbiosis of the gut microbiota is suggested to be responsible for certain diseases of the host, such as obesity, cancers, and inflammatory bowel diseases (Gilbert et al., 2018; Postler & Ghosh, 2017). The link between gut microbiota and the development of obesity and other metabolic diseases in hosts could be due to the microbiota-derived toxic metabolites, extra energy harvested from gut microbiota, and endotoxemia-related low-grade inflammation (Zhao, 2013). For instance, lipopolysaccharide (LPS), produced by Gram-negative bacteria, could cause an inflammatory response in the host (Shen, Obin, & Zhao, 2013). Compared with lean humans, obese persons are lower in the diversity of gut microbiota (Turnbaugh et al., 2009), and meanwhile, the relative abundance of the specific gut microbiota taxa in obese persons has been altered (Ley et al., 2005). Epidemiological studies also reveal that consumption of some dietary plants may be inversely associated with weight gain through modulating gut microbiota (Kang et al., 2016; Menni et al., 2017; Moreno-Indias et al., 2016). Thus, consumption of dietary plants, exploiting their effect on regulating gut microbiota, can be a novel strategy to combat obesity.

There are some recent reviews focusing on the topic of gut microbiota and their roles in obesity (Al-Assal, Martinez, Torrinhas, Cardinelli, & Waitzberg, 2018; Harsch & Konturek, 2018; Ottosson et al., 2018; Rastelli, Knauf, & Cani, 2018; Sun et al., 2018a, b), while these reviews mainly focused on the biomedical aspects of the topic. Herein, the current review discusses the topic mainly from the viewpoint of food and nutritional sciences, and summarizes the types of gut microbiota related to obesity and the anti-obesity activities of some dietary plants through modulating gut microbiota. Overall, this review may stimulate the development of dietary plants as functional foods, which have the potential to promote weight loss.

2. Obesogenic gut microbiota

Gut microbiota comprises numerous species, and some species may contribute to the development of obesity, which is defined as obesogenic gut microbiota (Prior et al., 2010), such as *Firmicutes* and *Bacteroidetes*.

2.1. Firmicutes

Phylum *Firmicutes* comprise a dominant part of the microbiota in the human gut (with phylum *Bacteroidetes* together accounting for 90% of human bacterial species), and mainly include *Ruminiococcus*, *Clostridium*, and *Lactobacillus* (Barlow, Yu, & Mathur, 2015; Eckburg et al., 2005). *Firmicutes* substantially decreased in diet-induced obese C57BL/6J mice treated with antibiotics (vancomycin and bacitracin), which could improve insulin resistance and ameliorate obesity by modulating glucagon-like peptide 1 secretion (Hwang et al., 2015). In contrast, an increase in *Firmicutes* was observed in high fat diet (HFD)-fed male C57BL/6J mice gut (Shang et al., 2017). A high ratio of *Firmicutes to Bacteroidetes* has been considered as an obesity-related pattern of the gut microbiota composition for obese humans and obese (ob/ob) mice (Ley et al., 2005). Gut *Firmicutes* were reportedly increased in endocarditis patients with vancomycin-related obesity (Million et al., 2013). Besides, women who had obese phenotype with high expression of toll-like receptor 5 (TLR5) genes had more *Firmicutes* (Pekkala et al., 2015). Moreover, a study compared the gut microbiota composition of 51 obese persons (including 23 children and 28 adults) with 28 normal weight persons (including 17 children and 11 adults) from Egypt, and found that phyla *Firmicutes* and *Bacteroidetes* significantly increased in the obese group ($p < 0.001$, $p = 0.003$) (Ismail et al., 2011).

Lactobacillus has many subspecies, some of which are related to weight gain and help induce obesity. Weight gain-promoted *Lactobacillus* species were found to lack some important enzymes, including glucose metabolic enzymes, antioxidant enzymes, and the synthetases of dextrin, L-rhamnose, and acetate (Drissi et al., 2014). A meta-analysis, including 17 randomized controlled trials (RCTs) in humans, 51 studies on farm animals, and 14 studies on experimental models, reported that *Lactobacillus acidophilus* administration was associated with weight gain in humans, and *Lactobacillus fermentum* and *Lactobacillus ingluviei* would cause weight gain in animals (Million et al., 2012). Treating newborn broiler chicks and ducks with *Lactobacillus* at a dose of 4×10^{10} bacteria per animal promoted weight gain (Angelakis & Raoult, 2010). In addition, *Lactobacillus ingluviei* was reported to speed the weight gain in female BALB/c mice (Angelakis et al., 2012). Moreover, in a human observational study, researchers found that endocarditis patients treated with vancomycin, a common antibiotic, showed body weight gain (12.2% of patients had a BMI increase of over 10%) with increased *Lactobacillus* (Million et al., 2013).

2.2. Bacteroidetes

Bacteroides, *Prevotella*, and *Porphyromonas* are the three main genera of *Bacteroidetes* in the human gut. *Bacteroides* alone accounts for an estimated 30% of all gut bacteria, and is most common in Western populations consuming high-fat or high-sucrose diet (Johnson, Heaver, Walters, & Ley, 2017). In a prospective study on 138 infants from 1 to 3 years, *Bacteroides fragilis* in their intestines was found positively related to body weight (Vael, Verhulst, Nelen, Goossens, & Desager, 2011). Similarly, Koleva, Bridgman, and Kozyrskyj (2015) reported that *Bacteroides* and *Lactobacillus* species were associated with weight gain in children.

2.3. Other obesogenic microbiota

Studies reported that several microbiota, such as *Rhizobium*, *Lactococcus*, and *Clostridium*, were also associated with the development of obesity (Hippe et al., 2016; Pekkala et al., 2015; Qiao, Sun, Xie, Shi, & Le, 2014a). A study has shown that the amount of intestinal *Rhizobium* and *Lactococcus* increased greatly in HFD-fed C57BL/6J male mice (Qiao et al., 2014a). Besides, HFD feeding also increased the amount of gut sulfidogenic bacteria in C57BL/6J male mice, which may be responsible for chronic intestinal and systemic inflammation (Shen et al., 2014). A study demonstrated that women with higher TLR5 expression and flagellated *Clostridium* cluster XIV bacteria count would have a tendency to obesity because the flagellin from *Clostridium* could activate TLR5 inflammatory pathway, enhance glycerol secretion, and reduce insulin signaling (Pekkala et al., 2015). Compared with the lean control group, obese people had higher *Faecalibacterium prausnitzii* count, which were considered to produce more butyrate, an essential energy substrate for gut epithelium metabolism, and overproduction of butyrate could cause gut inflammation to different degrees (Hippe et al., 2016).

To sum up, obesogenic gut microbiota, such as *Firmicutes,* certain *Bacteroidetes, Rhizobium*, *Lactococcus*, and *Clostridium*, could promote the development of obesity mainly through the production of SCFAs like butyrate, providing extra energy for the host, and the induction of low-grade inflammation caused by the metabolites of gut microbiota. It should be pointed out that the effects of SCFAs on obesity have been extensively studied in animal studies, but few conclusions have been drawn from human studies. Therefore, more clinical trials are required to test and verify their effects on human.

3. Anti-obesity gut microbiota

In contrast to the obesogenic gut microbiota, some species of gut microbiota have shown anti-obesity activity. In the following part, *Bifidobacterium*, certain subspecies of *Lactobacillus* and *Bacteroidetes* are discussed as anti-obesity gut microbiota.

3.1. Bifidobacterium

Treatment of *Bifidobacterium lactis* 420 (10^9 colony-forming units (CFU)/day, i. g.) to C57BL/6J mice for 12 weeks significantly reduced HFD-induced weight gains, which could be related to decreased intestinal mucosal adherence and plasma LPS (Stenman et al., 2014). Besides, *Bifidobacterium lactis* 420 dose-dependently enhanced the integrity and decreased the permeability of Caco-2 cells, which could fight against the low-grade inflammation-related diseases such as obesity (Mokkala, Laitinen, & Röytiö, 2016). *Bifidobacterium pseudocatenulatum* CECT 7765 could also protect C57BL/6 male mice against HFD-induced weight gain through modulating the expression of key regulators in fatty acid and cholesterol metabolism, including fatty acid transporter CD36, the transcription regulator of lipid biosynthesis early growth response 1, and patatin-like phospholipase domain containing 2 (PNPLA2) (Moya-Pérez, Romo-Vaquero, Tomás-Barberán, Sanz, & García-Conesa, 2014). Treating HFD-fed mice with *Bifidobacterium bifidum* BGN4 and *Bifidobacterium longum* BORI individually for 8 weeks greatly inhibited the weight gain of mice, and lowered the hepatic levels of triglyceride and total cholesterol, and the activities of serum aspartate transaminase and alanine transaminase, without influencing food intake (Li, Jin, Oh, & Ji, 2016). Moreover, *Bifidobacterium adolescentis* IM38 with a dose of 2×10^9 CFU/day suppressed body and epididymal fat weight gains caused by HFD in male C57BL/6 mice, via regulating the ratio of *Proteobacteria* to *Bacteroidetes,* which reduced LPS production in the gut. Meanwhile, an *in vitro* study found that *Bifidobacterium adolescentis* IM38 greatly inhibited the nuclear factor (NF)-κB activation and tumor necrosis factor (TNF) expression in LPS-stimulated Caco-2 cells (Lim & Kim, 2017). Treatment with *Bifidobacterium* MKK4 to obese mice for 8 weeks reduced body and organ weight, improved levels of serum glucose, triglyceride, and cholesterol, and regulated gut microbiota dysbiosis. Enhanced expressions of lipolytic transcription factors, such as peroxisome proliferator-activated receptor (PPAR)-α, PPAR-δ, and their downstream productions, were associated with the anti-obesity effect of *Bifidobacterium* MKK4 (Ray et al., 2018). Moreover, in an RCT, participants with BMI ranging 24–30 kg/m^2 were treated with 5×10^{10} CFU/d *Bifidobacterium breve* B-3, and it was found that alterations in levels of γ-glutamyltranspeptidase and high-sensitivity C-reactive protein might be associated with lowered fat mass (Minami et al., 2015).

3.2. Lactobacillus

Although certain *Lactobacillus* is associated with weight gain, most *Lactobacilli* has an anti-obesity effect (Barlow et al., 2015). A meta-analysis revealed that *Lactobacillus plantarum* promoted weight loss in animals and *Lactobacillus gasseri* promoted weight loss in both obese humans and animals (Million et al., 2012). *Lactobacillus acidophilus* 031 CE significantly inhibited obesity development and lipid deposition in the liver of ICR (Institute of Cancer Research) mice fed with HFD by reducing the level of triglyceride, and activities of aspartate transaminase and alanine transaminase (Li et al., 2016). Administration of *Lactobacillus sakei* OK67 to HFD-fed mice greatly reduced body and epididymal fat weight gains through down-regulating TNF-α, interleukin (IL)-1β, and NF-κB, as well as up-regulating IL-10 and tight junction proteins (Lim, Jeong, Woo, Han, & Kim, 2016). Besides, *Lactobacillus sakei* could reduce HFD-induced obesity, colitis, and anxiety through activating gut microbiota-mediated AMP-activated protein kinase (AMPK) and NF-κB pathways, and modulating SIRT-1 expression in mice (Jang et al., 2019). Moreover, *Lactobacillus reuteri* GMNL-263, both living and heat-killed, could decrease weight gain and the number of pathogenic bacteria, alleviate hepatic steatosis, and improve insulin resistance in mice fed with HFD (Hsieh et al., 2016). *Lactobacillus reuteri* 263 exhibited anti-obesity effect by promoting the browning of white adipose tissue through upregulating the expression of browning-related genes *Ppar-γ*, *PR domain containing 16* (*Prdm16*), *Ppar-γ coactivator-1α (Pgc-α)*, *bone morphogenetic protein 7 (Bmp7)*, and *fibroblast growth factor 21* (*Fgf21*) in Sprague-Dawley rats (Chen et al., 2018). *Lactobacillus plantarum* Ln4, obtained from napa cabbage kimchi, inhibited weight gains and epididymal fat mass in mice fed with HFD by decreasing levels of C-reactive protein, insulin-like growth factor binding proteins-3, and monocyte chemoattractant protein (MCP)-1 in white adipose tissue, and lowering total plasma triglyceride level (Lee et al., 2018a). Additionally, 10-oxo-12(Z)-octadecenoic acid, a linoleic acid metabolite produced by lactic acid bacteria, could elevate energy expenditure in mice by activating transient receptor potential vanilloid (TRPV) 1-mediated browning in white adipose tissue, which inhibited diet-induced obesity development (Kim et al., 2017). Treating C57BL/6J mice with a mixture of lactic acid bacteria isolated from cheese reduced the levels of pro-inflammatory cytokines, chemokines, triglyceride, and cholesterol, and inhibited fat accumulation, which led to the suppression of obesity and obesity-related inflammation (Roselli et al., 2017). Administration of *Lactobacillus JBD301* daily with 10^7 CFU to female C57BL/6 mice inhibited the free fatty acid absorption by increasing its fecal excretion and reducing its concentration in the gut fluid content, thus suppressing the weight gain induced by HFD (Chung et al., 2016). Furthermore, this study also found that people administered with *Lactobacillus JBD3*01 had less weight gain compared with the control group in a phaseIIRCT. In another 6-year prospective observational study, a negative association was found between a high level of oral *Lactobacillus* and weight gain among those with medium and low administrations of complex carbohydrates (Rosing, Walker, Jensen, & Heitmann, 2017). Moreover, a pilot study conducted on obese children revealed that *Lactobacillus casei* strain Shirota-containing beverage reduced body weight and increased high-density lipoprotein cholesterol level (Nagata, Chiba, Wang, & Yamashiro, 2017). Furthermore, in an RCT, *Lactobacillus gasseri* BNR17 effectively decreased visceral fat mass and waist circumferences in tested obese adults (Kim, Yun, Kim, Kwon, & Cho, 2018). However, in a 6-week, single-blinded, parallel-group intervention conducted on 58 obese postmenopausal women, *Lactobacillus paracasei* F19 at a dose of 9.4×10^{10} CFU/d showed no effects in the metabolic markers and gut microbiota composition (Brahe et al., 2015). Besides, the intake of *Lactobacillus salivarius* Ls-33 at a dose of 10^{10} CFU/d for 12 weeks in 50 obese Danish adolescents also had no beneficial effects (Gøbel, Larsen, Jakobsen, Mølgaard, & Michaelsen, 2012). The inconsistent effects of probiotics *Lactobacillus* on preventing obesity might be associated with the differences of bacterial strains used and their doses, intervention time, and dietary bioactive compounds in foods.

3.3. Bacteroidetes

Most *Bacteroidetes* in the gut harvested energy from the indigestible polysaccharides and produced SCFAs, which regulate host energy metabolism (Johnson et al., 2017). *Bacteroidetes* are negatively related to obesity, and were decreased by 50% in leptin-deficient obese mouse models compared with the lean mice (Ley et al., 2005). In an animal experiment, 12-week HFD-fed Wistar rats became obese with lowered *Bacteroidetes*, *Prevotella*, and *Lactobacillus* in the gut (Lau et al., 2016), and the similar alteration was also found in HFD-fed C57BL/6J mice (Shang et al., 2017). Besides, a study compared the gut microbial composition in 100 women from rural Ghana and urban US (including 50 lean women and 50 obese women), and found that lean women had more abundant *Bacteroides,* and lean Ghanaians had more butyrate-generating gut microbiota. Meanwhile, mice transplanted with feces

from the lean Ghanaian were resistant to obesity induced by 6-weeks high-fat diet feeding ($p < 0.01$) (Dugas et al., 2018).

3.4. Other anti-obesity gut microbiota

Yeast and *Akkermansia muciniphila* could also promote weight loss (Chelakkot et al., 2018; Tsai, Wang, Hsu, Li, & Chen, 2015). Administration of yeast with bacteriocin from ruminal bacteria inhibited weight gain and enhanced lipid catabolism through modulating gut microbiota in C57BL/6 male mice fed with a Western diet (Tsai et al., 2015). *Akkermansia muciniphila*, a mucin-degrading bacterium which can benefit host metabolism, could decrease the permeability of Caco-2 cells treated with LPS, thus regulating gut barrier integrity (Chelakkot et al., 2018).

Collectively, anti-obesity gut bacteria, such as *Bifidobacterium, Lactobacillus, Bacteroidetes*, and *Akkermansia muciniphila,* can induce weight loss in multiple ways, including lowering gut permeability, enhancing gut mucosa integrity with elevated levels of tight junction proteins, modulating the expression of key regulators involved in lipogenesis, attenuating gut inflammation with lowered NF-κB, TNF, and IL-1β levels, reducing insulin resistance, and promoting the browning of white adipose fat. It should be pointed out that different species of the same genus could have different effects on obesity. For example, some species of *Lactobacillus* (such as *Lactobacillus plantarum, Lactobacillus sakei,* and *Lactobacillus reuteri*) were associated with weight loss as they could express a certain amount of glucose permease and encode fewer bacteriocins than weight-promoting *Lactobacillus* (Driss et al., 2014). On the other hand, some *Lactobacillus* species (such as *Lactobacillus acidophilus, Lactobacillus fermentum*, and *Lactobacillus ingluviei*) were found to be weight-promoting in animal and human studies as they lacked the ability to breakdown fructose or glucose, and had more stronger replication, recombination, and repair activities, which may interrupt the host gut microbiota eco-balance.

4. Anti-obesity effect of dietary plants through modulating gut microbiota

Many dietary plants have been demonstrated to have anti-obesity effects via modulating gut microbiota composition and abundance, such as fruits, vegetables, spices, legumes, grains, and tea (Fu et al., 2016; Qiao et al., 2014b; Shen, Liu, & Ji, 2017a), which are further discussed below.

4.1. Fruits

Fruits are abundant in polyphenols, cellulose, and xylans, which could prevent many chronic diseases, such as obesity, cancers, and cardiovascular diseases (Zhang et al., 2015b; Zhao et al., 2017a). A randomized controlled trial (RCT) conducted on 122 individuals in Britain found that an increasing administration of fruit and vegetable could modulate human gut microbiota composition with the increase in *Clostidium leptum-Ruminococcus bromii/flavefaciens* and the decrease in potentially pathogenic *Clostridia*, which may be associated with obesity prevention (Klinder et al., 2016).

4.1.1. Grapes

Grapes are well-known as healthy fruit and are rich in resveratrol (3,5,4′-trihydroxy-*trans*-stilbene), a natural polyphenol with several health benefits (Zhang et al., 2015a, b). Resveratrol reduced the weight gain and visceral adipose weight greatly, increased the *Bacteroidetes* to *Firmicutes* ratio, *Lactobacillus*, and *Bifidobacterium,* as well as decreased *Enterococcus faecalis* in HFD-fed mice. The anti-obesity activity of resveratrol could be due to down-regulation of mRNA expression of genes associated with lipogenesis, such as *lipoprotein lipase* (*Lpl*), *stearoyl-CoA desaturase 1* (*Scd1*), *Ppar-γ*, *acetyl-CoA carboxylase 1* (*Acc1*), and *fatty acid synthase* (*Fas*) (Qiao et al., 2014b). Co-administration of *trans*-resveratrol and quercetin inhibited weight gains, elevated *Bacteroidetes* to *Firmicutes* ratio, and inhibited the growth of obesogenic bacteria like *Erysipelotrichaceae*, *Bacillus*, and *Eubacterium glindroides* in high-fat-sucrose diet-fed rats (Etxeberria et al., 2015). Similarly, the combination of resveratrol and quercetin also inhibited body weight gain and visceral adipose accumulation, increased the *Bacteroidetes* to *Firmicutes* ratio and reduced the amounts of Desulfovibrionaceae, *Acidaminococcaceae*, *Cozriobacteriaceae, Bilophilaz,* and Lachnospiraceae and its genus *Lachnoclostridium* in HFD-fed rats (Zhao et al., 2017b). Besides, piceatannol, an analog of resveratrol, decreased mouse body weight without affecting the food intake, dose-dependently lowered the levels of serum total cholesterol, low-density lipoprotein cholesterol, and blood glucose, and altered the abundance of *Firmicutes* and *Lactobacillus* (Tung et al., 2016). In addition, the intake of the extracts from grape pomace and cinnamon bark in C57BL/6J mice for 8 weeks, could reduce obesity through alleviating fat mass gain and adipose tissue inflammation, as well as alter gut microbiota and the markers of the gut barrier. After the treatment of mixed extracts, *Allobaculum* and *Roseburia* were up-regulated, while *Desulfovibrio* and *Lactococcus* were down-regulated in C57BL/6J mice (Van et al., 2018).

Feeding male C57BL/6J mice with grape seed extracts at a dose of 10 mg/kg body weight decreased the weight gain induced by HFD and lowered the counts of *Firmicutes* in the small intestine (Griffin et al., 2017). Besides, grape seed flour could decrease HFD-induced weight gain, liver and adipose tissue weight, and plasma lipid levels, as well as alter the population of intestinal *Lactobacillus, Roseburia*, and *Enterococcus* in male C57BL/6J mice, which were associated with the metabolism of bile acids and hepatic lipids, and the production of butyrate (Seo, Kim, Jeong, Yokoyama, & Kim, 2017a). Moreover, in research conducted on obese patients, consumption of red wine at a moderate dose remarkably improved obesity by increasing the amounts of *Bifidobacterium, Lactobacillus*, and butyrate-generating *Faecalibacterium* (Moreno-Indias et al., 2016).

4.1.2. Apples

Apples are abundant in fiber, polysaccharides, and other bioactive compounds, which are known to benefit health (Jiang et al., 2016). Apple was fermented with feces obtained from diet-induced obese mice, and the extracts could regulate the dysbiosis of microbiota induced by obesity through altering the amounts of *Firmicutes, Bacteroidetes, Enterococcus,* Enterobacteriaceae*, Escherichia coli*, and *Bifidobacterium* (Condezo-Hoyos, Mohanty, & Noratto, 2014). Also, pectin extracted from apple could inhibit weight gain by decreasing *Firmicutes,* increasing *Bacteroidetes*, and reducing metabolic endotoxemia and inflammation in HFD-fed rats (Jiang et al., 2016). Besides, in C57BL/6J mice fed with a high-fat or high-sucrose diet for 20 weeks, 0.5% polymeric non-absorbable apple procyanidins consumption could reduce obesity through modulating the expression of genes associated with lipid metabolism, lowering the ratio of *Firmicutes* to *Bacteroidetes*, and raising the proportion of *Akkermansia* with eight folds (Masumoto et al., 2016). Moreover, apple polysaccharides elevated *Bacteroidetes* and *Lactobacillus*, and decreased *Firmicutes* and *Fusobacteium*, as well as improved the gut permeability and dysbiosis-related gut inflammation with the increase of tight junction protein occludin and the decrease of pro-inflammatory factors TNF-α, IL-1β, MCP-1, and chemokine ligand 1 in HFD-fed rats (Wang et al., 2017a).

4.1.3. Berries

Several berries like blueberry, black raspberries, and lingonberries were found to possess anti-obesity effects via modulating gut microbiota (Heyman-Lindén et al., 2016; Lee et al., 2018b; Pan et al., 2017). Supplementary feeding of blueberry powder to Wistar rats could protect against HFD-induced inflammation through reducing TNF-α and IL-1β levels, improve insulin sensitivity, and increase the abundance of *Gammaproteobacteria* (Lee et al., 2018b). Besides, the administration of blueberry polyphenol extracts to high-fat diet-induced obesity C57BL/

6 J mice could alleviate obesity though altering gut microbiota composition by regulating *Proteobacteria*, *Deferribacteres*, *Actinobacteria*, *Bifidobacterium*, *Desulfovibrio*, *Adlercreutzia*, *Helicobacter*, *Flexispira*, and *Prevotella* (Jiao et al., 2019). In addition, whole black raspberries could inhibit gut inflammation by increasing the anti-inflammatory bacteria, i.e. *Akkermansia* and *Desulfovibrio* (Pan et al., 2017). However, another study reported that black raspberries anthocyanins intake showed no effect on obesity in high-fat diet feeding mice (Prior et al., 2010). Moreover, lingonberries showed anti-obesity and anti-inflammatory activities, which could elevate the amounts of gut mucosal beneficial *Akkermansia* and *Faecalibacterium* in C57BL/6J mice (Heyman-Lindén et al., 2016). Treating male New Zealand white rabbits with procyanidin B2, a proanthocyanidin dimer rich in berries, for 12 weeks, could ameliorate diet-induced obesity by increasing the abundance of *Bacteroidetes* at the phylum level and *Akkermansia* at the genus level (Xing, Lei, Wu, Jiang, & Huang, 2019).

4.1.4. Other fruits

Mango, citrus, persimmon, and kiwifruit also possess anti-obesity effect through modulating gut microbiota (Ojo et al., 2016; Tung et al., 2018; Zhu, Lin, Li, Deng, & Li, 2018). Mango at 10% (*m/m*) regulated the gut microbiota dysbiosis by restoring the abundance of *Bifidobacteria* and *Akkermansia* in C57BL/6 mice treated with HFD (Ojo et al., 2016). Polymethoxyflavones and hydroxyl polymethoxyflavones are two components with anti-obesity activities found in citrus peel. Both of them could lower the body weight and adipose tissue weight in HFD-fed mice by reducing the levels of lipid droplets, perilipin 1 protein, and sterol regulatory element binding protein 1, increasing the abundance of *Prevotella*, as well as decreasing *rc4-4* bacteria in the mouse gut (Tung et al., 2018). Persimmon tannin lowered the levels of serum lipids and cholesterol in high cholesterol-fed rats by altering the gut microbiota composition with increases in *Bifidobacterium* and *Lactobacillus,* as well as decreases in *Firmicutes*, *Escherichia coli*, and *Enterococcus* (Zhu et al., 2018). Long-term intake of kiwifruit seed oil could reduce obesity and the ratio of *Firmicutes* to *Bacteroidetes* with decreased inflammation and adipose thermogenesis (Qu et al., 2019).

In summary, fruits like grapes, apple, and berries are under extensive research for the anti-obesity activities through modulating gut microbiota, which could reduce the expression of genes associated with lipogenesis, down-regulate the levels of serum cholesterol, LDL, and glucose, mediate the metabolism of fatty acids and lipids, and attenuate low-grade inflammation in the gut. It should be pointed out that many fruits, such as grape, contain a high content of sugar, which may counteract their anti-obesity activities. Therefore, most studies were carried out using fruit extracts rather than the fruit itself, and the intake of fruit extracts could have better anti-obesity effects than the intake of the fruit itself, suggesting that bioactive compounds in fruits, such as polyphenols, should possess anti-obesity effect besides dietary fibers.

4.2. Vegetables

Thylakoid, a part of the chloroplast in all green vegetable tissue, could promote weight loss by increasing *Bacteriodes fragilis* and enhancing satiety in rats, induced by altering appetite hormones (Stenblom et al., 2016). In addition, dietary fiber of vegetables could inhibit weight gain and white adipose tissue accumulation with modulation of gut microbiota, including increases of *Bacteroidetes* to *Firmicutes* ratio and *Roseburia* abundance in HFD-induced fat mice (Wang, Hong, Li, Zang, & Wu, 2018a). Moreover, the powder of bitter melon was effective in elevating the ratio of *Bacteroidetes* to *Firmicutes* in HFD-treated rats (Zhu, Bai, Zhang, Xiao, & Dong, 2016). In a cross-sectional study of healthy females, high consumption of dietary fiber from vegetables and fruits could attenuate long-term weight gain with more abundance of Ruminococcaceae, which could improve energy metabolism (Menni et al., 2017).

In general, studies on the anti-obesity effect of vegetables through regulating gut microbiota were rare. Dietary fiber and bitter melon have shown the anti-obesity effect through modulating the ratio of *Bacteroidetes* to *Firmicutes*. In the future, more studies should be carried out to evaluate the anti-obesity activities of different vegetables by modulating gut microbiota, and active components should be separated and identified.

4.3. Spices

Spices have a long history of use in flavoring food, and the polyphenols from spices have been shown to possess many bioactive functions, such as anti-obesity, anticancer, anti-inflammatory activities and inhibiting growth of bacteria (Carrera-Quintanar et al., 2018; Zheng et al., 2016).

4.3.1. Turmeric

Curcumin is a main bioactive component in turmeric, which is a widely used spice with multiple health benefits. It has been found that curcumin could greatly influence the population of certain gut microbiota in C57BL/6 mice, such as *Prevotella*, *Bacteroidaceae*, and *Rikenella,* which are closely associated with obesity development (Shen et al., 2017a). In menopausal obese rat models, curcumin inhibited the weight gain without affecting the levels of estradiol, and restored the diversities of gut microbiota (Zhang et al., 2017a). Moreover, curcumin improved the intestinal barrier function through increasing the expression of tight junction proteins, which were beneficial for obesity prevention (Wang, Ghosh, & Ghosh, 2017b). Considering the poor bioavailability of curcumin, a newly developed nanoparticle curcumin with improved absorbability has been produced and could increase the abundance of butyrate-producing bacteria, lower the level of NF-κB, and improve gut mucosal permeability in BALB/c mice (Ohno et al., 2017).

4.3.2. Chili

Chili is one of the most popular spicy flavors, and capsaicin is the component playing a major role in the bioactivities of chili. A study found that capsaicin could inhibit weight gain with increasing abundance of butyrate-producing Ruminococcaceae and Lachnospiraceae, and inactivate cannabinoid receptor type 1 in mice fed with HFD (Kang et al., 2017). Similarly, capsaicin also showed anti-obesity effects through decreasing *Proteobacteria* and increasing *Akkermansia muciniphila* in HFD-fed C57BL/6 mice (Shen et al., 2017b). Moreover, in obese and diabetic ob/ob mice, capsaicin could reduce body weight, adiposity index, and Lee's obesity index, and alter the composition of gut microbiota. Specifically, capsaicin could increase the *Firmicutes* to *Bacteroidetes* ratio at the phylum level and the *Roseburia* abundance, and decrease the abundances of *Bacteroides* and *Parabacteroides* at the genus level, leading to improved glucose tolerance, increased fecal butyrate and plasma total glucagon-like peptide-1 (GLP-1) levels, and reduced plasma total ghrelin, TNF-α, IL-1 β, and IL-6 levels (Song et al., 2017). Furthermore, after oral intake for 6 weeks of chili powder in Chinese healthy adults, the level of plasma ghrelin, a regulator of appetite, was lowered and the gut microbiota composition was altered with changes in *Firmicutes* to *Bacteroidetes* ratio and *Faecalibacterium* abundance (Kang et al., 2016).

4.3.3. Other spices

Rosemary is an aromatic shrub belonging to the Lamiaceae family. Rosemary extract is rich in carnosic acid, which reduces body weight gain through increasing the abundance of *Blautia coccoides* and *Prevotella*, and decreasing the populations of *Lactobacillus/Leuconostoc/Pediococccus* (Romo-Vaquero et al., 2014). Cinnamon is a spice harvested from the inner bark of trees belonging to the genus *Cinnamomum.* Cinnamon bark extracts could reduce fat mass gain, adipose tissue inflammation, and the *Peptococcus*, accompanied with the upregulation of antimicrobial peptides and tight junction proteins in the gut

of C57BL/6J mice fed with HFD for 8 weeks (Van et al., 2018).

Collectively, turmeric, chili, rosemary, and cinnamon showed anti-obesity effects, at least partly via regulation of gut microbiota. The metabolites from gut microbiota could reduce the gut mucosa permeability with elevated levels of tight junction proteins, and mitigate the gut inflammation with reduced levels of inflammatory factors, like NF-κB. Many spices could inhibit the growth of bacteria, and are worthy of further investigation to find more spices and their active components with anti-obesity activity through modulating gut microbiota.

4.4. Legumes

Legumes, such as pea, soy, and mung bean, have been reported to inhibit weight gain and alter gut microbiota composition (Eslinger, Eller, & Reimer, 2014; Nakatani et al., 2018; Panasevich et al., 2017). The pea flour exhibited strong anti-obesity effect and increased the ratio of *Bacteroidetes* to *Firmicutes* in diet-induced obese rats (Eslinger et al., 2014). Soy proteins could reduce rat fat mass and percent fat to around 10%, ameliorate hepatic steatosis and secondary bile acids, increase the abundance of *Lactobacillus* as well as decrease the abundance of *Blautia* and Lachnospiraceae (Panasevich et al., 2017). Besides, mung bean proteins, rich in 8-globulin, could greatly inhibit adipose tissue accumulation and weight gain induced by HFD, and attenuate hepatic steatosis (Nakatani et al., 2018). Meanwhile, the anti-obesity effects of mung bean proteins were associated with the increase in *Bacteroidetes* and the decrease in *Firmicutes,* along with an enhancement in intestinal glucagon-like peptide-1 level and a raised secondary/primary bile acid ratio.

Generally, several legumes have been found to inhibit weight gain through decreasing *Firmicutes* and increasing *Bacteroidetes* and *Lactobacillus.* Until now, researches on the anti-obesity effect of legumes through regulating gut microbiota have been scarce, and most researches mainly emphasize the anti-obesity effect of legume proteins. In the future, more attention should be paid to other components of legumes, such as polyphenols rich in bean coats, which should possess anti-obesity activity via regulating gut microbiota.

4.5. Grains

Buckwheat, sorghum, barley, maize, and wheat are commonly cultivated grain crops, which have shown anti-obesity activity because of their rich fibre and other bioactive compounds (Neyrinck et al., 2018; Ou et al., 2016; Ramos-Romero et al., 2014; Shen, Zhang, Dong, Ren, & Chen, 2015; Zhong, Marungruang, Fak, & Nyman, 2015). Fagomine, an iminosugar first found in buckwheat, inhibits rat obesity development by selectively agglutinating *Enterobacteriales* in the gut and reducing its excretion (Ramos-Romero et al., 2014). Sorghum resistant starch could mitigate overweight and obesity by modulating adipokine levels and increasing *Lactobacillus* and *Bifidobacterium* counts in Sprague-Dawley rats (Shen et al., 2015). In male Wistar rats, two whole-grain barley varieties differing in dietary fibre and β-glucan contents, were found effective in reducing inflammation, with an increase in SCFA levels and a decrease in plasma LPS-binding protein and MCP-1, and altering the gut microbiota composition, presenting as increased *Lactobacillus* and *Bifidobacterium*, and decreased *Bacteroides fragilis* (Zhong, Marungruang, Fåk, & Nyman, 2015). Furthermore, wheat-derived arabinoxylan oligosaccharides could reduce fat-mass expansion and increase *Bifidobacterium animalis* and *Bifidobacterium pseudolongum* in the gut of obese mice fed with a Western diet (Neyrinck et al., 2018). Feruloylated oligosaccharides from maize bran, a byproduct generated from maize milling, could greatly increase the ratio of *Bacteroidetes* to *Firmicutes*, which was tightly associated with weight loss (Ou et al., 2016). Besides, dextrins from maize starch could increase the abundance of *Bacteroidetes* and *Actinobacteria*, which represented a majority of gut microbiota in lean individuals, and decrease the obesity-related *Firmicutes* in feces of children (Barczynska, Kapusniak, Litwin, Slizewska, & Szalecki, 2016).

In summary, grains have shown an anti-obesity effect via regulating gut microbiota, and related researches mainly studied grain starch and fibers. Future studies should pay more attention to the byproducts from grain processing, which contain abundant dietary fibers and other bioactive compounds and could possess an anti-obesity effect via gut microbiota modulation.

4.6. Tea

Tea has a long history of consumption as a popular beverage. Recently, tea has been reported to possess anti-obesity efficacy through multiple mechanisms, like decreasing lipid accumulation in cells and modulating gut microbiota (Pan, Tung, Yang, Li, & Ho, 2016). Infusions of green tea, oolong tea, and black tea were used through gavage to HFD-induced obese C57BL/6J mice, respectively, and the results showed that all three teas could prevent weight gain and alter the composition of gut microbiota including *Alistipes*, *Rikenella*, Lachnospiraceae*, Akkermansia, Bacteroides, Allobaculum*, and *Parabacteroides*, which were closely associated with host obesity development (Liu et al., 2016). Another study found that polyphenols from these teas could stimulate the proliferation of beneficial bacteria, decrease the abundance of *Bacteroides, Prevotella*, and *Clostridium histolyticum*, and increase the levels of SCFAs (Sun et al., 2018a, b). Besides, treatment of the water extracts of green tea, oolong tea, and black tea in C57BL/6J mice showed that these tea extracts could improve glucose tolerance and decrease weight gain through modulating gut microbiota. These tea extracts down-regulated the relative proportion of family *Rikenellaceae* and Desulfovibrionaceae*,* causing elevated SCFA levels, decreased endotoxin LPS, and improved glucose tolerance (Liu et al., 2019). Fermented green tea effectively decreased weight gain and fat mass of obese mice with no influence on food intake through improving the ratios of *Firmicutes* to *Bacteroidetes* and *Bacteroides* to *Prevotella*, as well as down-regulating the expression of lipogenic and inflammatory genes in white adipose tissue (Seo et al., 2015). Additionally, fermented green tea also prevented obesity development by increasing the energy expenditure, modulating mRNA expressions of lipid metabolism genes, and lowering the abundance of *Firmicutes* in hamsters (Seo et al., 2017b). Besides, green tea polyphenols could attenuate HFD-induced obesity via modulating gut microbiota composition in human flora-associated (HFA) C57BL/6J mice models (Guo et al., 2017; Wang et al., 2018b). Furthermore, oolong tea polyphenols could improve obesity-related metabolic disorders by restoring the alteration of gut microbiota composition induced by HFD in HFA mice (Zhang et al., 2017b). Moreover, (−)-epigallocatechin-3-gallate (EGCG), the main catechin in tea, could protect the integrity of DNA, alter the expression and DNA methylation of gene *MutL homologue 1*, and prevent the changes of gut microbiota in obese mice induced by high-fat diet with reduced ratio of *Firmicutes* to *Bacteroidetes* (Remely et al., 2017). The effects of tea on obesity through regulating gut microbiota have also been investigated in human. In a RCT studying the effects of tea polyphenols on gut microbiota on 37 overweight and obese men and women from Netherlands, the co-use of EGCG and resveratrol (282 and 80 mg/day, respectively) for 12 weeks reduced the *Bacteroidetes* and *Faecalibacterium prausnitzii* in men, but showed no effects in women (Most, Penders, Lucchesi, Goossens, & Blaak, 2017). However, another RCT conducted on 58 healthy Caucasian men and women aged 18–50 years old found that 12-week consumption of green tea extracts, containing more than 0.56 g/d EGCG and 0.28–0.45 g/d caffeine, didn't change the gut microbiota composition (Janssens et al., 2016). The different results of the anti-obesity and gut microbiota-modulating effects of tea on humans might be due to the gender difference or the diversity of gut microbiota in individuals from different geographical areas. In the future, more clinical trials should be carried out to confirm the anti-obesity effect of tea through regulating gut microbiota.

Finally, the alteration of obesogenic and anti-obesity gut bacteria

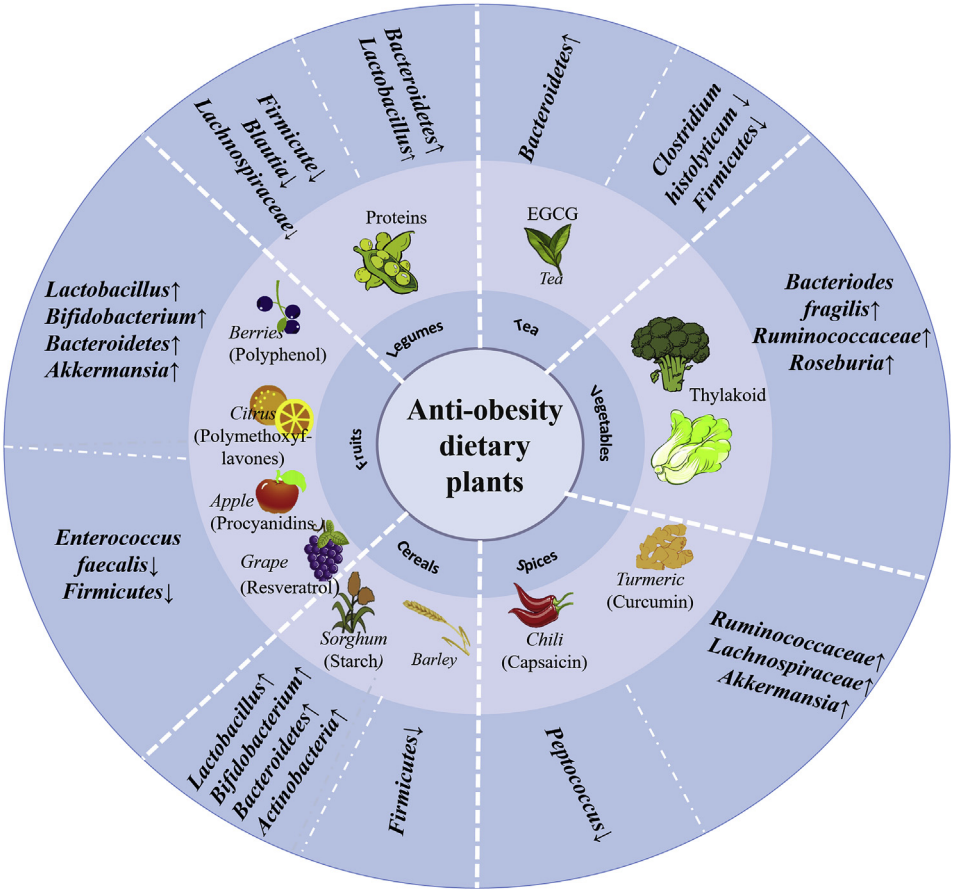

Fig. 1. The gut microbiota modulated by dietary natural plants. Up arrows mean up-regulation, and down arrows mean down-regulation.

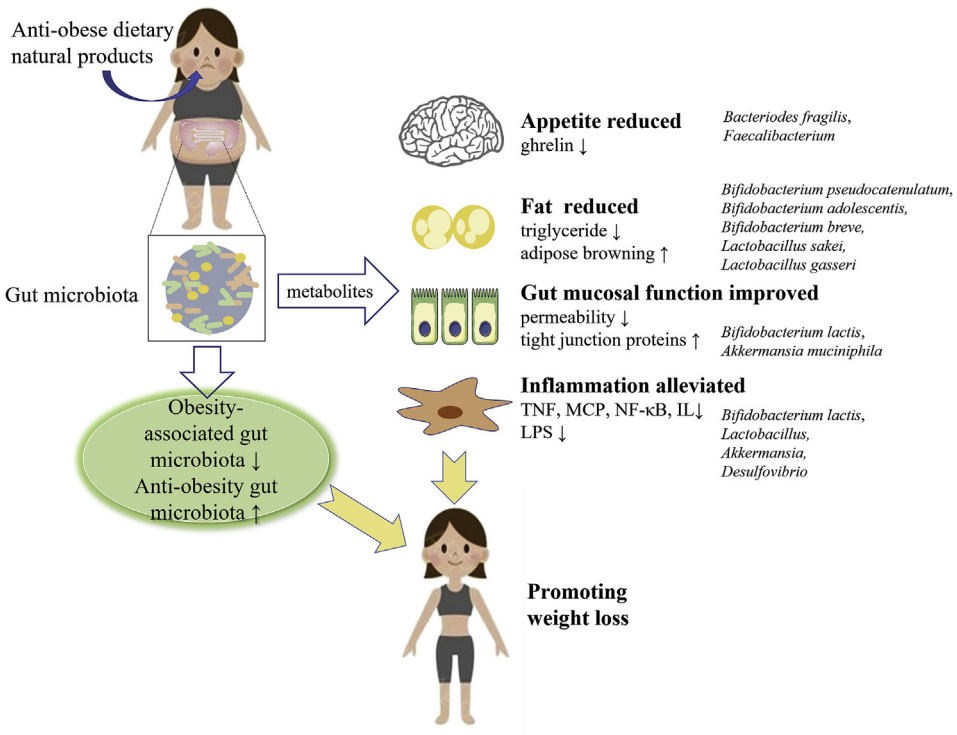

Fig. 2. The main mechanisms of anti-obesity effects of dietary plants through modulating gut microbiota. Intake of anti-obesity dietary natural plants could up-regulate anti-obesity gut bacteria and down-regulate obesogenic gut bacteria. The metabolites produced by modulated gut microbiota would promote weight loss through reducing appetite with lowered ghrelin, decreasing fat accumulation with down-regulation of triglyceride and up-regulation of adipose browning, improving gut mucosal function, and alleviating gut inflammation with lowered TNF, MCP, NF-κB, IL, and LPS.

caused by dietary plants are shown in Fig. 1, and the main mechanisms of anti-obesity effects of dietary plants through modulating gut microbiota are shown in Fig. 2.

5. Targeting gut microbiota for the development of anti-obesity functional foods

Nowadays, there has been increasing interest to develop anti-obesity functional foods with gut microbiota-regulating activity. In the literature, many animal studies have been carried out, and found that some gut microbiota regulated by functional foods could decrease weight, while other gut microbiota regulated by functional foods could increase weight. However, the reproducibility of different studies was usually poor, and the findings in one study might be contradictory or not observed in another study. This could be associated with the differences in gut microbiota, animal species, dosage, and duration. Furthermore, it is very difficult to translate the results of animal studies into human beings because of the differences of gut microbiota in animals and human, the interindividual differences, as well as over-high dosages used in animal studies, which are sometimes unrealistic in human. Therefore, a large number of studies are required for human in order to find differences or consistent effects before anti-obesity functional foods targeting gut microbiota can be developed. Moreover, the racial and interindividual differences of gut microbiota in human beings should be considered for designing potential anti-obesity therapeutics. Generally speaking, functional foods should increase the diversity of gut microbiota, increase the proportion of anti-obesity gut bacteria, but decrease the proportion of obesogenic gut microbiota.

Dietary polyphenols such as resveratrol and quercetin, dietary fibers such as pectin, β-glucan, xylan, arabinoxylan, inulin, resistant starch, and guar gum, and dietary proteins such as soy proteins, have been found to modulate certain gut microbiota and promote weight loss in human beings, and have been developed as capsule supplementary or food additives (Baboota et al., 2013). In the European Union, fructooligosaccharides, galactooligosaccharides, and lactulose have been approved as prebiotics to modulate obesity (Kolida & Gibson, 2011).

The anti-obesity functional foods could play beneficial roles in weight loss by different actions, such as inhibiting appetite, reducing the absorption of fat and carbohydrates, accelerating energy expenditure, and modulating gut microbiota, which has been increasingly paid attention to. In the future, more anti-obesity functional foods targeting gut microbiota should be developed.

6. Conclusion and perspective

Gut microbiota is essential in modulating human energy metabolism and is tightly associated with obesity. The effects of gut microbiota on obesity development are species/strain-dependent, since some gut bacteria belonging to *Lactobacillus*, *Firmicutes*, and *Bacteroidetes* are positively related to obesity development, while *Bifidobacterium*, most of *Lactobacillus*, and some *Bacteroidetes* show anti-obesity activities. Recently, a number of experimental and epidemiological studies have demonstrated that several dietary plants, such as fruits (grapes, apples, and berries), vegetables (green leafy vegetables and bitter melon), spices (turmeric, chili, rosemary, and cinnamon), legumes (pea, soy, and mung beans), grains (buckwheat, sorghum, barley, maize, and wheat) and tea (green, oolong, and black teas), could modulate the composition and abundance of gut microbiota, which play an essential role in their anti-obesity efficacy. The alteration of gut microbiota can have feedback effects on the development of obesity in hosts. Metabolites from gut microbiota can promote weight loss through multiple pathways, including regulating the metabolism of fatty acids, reducing appetite, alleviating the gut inflammation, regulating the genes involved in lipogenesis, decreasing serum levels of triglyceride, cholesterol, and glucose, and promoting the browning of white adipose tissue.

In the future, it is necessary to identify more obesogenic and anti-obesity gut microbiota. In addition, other anti-obese dietary plants should also be evaluated for their effects on gut microbiota. Meanwhile, the main anti-obesity compounds should be isolated and identified in dietary plants. Besides, the mechanisms on gut microbiota regulation by dietary plants should be further clarified. Furthermore, anti-obesity action of the dietary plants or their phytochemicals should be further studied by clinical trials to confirm their effects on human beings.

Acknowledgments

This study was supported by the National Key R&D Program of China [No. 2018YFC1604400], Technology Innovation Program of Chinese Academy of Agricultural Sciences (ASTIP), Shanghai Basic and Key Program [No. 18JC1410800], Startup Fund for Youngman Research at SJTU (SFYR at SJTU), the Agri-X Interdisciplinary Fund of Shanghai Jiao Tong University [No. Agri-X2017004], the National Natural Science Foundation of China [No. 81372976], and the Key Project of Guangdong Provincial Science and Technology Program [No. 2014B020205002].

Abbreviation

WHO	World Health Organization
SCFAs	short-chain fatty acids
HFD	high fat diet
TLR5	toll-like receptor 5
RCT	randomized controlled trial
CFU	colony-forming units
LPS	lipopolysaccharide
PNPLA2	patatin-like phospholipase domain containing 2
NF-κB	nuclear factor-κB
TNF	tumor necrosis factor
PPAR	peroxisome proliferator-activated receptor
ICR	Institute of Cancer Research
IL	interleukin
Prdm16	PR domain containing 16
Pgc-1α	Ppar-γ coactivator-1α
Bmp7	bone morphogenetic protein
Fgf21	fibroblast growth factor 21
MCP	monocyte chemoattractant protein
TRPV	transient receptor potential vanilloid
Lpl	lipoprotein lipase
Scd1	stearoyl-CoA desaturase 1
Acc1	acetyl-CoA carboxylase 1
Fas	fatty acid synthase
HFA	human flora-associated
EGCG	(−)-epigallocatechin-3-gallate

Conflicts of interest

The authors declare no conflict of interest.

References

Al-Assal, K., Martinez, A. C., Torrinhas, R. S., Cardinelli, C., & Waitzberg, D. (2018). Gut microbiota and obesity. *Clinical Nutrition Experimental, 20*, 60–64.

Angelakis, E., Bastelica, D., Ben Amara, A., El Filali, A., Dutour, A., Mege, J., et al. (2012). An evaluation of the effects of *Lactobacillus ingluviei* on body weight, the intestinal microbiome and metabolism in mice. *Microbial Pathogenesis, 52*(1), 61–68.

Angelakis, E., & Raoult, D. (2010). The increase of *Lactobacillus* species in the gut flora of newborn broiler chicks and ducks is associated with weight gain. *PLoS One, 5* Article No. e104635.

Baboota, R. K., Bishnoi, M., Ambalam, P., Kondepudi, K. K., Sarma, S. M., Boparai, R. K., et al. (2013). Functional food ingredients for the management of obesity and associated co-morbidities. *Journal of Functional Foods, 5*, 997–1012.

Bäckhed, F., Ley, R. E., Sonnenburg, J. L., Peterson, D. A., & Gordon, J. I. (2005). Host-bacterial mutualism in the human intestine. *Science, 307*(5717), 1915–1920.

Barczynska, R., Kapusniak, J., Litwin, M., Slizewska, K., & Szalecki, M. (2016). Dextrins

from maize starch as substances activating the growth of *Bacteroidetes* and *Actinobacteria* simultaneously inhibiting the growth of *Firmicutes*, responsible for the occurrence of obesity. *Plant Foods for Human Nutrition, 71*(2), 190–196.
Barlow, G. M., Yu, A., & Mathur, R. (2015). Role of the gut microbiome in obesity and diabetes mellitus. *Nutrition in Clinical Practice, 30*, 787–797.
Brahe, L. K., Le Chatelier, E., Prifti, E., Pons, N., Kennedy, S., Blaedel, T., et al. (2015). Dietary modulation of the gut microbiota - a randomised controlled trial in obese postmenopausal women. *British Journal of Nutrition, 114*, 406–417.
Carrera-Quintanar, L., López Roa, R. I., Quintero-Fabián, S., Sánchez-Sánchez, M. A., Vizmanos, B., & Ortuño-Sahagún, D. (2018). *Phytochemicals that influence gut microbiota as prophylactics and for the treatment of obesity and inflammatory diseases.* Mediators of Inflammation Article No. 9734845.
Chelakkot, C., Choi, Y., Kim, D. K., Park, H. T., Ghim, J., Kwon, Y., et al. (2018). *Akkermansia muciniphila*-derived extracellular vesicles influence gut permeability through the regulation of tight junctions. *Experimental & Molecular Medicine, 50* Article No. 450.
Chen, L. H., Chen, Y. H., Cheng, K. C., Chien, T. Y., Chan, C. H., Tsao, S. P., et al. (2018). Antiobesity effect of *Lactobacillus reuteri* 263 associated with energy metabolism remodeling of white adipose tissue in high-energy-diet-fed rats. *Journal of Nutritional Biochemistry, 54*, 87–94.
Chung, H. J., Yu, J. G., Lee, I. A., Liu, M. J., Shen, Y. F., Sharma, S. P., et al. (2016). Intestinal removal of free fatty acids from hosts by *Lactobacilli* for the treatment of obesity. *FEBS Open Bio, 6*, 64–76.
Condezo-Hoyos, L., Mohanty, I. P., & Noratto, G. D. (2014). Assessing non-digestible compounds in apple cultivars and their potential as modulators of obese faecal microbiota *in vitro*. *Food Chemistry, 161*, 208–215.
Drissi, F., Merhej, V., Angelakis, E., El Kaoutari, A., Carrière, F., Henrissat, B., et al. (2014). Comparative genomics analysis of *Lactobacillus* species associated with weight gain or weight protection. *Nutrition & Diabetes, 4* Article No. e109.
Dugas, L. R., Bernabe, B. P., Priyadarshini, M., Fei, N., Park, S. J., Brown, L., et al. (2018). Decreased microbial co-occurrence network stability and SCFA receptor level correlates with obesity in African-origin women. *Scientific Reports, 8* Article No. 17135.
Eckburg, P. B., Bik, E. M., Bernstein, C. N., Purdom, E., Dethlefsen, L., Sargent, M., et al. (2005). Diversity of the human intestinal microbial flora. *Science, 308*, 1635–1638.
Eslinger, A. J., Eller, L. K., & Reimer, R. A. (2014). Yellow pea fiber improves glycemia and reduces *Clostridium leptum* in diet-induced obese rats. *Nutrition Research, 34*(8), 714–722.
Etxeberria, U., Arias, N., Boqúe, N., Macarulla, M. T., Portillo, M. P., Martínez, J. A., et al. (2015). Reshaping faecal gut microbiota composition by the intake of *trans*-resveratrol and quercetin in high-fat sucrose diet-fed rats. *Journal of Nutritional Biochemistry, 26*(6), 651–660.
Fu, C. H., Jiang, Y., Guo, J., & Su, Z. Q. (2016). Natural products with anti-obesity effects and different mechanisms of action. *Journal of Agricultural and Food Chemistry, 64*, 9571–9585.
Gilbert, J. A., Blaser, M. J., Caporaso, J. G., Jansson, J. K., Lynch, S. V., & Knight, R. (2018). Current understanding of the human microbiome. *Nature Medicine, 24*(4), 392–400.
Gøbel, R. J., Larsen, N., Jakobsen, M., Mølgaard, C., & Michaelsen, K. F. (2012). Probiotics to adolescents with obesity: Effects on inflammation and metabolic syndrome. *Journal of Pediatric Gastroenterology and Nutrition, 55*(6), 673–678.
Griffin, L. E., Witrick, K. A., Klotz, C., Dorenkott, M. R., Goodrich, K. M., Fundaro, G., et al. (2017). Alterations to metabolically active bacteria in the mucosa of the small intestine predict anti-obesity and anti-diabetic activities of grape seed extract in mice. *Food & Function, 8*(10), 3510–3522.
Guo, X., Cheng, M., Zhang, X., Cao, J. X., Wu, Z. F., & Weng, P. F. (2017). Green tea polyphenols reduce obesity in high-fat diet-induced mice by modulating intestinal microbiota composition. *International Journal of Food Science and Technology, 52*(8), 1723–1730.
Harsch, I. A., & Konturek, P. C. (2018). The role of gut microbiota in obesity and type 2 and type 1 diabetes mellitus: New insights into "old" diseases. *Medical Science, 17* Article No. E32.
Heyman-Lindén, L., Kotowska, D., Sand, E., Bjursell, M., Plaza, M., Turner, C., et al. (2016). Lingonberries alter the gut microbiota and prevent low-grade inflammation in high-fat diet fed mice. *Food & Nutrition Research, 60* Article No. 29993.
Hippe, B., Remely, M., Aumueller, E., Pointner, A., Magnet, U., & Haslberger, A. G. (2016). *Faecalibacterium prausnitzii* phylotypes in type two diabetic, obese, and lean control subjects. *Beneficial Microbes, 7*(4), 511–517.
Hsieh, F. C., Lan, C. C. E., Huang, T. Y., Chen, K. W., Chai, C. Y., Chen, W. T., et al. (2016). Heat-killed and live *Lactobacillus reuteri* GMNL-263 exhibit similar effects on improving metabolic functions in high-fat diet-induced obese rats. *Food & Function, 7*(5), 2374–2388.
Hwang, I., Park, Y. J., Kim, Y. R., Kim, Y. N., Ka, S., Lee, H. Y., et al. (2015). Alteration of gut microbiota by vancomycin and bacitracin improves insulin resistance via glucagon-like peptide 1 in diet-induced obesity. *Federation of American Societies for Experimental Biology Journal, 29*(6), 2397–2411.
Ismail, N. A., Ragab, S. H., Abd ElBaky, A., Shoeib, A. R. S., Alhosary, Y., & Fekry, D. (2011). Frequency of *Firmicutes* and *Bacteroidetes* in gut microbiota in obese and normal weight Egyptian children and adults. *Archives of Medical Science, 7*(3), 501–507.
Jang, H. M., Han, S. K., Kim, J. K., Oh, S. J., Jang, H. B., & Kim, D. H. (2019). *Lactobacillus sakei* alleviates high-fat-diet-induced obesity and anxiety in mice by inducing AMPK activation and SIRT1 expression and inhibiting gut microbiota-mediated NF-κB activation. *Molecular Nutrition & Food Research, 63* Article No. 1800978.
Janssens, P. L. H. R., Penders, J., Hursel, R., Budding, A. E., Savelkoul, P. H. M., & Westerterp-Plantenga, M. S. (2016). Long-term green tea supplementation does not change the human gut microbiota. *PLoS One, 11*(4) Article No. e0153134.
Jiang, T. T., Gao, X. J., Wu, C., Tian, F., Lei, Q. C., Bi, J. C., et al. (2016). Apple-derived pectin modulates gut microbiota, improves gut barrier function, and attenuates metabolic endotoxemia in rats with diet-induced obesity. *Nutrients, 8*(3), 126. https://doi.org/10.3390/nu8030126.
Jiao, X. Y., Wang, Y. H., Lin, Y., Lang, Y. X., Li, E. H., Zhang, X. Y., et al. (2019). Blueberry polyphenols extract as a potential prebiotic with anti-obesity effects on C57BL/6 J mice by modulating the gut microbiota. *Journal of Nutritional Biochemistry, 64*, 88–100.
Johnson, E. L., Heaver, S. L., Walters, W. A., & Ley, R. E. (2017). Microbiome and metabolic disease: Revisiting the bacterial phylum *Bacteroidetes*. *Journal of Molecular Medicine, 95*(1), 1–8.
Kang, C., Wang, B., Kaliannan, K., Wang, X. L., Lang, H. D., Hui, S. C., et al. (2017). Gut microbiota mediates the protective effects of dietary capsaicin against chronic low-grade inflammation and associated obesity induced by high-fat diet. *mBio, 8* Article No. e00470-173.
Kang, C., Zhang, Y., Zhu, X. H., Liu, K., Wang, X. L., Chen, M. T., et al. (2016). Healthy subjects differentially respond to dietary capsaicin correlating with specific gut enterotypes. *Journal of Clinical Endocrinology & Metabolism, 101*(12), 4681–4689.
Kazemipoor, M., Cordell, G. A., Sarker, M. M. R., Radzi, C. W. J. B. W. M., Hajifaraji, M., & Kiat, P. E. (2015). Alternative treatments for weight loss: Safety/risks and effectiveness of anti-obesity medicinal plants. *International Journal of Food Properties, 18*(9), 1942–1963.
Kim, M., Furuzono, T., Yamakuni, K., Li, Y., Kim, Y., Takahashi, H., et al. (2017). 10-Oxo-12(Z)-octadecenoic acid, a linoleic acid metabolite produced by gut lactic acid bacteria, enhances energy metabolism by activation of TRPV1. *Federation of American Societies for Experimental Biology Journal, 31*(11), 5036–5048.
Kim, J., Yun, J. M., Kim, M. K., Kwon, O., & Cho, B. (2018). *Lactobacillus gasseri* BNR17 supplementation reduces the visceral fat accumulation and waist circumference in obese adults: A randomized, double-blind, placebo-controlled trial. *Journal of Medicinal Food, 21*(5), 454–461.
Klinder, A., Shen, Q., Heppel, S., Lovegrove, J. A., Rowland, I., & Tuohy, K. M. (2016). Impact of increasing fruit and vegetables and flavonoid intake on the human gut microbiota. *Food & Function, 7*(4), 1788–1796.
Koleva, P. T., Bridgman, S. L., & Kozyrskyj, A. L. (2015). The infant gut microbiome: Evidence for obesity risk and dietary intervention. *Nutrients, 7*(4), 2237–2260.
Kolida, S., & Gibson, G. R. (2011). Synbiotics in health and disease. *Annual Review of Food Science and Technology, 2*, 373–393.
Lau, E., Marques, C., Pestana, D., Santoalha, M., Carvalho, D., Freitas, P., et al. (2016). The role of I-FABP as a biomarker of intestinal barrier dysfunction driven by gut microbiota changes in obesity. *Nutrition & Metabolism, 13* Article No. 31.
Lee, E., Jung, S. R., Lee, S. Y., Lee, N. K., Paik, H. D., & Lim, S. I. (2018a). *Lactobacillus plantarum* strain Ln4 attenuates diet-induced obesity, insulin resistance, and changes in hepatic mRNA levels associated with glucose and lipid metabolism. *Nutrients, 10* Article No. 643.
Lee, S., Keirsey, K. I., Kirkland, R., Grunewald, Z. I., Fischer, J. G., & de La Serre, C. B. (2018b). Blueberry supplementation influences the gut microbiota, inflammation, and insulin resistance in high-fat-diet-fed rats. *Journal of Nutrition, 148*(2), 209–219.
Ley, R. E., Bäckhed, F., Turnbaugh, P., Lozupone, C. A., Knight, R. D., & Gordon, J. I. (2005). Obesity alters gut microbial ecology. *Proceedings of the National Academy of Sciences of the United States of America, 102*, 11070–11075.
Li, Z., Jin, H., Oh, S. Y., & Ji, G. E. (2016). Anti-obese effects of two *Lactobacilli* and two *Bifidobacteria* on ICR mice fed on a high fat diet. *Biochemical and Biophysical Research Communications, 480*(2), 222–227.
Lim, S. M., Jeong, J. J., Woo, K. H., Han, M. J., & Kim, D. H. (2016). *Lactobacillus sakei* OK67 ameliorates high-fat diet-induced blood glucose intolerance and obesity in mice by inhibiting gut microbiota lipopolysaccharide production and inducing colon tight junction protein expression. *Nutrition Research, 36*(4), 337–348.
Lim, S. M., & Kim, D. H. (2017). *Bifidobacterium adolescentis* IM38 ameliorates high-fat diet-induced colitis in mice by inhibiting NF-κB activation and lipopolysaccharide production by gut microbiota. *Nutrition Research, 41*, 86–96.
Liu, Z. B., Chen, Z. C., Guo, H. W., He, D. P., Zhao, H. R., Wang, Z. Y., et al. (2016). The modulatory effect of infusions of green tea, oolong tea, and black tea on gut microbiota in high-fat-induced obese mice. *Food & Function, 7*(12), 4869–4879.
Liu, J. H., Hao, W. J., He, Z. Y., Kwek, E., Zhao, Y. M., Zhu, H. Y., et al. (2019). Beneficial effects of tea water extracts on the body weight and gut microbiota in C57BL/6J mice fed with a high-fat diet. *Food & Function, 10*, 2847–2860.
Masumoto, S., Terao, A., Yamamoto, Y., Mukai, T., Miura, T., & Shoji, T. (2016). Non-absorbable apple procyanidins prevent obesity associated with gut microbial and metabolomic changes. *Scientific Reports, 6* Article No. 31208.
Menni, C., Jackson, M. A., Pallister, T., Steves, C. J., Spector, T. D., & Valdes, A. M. (2017). Gut microbiome diversity and high-fibre intake are related to lower long-term weight gain. *International Journal of Obesity, 41*(7), 1099–1105.
Million, M., Angelakis, E., Paul, M., Armougom, F., Leibovici, L., & Raoult, D. (2012). Comparative meta-analysis of the effect of *Lactobacillus* species on weight gain in humans and animals. *Microbial Pathogenesis, 53*(2), 100–108.
Million, M., Thuny, F., Angelakis, E., Casalta, J. P., Giorgi, R., Habib, G., et al. (2013). *Lactobacillus reuteri* and *Escherichia coli* in the human gut microbiota may predict weight gain associated with vancomycin treatment. *Nutrition & Diabetes, 3* Article No. 87.
Minami, J., Kondo, S., Yanagisawa, N., Odamaki, T., Xiao, J. Z., Abe, F., et al. (2015). Oral administration of *Bifidobacterium breve* B-3 modifies metabolic functions in adults with obese tendencies in a randomised controlled trial. *Journal of Nutrition Sciences, 4* Article No. 17.
Mokdad, A. H., Ford, E. S., Bowman, B. A., Dietz, W. H., Vinicor, F., Bales, V. S., et al. (2003). Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA-Journal of the American Medical Association, 289*(1), 76–79.

Mokkala, K., Laitinen, K., & Röytiö, H. (2016). *Bifidobacterium lactis* 420 and fish oil enhance intestinal epithelial integrity in Caco-2 cells. *Nutrition Research, 36*(3), 246–252.
Moreno-Indias, I., Sánchez-Alcoholado, L., Pérez-Martinez, P., Andrés-Lacueva, C., Cardona, F., Tinahones, F., et al. (2016). Red wine polyphenols modulate fecal microbiota and reduce markers of the metabolic syndrome in obese patients. *Food & Function, 7*(4), 1775–1787.
Most, J., Penders, J., Lucchesi, M., Goossens, G. H., & Blaak, E. E. (2017). Gut microbiota composition in relation to the metabolic response to 12-week combined polyphenol supplementation in overweight men and women. *European Journal of Clinical Nutrition, 71*, 1040–1045.
Moya-Pérez, A., Romo-Vaquero, M., Tomás-Barberán, F., Sanz, Y., & García-Conesa, M. T. (2014). Hepatic molecular responses to *Bifidobacterium pseudocatenulatum* CECT 7765 in a mouse model of diet-induced obesity. *Nutrition, Metabolism, and Cardiovascular Diseases, 24*(1), 57–64.
Nagata, S., Chiba, Y., Wang, C., & Yamashiro, Y. (2017). The effects of the *Lactobacillus casei* strain on obesity in children: A pilot study. *Beneficial Microbes, 8*(4), 535–543.
Nakatani, A., Li, X., Miyamoto, J., Igarashi, M., Watanabe, H., Sutou, A., et al. (2018). Dietary mung bean protein reduces high-fat diet-induced weight gain by modulating host bile acid metabolism in a gut microbiota-dependent manner. *Biochemical and Biophysical Research Communications, 501*(4), 955–961.
Neyrinck, A. M., Hiel, S., Bouzin, C., Campayo, V. G., Cani, P. D., Bindels, L. B., et al. (2018). Wheat-derived arabinoxylan oligosaccharides with bifidogenic properties abolishes metabolic disorders induced by western diet in mice. *Nutrition & Diabetes, 8* Article No. 15.
Ohno, M., Nishida, A., Sugitani, Y., Nishino, K., Inatomi, O., Sugimoto, M., et al. (2017). Nanoparticle curcumin ameliorates experimental colitis via modulation of gut microbiota and induction of regulatory T cells. *PLoS One, 12* Article No. 0185999.
Ojo, B., El-Rassi, G., Payton, M. E., Perkins-Veazie, P., Clarke, S., Smith, B. J., et al. (2016). Mango supplementation modulates gut microbial dysbiosis and short-chain fatty acid production independent of body weight reduction in C57BL/6 mice fed a high-fat diet. *Journal of Nutrition, 146*(8), 1483–1491.
Ottosson, F., Brunkwall, L., Ericson, U., Nilsson, P. M., Almgren, P., Fernandez, C., et al. (2018). Connection between BMI-related plasma metabolite profile and gut microbiota. *Journal of Clinical Endocrinology & Metabolism, 103*, 1491–1501.
Ou, J. Y., Huang, J. Q., Song, Y., Yao, S. W., Peng, X. C., Wang, M. F., et al. (2016). Feruloylated oligosaccharides from maize bran modulated the gut microbiota in rats. *Plant Foods for Human Nutrition, 71*(2), 123–128.
Panasevich, M. R., Schuster, C. M., Phillips, K. E., Meers, G. M., Chintapalli, S. V., Wankhade, U. D., et al. (2017). Soy compared with milk protein in a Western diet changes fecal microbiota and decreases hepatic steatosis in obese OLETF rats. *Journal of Nutritional Biochemistry, 46*, 125–136.
Pan, P., Lam, V., Salzman, N., Huang, Y. W., Yu, J., Zhang, J., et al. (2017). Black raspberries and their anthocyanin and fiber fractions alter the composition and diversity of gut microbiota in F-344 rats. *Nutrition and Cancer-An International Journal, 69*(6), 943–951.
Pan, M. H., Tung, Y. C., Yang, G., Li, S., & Ho, C. T. (2016). Molecular mechanisms of the anti-obesity effect of bioactive compounds in tea and coffee. *Food & Function, 7*(11), 4481–4491.
Pekkala, S., Munukka, E., Kong, L., Pollanen, E., Autio, R., Roos, C., et al. (2015). Toll-like receptor 5 in obesity: The role of gut microbiota and adipose tissue inflammation. *Obesity, 23*(3), 581–590.
Postler, T. S., & Ghosh, S. (2017). Understanding the holobiont: How microbial metabolites affect human health and shape the immune system. *Cell Metabolism, 26*(1), 110–130.
Prior, R. L., Wilkes, S., Rogers, T., Khanal, R. C., Wu, X., Hager, T. J., et al. (2010). Dietary black raspberry anthocyanins do not alter development of obesity in mice fed an obesogenic high-fat diet. *Journal of Agricultural and Food Chemistry, 58*, 3977–3983.
Qiao, Y., Sun, J., Xia, S., Tang, X., Shi, Y., & Le, G. (2014b). Effects of resveratrol on gut microbiota and fat storage in a mouse model with high-fat-induced obesity. *Food & Function, 5*(6), 1241–1249.
Qiao, Y., Sun, J., Xie, Z., Shi, Y., & Le, G. (2014a). Propensity to high-fat diet-induced obesity in mice is associated with the indigenous opportunistic bacteria on the interior of Peyer's patches. *Journal of Clinical Biochemistry & Nutrition, 55*(2), 120–128.
Qu, L., Liu, Q., Zhang, Q., Tuo, X., Fan, D., Deng, J., et al. (2019). Kiwifruit seed oil prevents obesity by regulating inflammation, thermogenesis, and gut microbiota in high-fat diet-induced obese C57BL/6 mice. *Food and Chemical Toxicology, 125*, 85–94.
Ramos-Romero, S., Molinar-Toribio, E., Gómez, L., Pérez-Jiménez, J., Casado, M., Clapés, P., et al. (2014). Effect of *D*-fagomine on excreted *Enterobacteria* and weight gain in rats fed a high-fat high-sucrose diet. *Obesity, 22*(4), 976–979.
Rastelli, M., Knauf, C., & Cani, P. D. (2018). Gut microbes and health: A focus on the mechanisms linking microbes, obesity, and related disorders. *Obesity, 26*, 792–800.
Ray, M., Hor, P. K., Ojha, D., Soren, J. P., Singh, S. N., & Mondal, K. C. (2018). *Bifidobacteria* and its rice fermented products on diet induced obese mice: Analysis of physical status, serum profile and gene expressions. *Beneficial Microbes, 9*(3), 441–452.
Remely, M., Ferk, F., Sterneder, S., Setayesh, T., Roth, S., Kepcija, T., et al. (2017). EGCG prevents high fat diet-induced changes in gut microbiota, decreases of DNA strand breaks, and changes in expression and DNA methylation of Dnmt1 and MLH1 in C57BL/6J male mice. *Oxidative Medicine and Cellular Longevity*3079148.
Romo-Vaquero, M., Selma, M. V., Larrosa, M., Obiol, M., García-Villalba, R., González-Barrio, R., et al. (2014). A rosemary extract rich in carnosic acid selectively modulates caecum microbiota and inhibits β-glucosidase activity, altering fiber and short chain fatty acids fecal excretion in lean and obese female rats. *PLoS One, 9* Article No. 946874.
Roselli, M., Devirgiliis, C., Zinno, P., Guantario, B., Finamore, A., Rami, R., et al. (2017). Impact of supplementation with a food-derived microbial community on obesity-associated inflammation and gut microbiota composition. *Genes and Nutrition, 12* Article No. 25.
Rosing, J. A., Walker, K. C., Jensen, B. A. H., & Heitmann, B. L. (2017). Oral *Lactobacillus* counts predict weight gain susceptibility: A 6-year follow-up study. *Obesity Facts, 10*(5), 473–482.
Round, J. L., & Mazmanian, S. K. (2009). The gut microbiota shapes intestinal immune responses during health and disease. *Nature Reviews Immunology, 9*, 313–323.
Sayin, S. I., Wahlstrom, A., Felin, J., Jantti, S., Marschall, H. U., Bamberg, K., et al. (2013). Gut microbiota regulates bile acid metabolism by reducing the levels of tauro-β-muricholic acid, a naturally occurring FXR antagonist. *Cell Metabolism, 17*, 225–235.
Schugar, R. C., Shih, D. M., Warrier, M., Helsley, R. N., Burrows, A., Ferguson, D., et al. (2017). The TMAO-producing enzyme flavin-containing monooxygenase 3 regulates obesity and the beiging of white adipose tissue. *Cell Reports, 19*, 2451–2461.
Seo, D. B., Jeong, H. W., Cho, D., Lee, B. J., Lee, J. H., Choi, J. Y., et al. (2015). Fermented green tea extract alleviates obesity and related complications and alters gut microbiota composition in diet-induced obese mice. *Journal of Medicinal Food, 18*(5), 549–556.
Seo, D. B., Jeong, H. W., Kim, Y. J., Kim, S., Kim, J., Lee, J. H., et al. (2017b). Fermented green tea extract exhibits hypolipidaemic effects through the inhibition of pancreatic lipase and promotion of energy expenditure. *British Journal of Nutrition, 117*(2), 177–186.
Seo, K. H., Kim, D. H., Jeong, D., Yokoyama, W., & Kim, H. (2017a). Chardonnay grape seed flour supplemented diets alter intestinal microbiota in diet-induced obese mice. *Journal of Food Biochemistry, 41*(5).
Shang, Y., Khafipour, E., Derakhshani, H., Sarna, L. K., Woo, C. W., Siow, Y. L., et al. (2017). Short term high fat diet induces obesity-enhancing changes in mouse gut microbiota that are partially reversed by cessation of the high fat diet. *Lipids, 52*(6), 499–511.
Shen, L., Liu, L., & Ji, H. F. (2017a). Regulative effects of curcumin spice administration on gut microbiota and its pharmacological implications. *Food & Nutrition Research, 61* Article No. 1361780.
Shen, J., Obin, M. S., & Zhao, L. (2013). The gut microbiota, obesity and insulin resistance. *Molecular Aspects of Medicine, 34*, 39–58.
Shen, W., Shen, M., Zhao, X., Zhu, H., Yang, Y., Lu, S., et al. (2017b). Anti-obesity effect of capsaicin in mice fed with high-fat diet is associated with an increase in population of the gut bacterium *Akkermansia muciniphila*. *Frontiers in Microbiology, 8*, 1–10.
Shen, W., Wolf, P. G., Carbonero, F., Zhong, W., Reid, T., Gaskins, H. R., et al. (2014). Intestinal and systemic inflammatory responses are positively associated with sulfidogenic bacteria abundance in high-fat-fed male C57BL/6J mice. *Journal of Nutrition, 144*(8), 1181–1187.
Shen, R. L., Zhang, W. L., Dong, J. L., Ren, G. X., & Chen, M. (2015). Sorghum resistant starch reduces adiposity in high-fat diet-induced overweight and obese rats via mechanisms involving adipokines and intestinal flora. *Food and Agricultural Immunology, 26*(1), 120–130.
Song, J. X., Ren, H., Gao, Y. F., Lee, C. Y., Li, S. F., Zhang, F., et al. (2017). Dietary capsaicin improves glucose homeostasis and alters the gut microbiota in obese diabetic ob/ob mice. *Frontiers in Physiology, 8* Article No. 602.
Stenblom, E. L., Weström, B., Linninge, C., Bonn, P., Farrell, M., Rehfeld, J. F., et al. (2016). Dietary green-plant thylakoids decrease gastric emptying and gut transit, promote changes in the gut microbial flora, but does not cause steatorrhea. *Nutrition & Metabolism, 13* Article No. 67.
Stenman, L. K., Waget, A., Garret, C., Klopp, P., Burcelin, R., & Lahtinen, S. (2014). Potential probiotic *Bifidobacterium animalis* ssp. *lactis* 420 prevents weight gain and glucose intolerance in diet-induced obese mice. *Beneficial Microbes, 5*(4), 437–445.
Sun, H., Chen, Y., Cheng, M., Zhang, X., Zheng, X., & Zhang, Z. (2018a). The modulatory effect of polyphenols from green tea, oolong tea and black tea on human intestinal microbiota *in vitro*. *Journal of Food Science and Technology-Mysore, 55*(1), 399–407.
Sun, L., Ma, L., Ma, Y., Zhang, F., Zhao, C., & Nie, Y. (2018b). Insights into the role of gut microbiota in obesity: Pathogenesis, mechanisms, and therapeutic perspectives. *Protein Cell, 9*(5), 397–403.
Tremaroli, V., & Bäckhed, F. (2012). Functional interactions between the gut microbiota and host metabolism. *Nature, 489*, 242–249.
Tsai, Y. C., Wang, H. T., Hsu, J. T., Li, Y. H., & Chen, C. Y. (2015). Yeast with bacteriocin from ruminal bacteria enhances glucose utilization, reduces ectopic fat accumulation, and alters cecal microbiota in dietary-induced obese mice. *Food & Function, 6*(8), 2727–2735.
Tung, Y. C., Chang, W. T., Li, S., Wu, J. C., Badmeav, V., Ho, C. T., et al. (2018). Citrus peel extracts attenuated obesity and modulated gut microbiota in mice with high-fat diet-induced obesity. *Food & Function, 9*(6), 3363–3373.
Tung, Y. C., Lin, Y. H., Chen, H. J., Chou, S. C., Cheng, A. C., Kalyanam, N., et al. (2016). Piceatannol exerts anti-obesity effects in C57BL/6 mice through modulating adipogenic proteins and gut microbiota. *Molecules, 21* Article No. 141911.
Turnbaugh, P. J., Hamady, M., Yatsunenko, T., Cantarel, B. L., Duncan, A., Ley, R. E., et al. (2009). A core gut microbiome in obese and lean twins. *Nature, 457*, 480–484.
Vael, C., Verhulst, S. L., Nelen, V., Goossens, H., & Desager, K. N. (2011). Intestinal microflora and body mass index during the first three years of life: An observational study. *Gut Pathogens, 3* Article No.8.
Van Hul, M., Geurts, L., Plovier, H., Druart, C., Everard, A., Ståhlman, M., et al. (2018). Reduced obesity, diabetes, and steatosis upon cinnamon and grape pomace are associated with changes in gut microbiota and markers of gut barrier. *American Journal of Physiology - Endocrinology And Metabolism, 314*(4), 334–352.
Wang, J., Ghosh, S. S., & Ghosh, S. (2017b). Curcumin improves intestinal barrier function: Modulation of intracellular signaling, and organization of tight junctions. *American Journal of Physiology - Cell Physiology, 312*(4), C438–C445.

Wang, H., Hong, T., Li, N., Zang, B., & Wu, X. (2018a). Soluble dietary fiber improves energy homeostasis in obese mice by remodeling the gut microbiota. *Biochemical and Biophysical Research Communications, 498*(1), 146–151.

Wang, S., Li, Q., Zang, Y., Zhao, Y., Liu, N., Wang, Y., et al. (2017a). Apple polysaccharide inhibits microbial dysbiosis and chronic inflammation and modulates gut permeability in HFD-fed rats. *International Journal of Biological Macromolecules, 99*, 282–292.

Wang, L., Zeng, B., Liu, Z., Liao, Z., Zhong, Q., Gu, L., et al. (2018b). Green tea polyphenols modulate colonic microbiota diversity and lipid metabolism in high-fat diet treated HFA mice. *Journal of Food Science, 83*(3), 864–873.

Whitehead, J. P., Simpson, F., Hill, M. M., Thomas, E. C., Connolly, L. M., Collart, F., et al. (2004). Insulin and oleate promote translocation of inosine-5 ' monophosphate dehydrogenase to lipid bodies. *Traffic, 5*, 739–749.

Xing, Y. W., Lei, G. T., Wu, Q. H., Jiang, Y., & Huang, M. X. (2019). Procyanidin B2 protects against diet-induced obesity and nonalcoholic fatty liver disease via the modulation of the gut microbiota in rabbits. *World Journal of Gastroenterology, 25*, 955–966.

Zhang, Z., Chen, Y., Xiang, L., Wang, Z., Xiao, G. G., & Hu, J. (2017a). Effect of curcumin on the diversity of gut microbiota in ovariectomized rats. *Nutrients, 9* Article No. 1146.

Zhang, Y. J., Gan, R. Y., Li, S., Zhou, Y., Li, A. N., Xu, D. P., et al. (2015b). Antioxidant phytochemicals for the prevention and treatment of chronic diseases. *Molecules, 20*, 21138–21156.

Zhang, Y. J., Li, S., Gan, R. Y., Zhou, T., Xu, D. P., & Li, H. B. (2015a). Impacts of gut bacteria on human health and diseases. *International Journal of Molecular Sciences, 16*, 7493–7519.

Zhang, L., Zhang, X., Cheng, M., Cao, J., Wu, Z. F., Weng, P. F., et al. (2017b). Oolong tea polyphenols-phospholipids complex reduces obesity in high fat diet-induced mice model. *European Journal of Lipid Science and Technology, 119* Article No. 1600394.

Zhao, L. P. (2013). The gut microbiota and obesity: From correlation to causality. *Nature Reviews Microbiology, 11*, 639–647.

Zhao, C. N., Meng, X., Li, Y., Li, S., Liu, Q., Tang, G. Y., et al. (2017a). Fruits for prevention and treatment of cardiovascular diseases. *Nutrients, 9* Article No. 598.

Zhao, L., Zhang, Q., Ma, W. N., Tian, F., Shen, H. Y., & Zhou, M. M. (2017b). A combination of quercetin and resveratrol reduces obesity in high-fat diet-fed rats by modulation of gut microbiota. *Food & Function, 8*(12), 4644–4656.

Zheng, J., Zhou, Y., Li, Y., Xu, D. P., Li, S., & Li, H. B. (2016). Spices for prevention and treatment of cancers. *Nutrients, 8* Article No. 495.

Zhong, Y., Marungruang, N., Fåk, F., & Nyman, M. (2015). Effects of two whole-grain barley varieties on caecal SCFA, gut microbiota and plasma inflammatory markers in rats consuming low- and high-fat diets. *British Journal of Nutrition, 113*(10), 1558–1570.

Zhu, Y., Bai, J., Zhang, Y., Xiao, X., & Dong, Y. (2016). Effects of bitter melon (*Momordica charantia* L.) on the gut microbiota in high fat diet and low dose streptozocin-induced rats. *International Journal of Food Sciences & Nutrition, 67*(6), 686–695.

Zhu, W., Lin, K., Li, K. K., Deng, X. Y., & Li, C. M. (2018). Reshaped fecal gut microbiota composition by the intake of high molecular weight persimmon tannin in normal and high-cholesterol diet-fed rats. *Food & Function, 9*(1), 541–551.