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Dietary natural products alleviate obesity by regulating gut microbiota: Effects, mechanisms, challenges, and perspectives

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ABSTRACT: Obesity is closely related to some diseases, such as cardiovascular disease, diabetes and cancers, and is one of the major public health challenges globally. Studies have shown that obesity is related to gut microbiota. Targeting gut microbiota could serve as a promising approach for the prevention and treatment of obesity. Dietary natural products have received widespread attention due to their anti-obesity effects by regulating gut microbiota, providing a safer and more sustainable treatment method for the prevention and treatment of obesity. This narrative review provides an overview of the anti-obesity effects of different dietary natural products, along with an exploration of their mechanisms in regulating the gut microbiota. Some dietary natural products, such as grains, fruits, vegetables, herbs, teas, algae, seafoods, edible macrofungi, spices, nuts, legumes, probiotics, prebiotics, synbiotics and postbiotics, can alleviate obesity by regulating gut microbiota. Furthermore, this review also discusses the strategies for enhancing anti-obesity effects, safety of dietary natural products, current research challenges, and future research directions. Methods to improve the anti-obesity effects of dietary natural products include fermentation, combination, and preparation of hydrogels. Future research should focus on personalized and precision nutrition through multi-omics technology and artificial intelligence, and combine multiple delivery systems to improve bioavailability and targeted delivery of dietary natural products. Moreover, attention should be paid to the dosage effect and long-term safety of dietary natural products. In short, dietary natural products could be developed into functional foods for the prevention and treatment of obesity.

Keywords: Obesity; Anti-obesity; Dietary natural products; Gut microbiota; Molecular mechanisms

1. Introduction

In recent years, the prevalence of obesity has been on the rise and is expected to increase to 1.02 billion by 2030 ^[1]. Obesity could increase the risk of a variety of diseases, such as obstructive sleep apnea, diabetes,

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chronic kidney disease, gastrointestinal diseases, cancer and cardiovascular disease, resulting in increase of healthcare costs ^[2-3]. In addition, obesity can shorten disease-free life expectancy by 3-8 years ^[4]. Obesity has become a significant global public health challenge. Currently, the main treatments for obesity include changing lifestyle, adjusting diet, increasing physical activity, using medications, and surgical treatment ^[3]. However, these weight loss methods have limited efficacy and often fail to achieve long-term success ^[5]. Therefore, exploring the strategies of prevention and treatment for obesity has become a research hotspot.

Studies have revealed a strong connection between obesity and gut microbiota disorders. In individuals with obesity, there is a reduction in gut microbiota diversity, along with an increased *Firmicutes/Bacteroidetes* ratio ^[6]. Furthermore, the mechanisms related to obesity and gut microbiota have been reported. For example, gut microbiota is closely associated with inflammation in obesity. Elevated levels of lipopolysaccharide (endotoxins present in the cell walls of Gram-negative bacteria) contribute to obesity-related low-grade inflammation ^[7]. Furthermore, the fermentation of indigestible carbohydrates by gut microbiota results in the production of short-chain fatty acids (SCFAs), such as butyrate, acetate and propionate, which have positive effects on weight loss, glucose regulation and insulin sensitivity ^[8]. Additionally, gut microbiota also plays an important role in regulating appetite and satiety via the gut-brain axis ^[6]. Therefore, modulating the gut microbiota has become a promising target for the development of novel anti-obesity therapies.

The composition and functions of the gut microbiota are determined by a variety of factors, such as birth mode, nutrition, exercise and environmental factors ^[7]. Studies have reported that diet is the primary determinant of gut microbiota composition and diversity, with dietary changes accounting for 57% of the overall alterations in gut microbiota structure ^[7]. Additionally, numerous studies have shown that some dietary natural products, such as fruits, vegetables, teas and herbs, can attenuate obesity by modulating gut microbiota ^[9-12]. For instance, polysaccharide from *Agrocybe cylindracea* could ameliorate obesity by improving insulin resistance, suppressing inflammation, and reducing adipose accumulation via regulating the gut microbiota and associated metabolites in high-fat diet (HFD)-fed C57BL/6J mice ^[13]. Besides, thinned peach polyphenols could attenuate obesity in HFD-fed C57BL/6N mice through lowering genera *Anaeroplasm*a and *Helicobacter*, and raising genera *Akkermansia*, *Alistipes* and *Klebsiella*, *Bacteroides* ^[14].

This narrative review collects the literature from the Web of Science and PubMed databases in recent five years, and combines the results from both experimental and clinical studies. It summarizes the anti-obesity effects of dietary natural products by regulating gut microbiota, and explores their potential mechanisms of action. In addition, we also focus on strategies to improve the anti-obesity effect of dietary natural products. Furthermore, the current challenges and future research directions of dietary natural products in ameliorating obesity are discussed. This review aims to provide a basis for further research and application of dietary natural products in the prevention and treatment of obesity.

2. Effects and mechanisms of dietary natural products on obesity by modulating gut microbiota from experimental studies

In recent years, numerous studies have demonstrated that various dietary natural products, such as fruits, vegetables, grains, teas, herbs, seafoods, macrofungi, algae, spices, legumes, nuts, probiotics, prebiotics, synbiotics and postbiotics, could reduce obesity via regulating gut microbiota. The associated effects and underlying mechanisms were discussed below (Table 1 and Fig. 1).

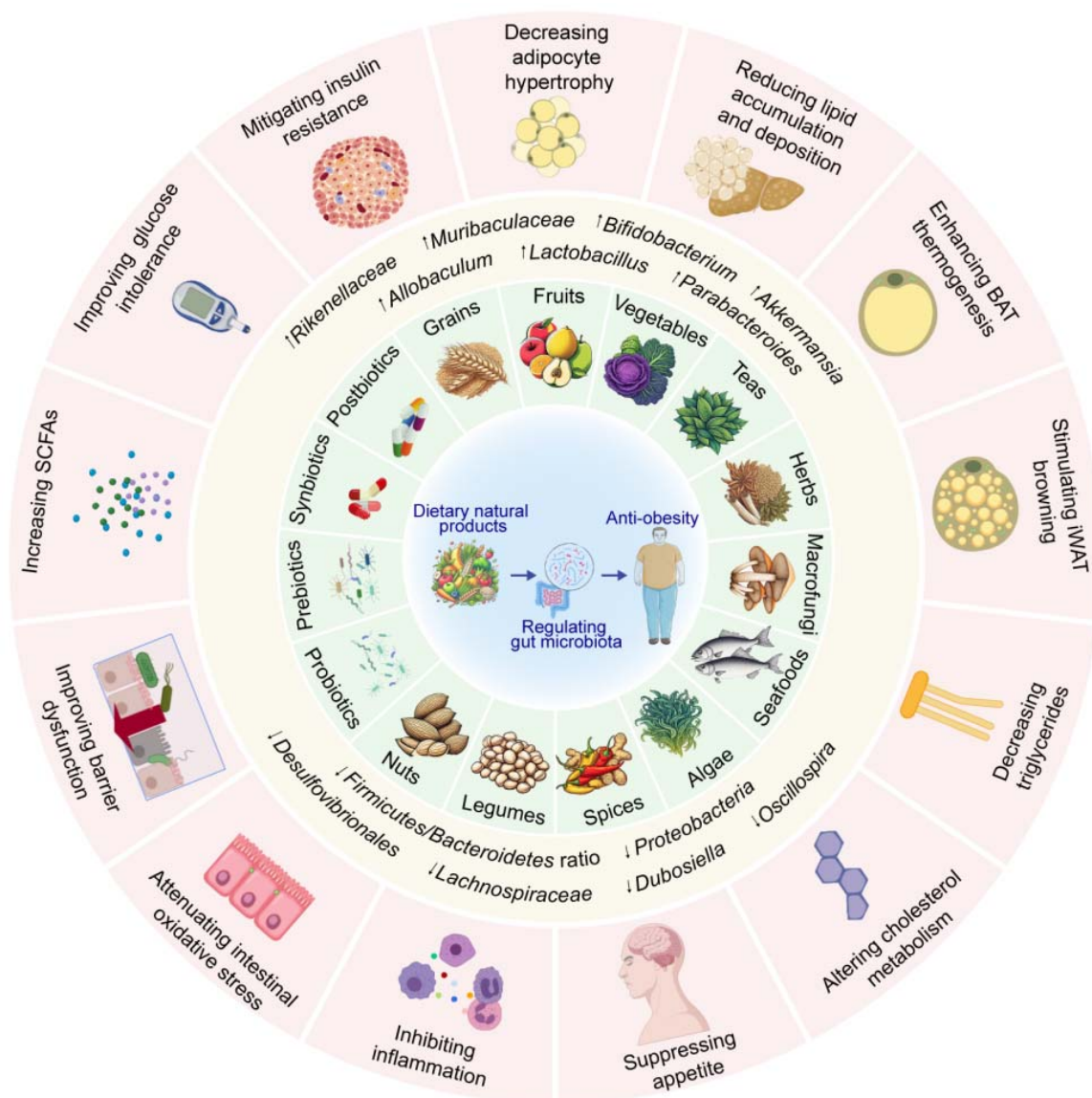


Fig. 1. The effects and mechanisms of dietary natural products on obesity by regulating gut microbiota. Abbreviations: BAT, brown adipose tissue; iWAT, inguinal white adipose tissue; SCFAs, short-chain fatty acids.

Name	Components	Models	Methods	Alterations of gut microbiota	Ref.
Fruits					
Apple	Phlorizin	HFD-fed C57BL/6J mice	Intragastrical administration: 80 mg/kg/day for 12 weeks	↑Phylum Bacteroidetes, class Bacteroidia, order Bacteroidales and family Muribaculaceae; ↓Phylum Firmicutes, class Clostridia, order Desulfovibrionales, family Desulfovibrion and genus Bilophila	[18]
Apple	Pectin	HFD-fed C57BL/6J mice	Diet supplementation: 1%, 3%, 5%, 8% and 12% in diet for 8 weeks	↑Family Coriobacteriaceae, genera Faecalibaculum and Ruminococcus	[101]
Euterpe oleracea Mart.	Anthocyanin-rich extract	HFD-fed C57BL/6J mice	Gavage: 150 mg/kg/day for 14 weeks	↑Species Akkermansia muciniphila	[102]
Pomegranate	Polyphenols from fruit pulp	HFD-fed C57BL/6J mice	Intragastrical administration: 200 mg/kg/day for 14 weeks	↑Species Akkermansia muciniphila, Lachnospiraceae bacterium 28-4, Parabacteroides distasonis, Mucispirillum schaedleri and Bacteroides acidifaciens; ↓Firmicutes/Bacteroidetes ratio, species Lactococcus lactis, Escherichia coli, Ruminococcus bicirculans and Blautia producta	[103]
Pomegranate	Anthocyanins from peel	HFD-fed C57BL/6J mice	Gavage: 150 mg/kg/day for 15 weeks	↑Phylum Bacteroidetes, genera Anaerotruncus, Akkermansia, Lachnoclostridium and Parabacteroides; ↓Phyla Firmicutes and Proteobacteria	[104]
Hippophae rhamnoides Linn.	Polysaccharide	HFD-fed C57BL/6J mice	Dietary supplementation: 0.1% for 12 weeks	↑Genera Bifidobacterium, Alistipes, Bacteroides, Muribaculaceae_unclassified and Rikenellaceae_RC9_gut_group; ↓Genera Bilophila, Lactobacillus, Dubosiella, Firmicutes_unclassified and Streptococcus	[19]
Citrus tangerina Tanaka cv. Dahongpao	Tangeretin	HFD-fed C57BL/6 mice	Gavage: 100 mg/kg/day for 12 weeks	↑Genera Bacteroides and Lactobacillus; ↓Firmicutes/Bacteroidetes ratio	[105]
Thinned peach	Polyphenols	HFD-fed C57BL/6N mice	Drinking: 0.1% (w/v) for 8 weeks	↑Genera Akkermansia, Alistipes, Bacteroides and Klebsiella; ↓Genera Anaeroplasma and Helicobacter	[14]
Guava	Polysaccharides	HFD-fed C57BL/6 mice	Gavage: 100 mg/kg/day every other day for 11 weeks	↑Genera Enterorhabdus, Clostridium XIVa and Parvibacter; ↓Firmicutes/Bacteroidetes ratio and genus Mucispirillum	[106]
Morinda citrifolia L.	Phenolic extract	HFD-fed C57BL/6 mice	Intragastric gavage: 100 and 200 mg/kg/day for 10 weeks	↑Genera norank_f_Muribaculaceae, Oscillibacter, Lachnospiraceae_NK4A136_group and Blautia; ↓Genera Lactobacillus, Clostridium_sensu_stricto_1, norank_f_Desulfovibrionaceae and Desulfovibrio	[20]
Artocarpus heterophyllus Lam.	Polysaccharides	HFD-fed SD rats	Gavage: 50, 100 and 200 mg/kg/day for 12 weeks	↑Family Ruminococcaceae, genera Prevotellaceae_Ga6A1_group, Sphaerochaeta and Alloprevotella	[107]

Citrus fruits	Naringin	HFD-fed C57BL/6J mice	Gavage: 100 mg/kg/day for 12 weeks	↑Genera Bifidobacterium and Lachnospiraceae_bacterium_28-4; ↓Genera Lachnospiraceae_bacterium_DW59 and Dubosiella_newyorkensis	[21]
Prunus salicina L.	Polyphenols	HFD-fed C57BL/6J mice	Gavage: 150 mg/kg/day for 14 weeks	↑Genera Parabacteroides, Akkermansia and Roseburia; ↓Genera Enterobacter and Oscillibacter	[108]
Vegetables					
Brassica oleracea var. acephala	/	HFD-fed C57BL/6J mice	Diet supplementation: 9% in diet for 12 weeks	↑Order Coriobacteriales/family Coriobacteriaceae and species Bacteroides thetaiotaomicron; ↓Firmicutes/Bacteroidetes ratio, classes Bacilli and Erysipelotrichi	[23]
Celery	Apigenin	HFD-fed C57BL/6J mice	Intragastric gavage: 50 mg/kg/day for 16 weeks	↑Genera Akkermansia and Incertae_Sedis; ↓Genera Faecalibaculum and Dubosiella	[24]
Red cabbage microgreens	/	HFD-fed C57BL/6NCr mice	Diet supplementation: 10.9 g/kg in diet for 8 weeks	↓Genus AF12	[26]
Red Cabbage	/	HFD-fed C57BL/6NCr mice	Diet supplementation: 10.9 g/kg in diet for 8 weeks	↓Genus AF12	[25]
Spinach	Betaine	HFD-fed Kunming female mice	Drinking: 1 % (w/v) for 23 weeks	↑Genera Bifidobacterium and Lactobacillus, species Akkermansia muciniphila	[109]
Grains					
Corn	Zeaxanthin	HFD-fed C57BL/6N mice	Intragastrical administration: 20 mg/kg/day for 22 weeks	↑Phylum Firmicutes and class Clostridia; ↓Phylum Proteobacteria and genus Desulfovibrio	[29]
Whole grain Qingke	/	HFD-fed C57BL/6J mice	Diet supplementation: 30% in diet for 16 weeks	↑Genera Akkermansia, Candidatus_Saccharimonas, Bifidobacterium and Lactobacillus; ↓Phylum Firmicutes	[30]
Chenopodium quinoa Willd.	Total saponins from bran	HFD-fed SD rats	Gavage: 100 mg/kg/day for 7 weeks	↑Phylum Lactobacillus, class Bacteroidetes and genus Bacilli; ↓Phylum Desulfovibrio and genus Proteobacteria	[31]
Chenopodium quinoa Willd.	Peptides	HFD-fed C57BL/6 mice	Intragastrical administration: 1000 mg/kg/day for 8 weeks	↑Phylum Bacteroidota, class Bacteroidia, order Bacteroidales and family Muribaculaceae; ↓Firmicutes/Bacteroidetes ratio	[110]
Refined Hordeum vulgare L. var. nudum Hook. f.	/	HFD-fed C57BL/6J mice	Diet supplementation: 30% in diet for 12 weeks	↑Genera Akkermansia, Alloprevotella, Bifidobacterium, Lachnospiraceae_UCG-001 and Lachnospiraceae_NK4A136_group; ↓Firmicutes/Bacteroidetes ratio	[32]
Teas					
Camellia sinensis L.	/	HFD-fed C57BL/6J mice	Diet supplementation: 1% and 3% in diet for 10 weeks	↑Families Ruminococcaceae, Lachnospiraceae, and genus Barnesiella	[111]
Pu-erh tea	Raw and ripened water extract	HFD-fed C57BL/6 mice	Gavage: 600 mg/kg/day for 15 weeks	↑Families Bacteroidaceae, Muribaculaceae, Lachnospiraceae, Ruminococcaceae and Rikenellaceae; ↓Families Lactobacillaceae and Erysipelotrichaceae	[35]

Fu brick tea	Polyphenols	HFD-fed SD rats	Intragastric gavage: 100 mg/kg/day for 12 weeks	↑Genera Bacteroides, Faecalibaculum and Alloprevotella, and species Akkermansia muciniphila; ↓Firmicutes/Bacteroidetes ratio, genera Blautia, Allobaculum, Desulfovibrio, Parasutterella, Lachnoclostridium and Roseburia	[112]
Fu brick tea	Aqueous extract	HFD-fed C57BL/6J mice	Oral administration: 4% and 8% for 8 weeks	↑Genera Akkermansia, Prevotella, Lactobacillus, Bifidobacterium, Parabacteroides and Roseburia	[113]
Fu brick tea	Polysaccharides	HFD-fed C57BL/6J mice	Oral administration: 100, 200 and 400 mg/kg for 8 weeks	↑Genera Lactobacillus, Bifidobacterium, Roseburia, Parabacteroides and Akkermansia	[36]
Fu brick tea	Polysaccharides	HFD-fed SD rats	Intragastric gavage: 400 and 800 mg/kg for 12 weeks	↑Genera Bacteroides, Alistipes, and species Akkermansia muciniphila; ↓Genera Parasutterella, Blautia, Desulfovibrio, Lachnoclostridium and Roseburia	[114]
Black tea	Water extract	HFD-fed C57BL/6J mice	Intragastrical administration: 760 mg/kg/day for 18 weeks	↑Species Lactobacillus gasseri, Eubacterium coprostanoligenes and Bacteroidales S24-7; ↓Genera Desulfovibrio, Eisenbergiella, Akkermansia and Blautia, species Roseburia spp., Ruminococcaceae UCG-009, Clostridium sp. ND2, Lactobacillus casei, Lachnospiraceae UCG-006, Escherichia coli,	[115]
Huangshan Maofeng green tea	Water extracts	Leptin receptor knockout (Lepr ^{-/-}) SD rats	Gavage: 700 mg/kg/day for 24 weeks	↑Families Ruminococcaceae, Veillonellaceae and genus Faecalibaculum	[116]
Heimao tea	Polysaccharides	HFD-fed C57BL/6J mice	Oral administration: 400 mg/kg/day for 12 weeks	↑Genera Dubosiella and Romboutsia; ↓Genus Allobaculum	[117]
Ya'an Tibetan tea	/	HFD-fed SD rats	Gavage: 500 and 2000 mg/kg/day for 7 weeks	↑Genera Akkermansia and unclassified_Lachnospiraceae; ↓Genera Romboutsia, Corynebacterium and Aerococcus	[118]
Junshanyinzen tea	Extract	HFD-fed SD rats	Gavage: 75, 150 and 300 mg/kg/day for 8 weeks	↑Families Bifidobacteriaceae, Bacteroidaceae, and genera Clostridium, Akkermansia; ↓Firmicutes/Bacteroidetes ratio, families Desulfovibriaceae and Erysipelotrichaceae	[37]
Green tea	EGCG	HFD-fed C57BL/6 mice	Gavage: 50 mg/kg/day for 12 weeks	↑Genera Dubosiella and Akkermansia	[39]
Dark tea	Theabrownin	HFD-fed C57BL/6J mice	Intragastrical administration: 2300 mg/kg/day for 14 and 28 weeks	↑Genera Akkermansia, Parabacteroides and Bacteroides	[38]
Herbs					
Mulberry leaf	Polyphenols and fiber	High-calorie diet-fed SD rats	Gavage: 0.6 g/kg/day for 6 weeks	↑Genus Lactobacilli and species Lactobacillus_johnsonii; ↓Firmicutes/Bacteroidetes ratio and family Lachnospiraceae	[119]
Mulberry leaf	Extract	HFD-fed C57BL/6 mice	Gavage: 167 and 333 mg/kg/day for 16 weeks	↑Genera Faecalibaculum, Dubosiella, Bifidobacterium and Coriobacteriaceae_UCG-002; ↓Firmicutes/Bacteroidetes ratio	[120]
Lycium barbarum	Homogeneous polysaccharide	HFD-fed C57BL/6 mice	Gavage: 50 mg/kg/day for 12 weeks	↑Genus Lactobacillus; ↓Firmicutes/Bacteroidetes ratio and phylum Proteobacteria	[121]

Lycium barbarum	Polysaccharides	HFD-fed ICR mice	Drinking: 0.2% (w/v) for 10 weeks	↑Genera Bacteroides, Lactococcus, Lachnospiraceae_NK4A136_group and Butyrivibrio; ↓Firmicutes/Bacteroidetes ratio and genus Lactobacillus	[122]
Lycium ruthenicum Murray	Petunidin-3-O-[rhamnopyranosyl-(trans-p-coumaroyl)]-5-O-(β-D-glucopyranoside)	HFD-fed C57BL/6J mice	Oral administration: 100 mg/kg/day for 12 weeks	↑Families Deferribacteraceae, Helicobacteraceae and Bifidobacteriaceae; ↓Phylum Firmicutes, families Erysipelotrichaceae, Ruminococcaceae, Streptococcaceae and Lactobacillaceae	[123]
Rosa davurica Pall.	Flavonoids	HFD-fed C57BL/6J mice	Gavage: 200 mg/kg/day for 7 weeks	↑Family Ruminococcaceae and genus Blautia; ↓Families Erysipelotrichaceae, Lachnospiraceae, genera Roseburia, Desulfovibrio, Bacteroides, Lactobacillus, Parvibacter, Parabacteroides, Marvinbryantia and Lactococcus	[124]
Astragalus membranaceus	Formononetin	Western-style diet-fed C57BL/6 mice	Oral administration: 20, 60 and 100 mg/kg for 28 days	↑Families Lachnospiraceae, Clostridiaceae, and species Clostridium aldenense, Eubacterium plexicaum, Clostridiaceae unclassified; ↓Family Porphyromonadaceae	[125]
Dendrobium officinale	Dietary fiber	HFD-fed C57BL/6 mice	Intragastric gavage: 1 g/kg/day for 11 weeks	↑Genera Akkermansia, Muribaculum and Bifidobacterium; ↓Genus Bilophila	[126]
Siraitia grosvenorii	Mogrosin-rich extract from fruits	HFD-fed C57BL/6 mice	Oral administration: 300 and 600 mg/kg for 18 weeks	↓Firmicutes/Bacteroidetes ratio, genera Ruminiclostridium and Oscillibacter	[127]
Eriobotrya japonica Lindl leaves	Total Sesquiterpenoids	HFD-fed C57BL/6J mice	Oral administration: 25 and 100 mg/kg for 8 weeks	↑Genera Lactobacillus, Alloprevotella, Alistipes and Bacteroides; ↓Genera Ileibacterium, Dubosiella and Enterorhabdus	[128]
Curcuma longa L., Zingiberaceae	Calebin A	HFD-fed C57BL/6 mice	Diet supplementation: 0.1% and 0.5% in diet for 12 weeks	↑Genera Butyrivibrio, Ruminiclostridium_9, unidentified_Ruminococcaceae and Akkermansia	[129]
Hawk tea	Extract	HFD-fed C57BL/6J mice	Gavage: 1.5 g/kg/day for 12 weeks	↑Species Faecalibaculum_rodentium, Bacteroides_vulgatus and Akkermansia_muciniphila; ↓Firmicutes/Bacteroidetes ratio, families Lachnospiraceae and Desulfovibrionaceae	[46]
Platycodon grandiflorus	Polysaccharides	HFD-fed C57BL/6 mice	Gavage: 500 mg/kg/day for 8 weeks	↑Family Muribaculaceae, genera Faecalibaculum, Akkermansia; ↓Families Lachnospiraceae, Oscillospiraceae and genus Dubosiella ↑Genus Turicibacter, species Ruminococcaceae_UCG-014, Bifidobacterium_pseudolongum and Lactobacillus_taiwanensis; ↓Genera Parasutterella, Olsenella, Enterorhabdus, species Paramuribaculum_intestinale, Prevotellaceae_UCG-001, and Ruminiclostridium_9	[42]
Rubus chingii Hu unripe fruits	Polysaccharides	HFD-fed C57BL/6 mice	Gavage: 200 and 400 mg/kg/day for 12 weeks		[43]

Polygonatum kingianum Coll. et Hemsl	Enzymatic saccharifying extract	HFD-fed C57BL/6J mice	Gavage: 60, 90 and 130 mg/kg/day for 4 weeks	↑Genera Akkermansia, Bifidobacterium and Lactobacillus; ↓Genera Desulfovibrio, Dubosiella and Acinetobacter	[44]
Momordica cochinchinensis aril	Polysaccharides	HFD-fed C57BL/6J mice	Gavage: 50 mg/kg/day for 12 weeks	↑Genera Akkermansia and Bacteroides	[130]
Raphanus sativus L. seed	Glucosinolates	HFD-fed C57BL/6J mice	Gavage: 100, 200 and 400 mg/kg/day for 8 weeks	↑Genera Allobaculum, Romboutsia, Turicibacter, and Akkermansia; ↓Genus Faecalibaculum	[131]
Radix bupleuri	Saikosaponin D	HFD-fed C57BL/6J mice	Oral administration: 20 mg/kg for 12 weeks	↑Genera Lactobacillus, Bilophila, Oscillibacter, Tyzzerella, Lactiplantibacillus, Romboutsia, weissella and Companilactobacillus; ↓Genera Roseburia, Ralstonia, Sphingomonas and Bifidobacterium and Achromobacter	[132]
Psoralea corylifolia L. Seafoods	Bavachin	HFD-fed C57BL/6 mice	Gavage: 20 mg/kg/day for 12 weeks	↑Genera Akkermansia, Lactobacillus, Romboutsia, Bilophila, unidentified_Clostridia and Tyzzerella	[45]
Portunus trituberculatus	Egg oil	HFD-fed C57BL/6J mice	Intragastrical administration: 600 mg/kg/day for 16 weeks	↑Phylum Verrucomicrobia and class Bacteroidia; ↓Phyla Proteobacteria and Actinobacteria, and class Epsilonproteobacteria	[50]
Coregonus peled	Fish oil	HFD-fed C57BL/6J mice	Gavage: 100 mg/kg/day for 4 and 8 weeks	↑Order Coriobacteriales, genera Bifidobacterium and Adlercreutzia; ↓Phylum Firmicutes, order Clostridiales, genera Clostridium and Prevotella	[51]
Tuna	Oil with high DHA (60 mg of EPA and 340 mg of DHA per gram of oil)	HFD-fed ICR mice	Gavage: 260 mg/kg/day for 6 weeks	↑Genera Bifidobacterium, Muribaculum and Parabacteroides; ↓Genera Terrisporobacter, Anaerobacterium, Millionella, Desulfovibrio, Paraeggerthella, Ruminiclostridium and Lachnoclostridium	[49]
Crassostrea gigas	Polysaccharide	HFD-fed C57BL/6 mice	Gavage: 200 and 600 mg/kg/day for 10 weeks	↑Genera Bifidobacterium, Faecalibaculum, Dubosiella and Lactobacillus; ↓Genera Erysipelatoclostridium, Mucispirillum and Helicobacter	[48]
Algae Chlorella pyrenoidosa and Spirulina platensis	Polysaccharides	HFD-fed C57BL/6 mice	Intragastrical administration: 400 mg/kg/day for 10 weeks	↑Classes Clostridia, Mollicutes and Bacteroidia; ↓Phyla Actinobacteria and Verrucomicrobia	[53]
Laminaria japonica	Low-molecular alginate	HFD-fed BALB/c mice	Drinking: 0.3% (w/v) for 11 weeks	↑Order Bacteroidales; ↓Order Clostridiales	[54]
Haematococcus pluvialis	Astaxanthin	HFD-fed C57BL/6 mice	Intragastrical administration: 5, 50 and 100 mg/kg for 3 weeks	↑Phylum Bacteroidetes, order Coriobacteriales, families Rikenellaceae and S24-7, genus Olsenella; ↓Phylum Firmicutes	[55]
Macrofungi Ganoderma lucidum	Polysaccharide from	HFD-fed C57BL/6 mice	Gavage: 100 and 300 mg/kg/day for 12 weeks	↑Genera Allobaculum, Christensenellaceae_R-7_group and Bifidobacterium;	[57]

	sporoderm- broken spores			↓Species Firmicutes_bacterium_ASF500, Alistipes_sp._627 and Clostridium_leptum	
Agrocybe cylindracea	/	HFD-fed C57BL/6 mice	Diet supplementation: 3% and 5% in diet for 9 weeks	↑Genera Bifidobacterium, Prevotellaceae UCG 001, and Parabacteroides; ↓Genera Eubacterium_fissicatena_group, Roseburia, Blautia and Oscillibacter	[133]
Agrocybe cylindracea	Polysaccharides	HFD-fed C57BL/6J mice	Oral administration: 300 mg/kg for 9 weeks	↑Genera Bacteroides, Dubosiella, Butyricimonas, and Parabacteroides; ↓Genera Oscillibacter and Desulfovibrio	[13]
Cordyceps militaris	Polysaccharides	HFD-fed C57BL/6J mice	Gavage: 200 and 400 mg/kg/day for 12 weeks	↑Genera Alloprevotella, Alistipes, Parabacteroides and Butyricimonas; ↓Negativebacillus	[134]
Morchella esculenta	Polysaccharide	HFD-fed BALB/c mice	Gavage: 200 and 400 mg/kg/day for 12 weeks	↑Genera Lactobacillus; ↓Genera Enterococcus	[135]
Cordyceps guangdongensis	Ethanollic extract	HFD-fed C57BL/6J mice	Gavage: 100 mg/kg/day for 10 weeks	↑Species Akkermansia muciniphila and Bifidobacterium animalis	[58]
Auricularia auricula-judae (Bull.)	Polysaccharides	HFD-fed C57BL/6J mice	Gavage: 50 and 100 mg/kg/day for 8 weeks	↑Genera Lactobacillus, Allobaculum, Bacteroides, Lactococcus and Parabacteroides; ↓Firmicutes/Bacteroidetes ratio, genera Bilophila, Desulfovibrio and Streptococcus	[59]
Pleurotus eryngii	/	HFD-fed C57BL/6 mice	Diet supplementation: 1% and 3% in diet for 8 weeks	↑Genera Bifidobacterium, Sutterella, Akkermansia, and Lactobacillus; ↓Genera Dorea, Ruminococcus, Coprococcus, rc4-4, and Oscillospira	[60]
Hericium erinaceus	Insoluble dietary fiber	HFD-fed C57BL/6J mice	Gavage: 100, 200 and 400 mg/kg/day for 9 weeks	↑Genus Akkermansia ↓Phylum Firmicutes and genus Desulfovibrio	[136]
Torreya grandis cv. Merrilli seed	Oil	HFD-fed ICR mice	Nuts Gavage: 250, 550 and 850 mg/kg/day for 8 weeks	↑Genera Lactobacillus, Allobaculum, Faecalibaculum and Bifidobacterium	[68]
Fermented soybean products	3'- hydroxydaidzei n	HFD-fed C57BL/6 mice	Legumes Diet supplementation: 0.05% and 0.1% in diet for 13 weeks	↓Genera Lachnospira and GCA_900066225	[66]
Soybean	Insoluble dietary fiber	HFD-fed C57BL/6J mice	Oral administration: 250, 500 and 100 mg/kg/day for 20 weeks	↑Order Lactobacillales, genera Lactobacillus and Lachnospirace_Nk4A136_group; ↓Family Lachnospiraceae and species Bacteroides_acidifaciens	[67]
Chili	Capsaicin	HFD-fed C57BL/6J mice	Spices Intragastrical administration: 2 mg/kg on alternate days for 12 weeks	↑Genera Akkermansia, Bacteroides, Prevotella, Odoribacter, Allobaculum and Coprococcus; ↓Genera Escherichia, Desulfovibrio, Sutterella and Helicobacter	[63]
Ginger	/	HFD-fed C57BL/6J mice	Oral administration: 500 mg/kg/day for 16 weeks	↑Genera Alloprevotella, Faecalibaculum, Bifidobacterium, Allobaculum and Parasutterella	[64]
			Probiotics		

Ligilactobacillus salivarius LCK11	/	HFD-fed C57BL/6J mice	Gavage: 200 μ L/day (5×10^8 CFU/mL) for 8 weeks	↑Phylum Bacteroidetes, orders Verrucomicrobiales Bacteroidales and Coriobacteriales; ↓Firmicutes/Bacteroidetes ratio, orders Clostridiales, Desulfovibrionales and Deferribacterales	[70]
Lactobacillus plantarum FRT4	/	HFD-fed Kunming mice	Gavage: 200 μ L/day (1×10^9 and 1×10^{10} CFU/mL) for 8 weeks	↑Genera Bacteroides, Butyricimonas, Intestinimonas, Anaerotruncus, Alistipes, Butyricoccus and Parabacteroides	[71]
Eurotium cristatum	/	HFD-fed C57BL/6J mice	Gavage: 0.4 mL/day (1×10^4 , 1×10^6 and 1×10^8 CFU/mL) for 12 weeks	↑Genus Akkermansia; ↓Firmicutes/Bacteroidetes ratio	[72]
Lactacisobacillus paracasei AO356	/	HFD-fed C57BL/6J mice	Gavage: 100 μ L/day (5×10^7 CFU/g) for 8 weeks	↑Genera Lactobacillus, Oscillospira, Ruminococcus and Allobaculum; ↓Genus Bacteroides	[73]
Prebiotics					
Type 3 resistant starch from Canna edulis	/	HFD-fed C57BL/6J mice	Gavage: 0.75, 1.5 and 3 g/kg/day for 13 weeks	↑Genera Bifidobacterium and Roseburia	[137]
Type 4 resistant starch from tapioca	/	HFD-fed C57BL/6JNarl mice	Intragastrical administration: 3 and 6 g/kg/day for 8 weeks	↑Genera Bacteroides, Lactobacillus, Bifidobacterium and Parabacteroides; ↓Genera [Eubacterium]_xylanophilum_group, Dubosiella, Clostridia_UCG-014 and Allobaculum	[76]
Insoluble yeast β -glucan	/	HFD-fed SD rats	Gavage: 50 mg/kg/day for 24 weeks	↑Genera Bacteroides, Erysipelotrichaceae, Romboutsia, Turicibacter, Parasutterella, Holdemanella, Helicobacter, Peptostreptococcaceae, Anaerovorax, Eggerthellaceae, Sutterella, Peptococcaceae, Faecalibacterium, Parvibacter and Anaerofilum; ↓Genera Erysipelatoclostridium and Candidatus_Soleaferrea	[77]
2'-fucosyllactose	/	HFD-fed C57BL/6J mice	Intragastrical administration: 400 mg/kg/day for 8 weeks	↑Bacteroides/Firmicutes ratio and genus Bifidobacterium; ↓Family Lachnospiraceae	[78]
Stachyose	/	HFD-fed C57BL/6J mice	Gavage: 200 mg/kg/day for 8 weeks	↑Genera Limosilactobacillus, Phocaecicola and Faecalibaculum Phocaecicola vulgatus, species Faecalibaculum rodentium, Limosilactobacillus reuteri, Parabacteroides distasonis; ↓Genera Erysipelatoclostridium, Enterocloster and Mucispirillum	[79]
Synbiotics					
Cudrania tricuspidata and Lactacisobacillus rhamnosus	/	HFD-fed C57BL/N6 mice	Gavage: 200 μ L/day (Lactacisobacillus rhamnosus: 1×10^9 CFU/g, Cudrania tricuspidata: 1500 mg/mL) for 8 weeks	↑Genera Desulfovibrio, Adlercreutzia, Allobaculum, Coprococcus, Lactococcus, Lactobacillus and Dorea	[82]
Postbiotics					
Rice Kefiran	/	HFD-fed C57BL/6J mice	Gavage: 10, 50 and 100 mg/kg, 5 times per week for 17 weeks	↑Genera Bacteroides and Alistipes; ↓Family Lachnospiraceae and family Lachnoclostridium	[83]

2.1. Fruits

Fruits are rich in vitamins, minerals, dietary fiber and other active ingredients, all of which contribute to health benefits [15–17]. They are an integral part of dietary guidelines and have been shown to exert anti-obesity effects. For instance, a study demonstrated that supplementation with apple phlorizin for 12 weeks could reduce body weight gain and alleviate insulin resistance by increasing phylum *Bacteroidetes*, class *Bacteroidia*, order *Bacteroidales* and family *Muribaculaceae*, and decreasing phylum *Firmicutes*, class *Clostridia*, order *Desulfovibrionales*, family *Desulfovibrion* and genus *Bilophila* in HFD-fed C57BL/6J mice [18]. In addition, polysaccharide from *Hippophae rhamnoides* Linn. could reduce body weight gain, decrease the levels of serum lipid and liver triglycerides, increase the protein expression of phosphorylated AMP-activated protein kinase alpha subunit (p-AMPK α), phosphorylated acetyl-CoA carboxylase 1 (p-ACC1) and peroxisome proliferator activated receptor alpha (PPAR α), inhibit the proteins expression of peroxisome proliferator activated receptor gamma (PPAR γ), fatty acid synthetase (FAS) and CD36 molecule in the liver, and enhance the levels of acetate, propionate, butyrate and isovalerate in HFD-fed obese C57BL/6J mice. These beneficial effects were likely mediated by shifts in the gut microbiota, including an increase in genera *Bifidobacterium*, *Alistipes*, *Bacteroides*, *Muribaculaceae_unclassified* and *Rikenellaceae_RC9_gut_group*, along with a decrease in genera *Bilophila*, *Lactobacillus*, *Dubosiella*, *Firmicutes_unclassified* and *Streptococcus* [19]. Furthermore, phenolics from *Morinda citrifolia* L. fruit could decrease body weight, attenuate intestinal oxidative stress, reduce lipid accumulation in liver and adipose tissues, inhibit inflammation and gut-barrier dysfunction, and raise the levels of acetic, i-butyric, n-butyric, propionic, n-valeric and i-valeric acids in HFD-fed C57BL/6 mice through reducing genera *Lactobacillus*, *Clostridium_sensu_stricto_1*, *norank_f_Desulfovibrionaceae* and *Desulfovibrio*, and enriching genera *norank_f_Muribaculaceae*, *Oscillibacter*, *Lachnospiraceae_NK4A136_group* and *Blautia* [20]. Moreover, naringin from citrus fruits could ameliorate obesity in HFD-fed C57BL/6J mice via decreasing liver weight, inhibiting body weight gain, altering body compositions, stimulating browning of inguinal white adipose tissue (iWAT), and enhancing the thermogenic activity of brown adipose tissue (BAT) through increasing genera *Lachnospiraceae_bacterium_28-4* and *Bifidobacterium*, and decreasing genera *Dubosiella_newyorkensis* and *Lachnospiraceae_bacterium_DW59* [21].

In short, some fruits and their components, such as apple phlorizin, citrus fruits, *Morinda citrifolia* L. fruit and *Hippophae rhamnoides* Linn., exert anti-obesity effects, which could mitigate insulin resistance, decrease the levels of serum lipid and liver triglycerides, stimulate iWAT browning, increase SCFAs levels, enhance BAT thermogenesis, and alleviate the intestinal inflammation and gut-barrier dysfunction by regulating gut microbiota.

2.2. Vegetables

Vegetables are a vital part of the diet, providing essential vitamins, dietary fiber, and minerals, all of which are widely acknowledged for their health benefits [22]. It was reported that vegetables could alleviate obesity. For example, *Brassica oleracea* var. *acephala* could alleviate inflammation in HFD-fed obese C57BL/6J mice by enriching order *Coriobacteriales*/family *Coriobacteriaceae* and species *Bacteroides thetaiotaomicron*, and decreasing phylum *Firmicutes*/phylum *Bacteroidetes* ratio, classes *Bacilli* and *Erysipelotrichi* [23]. Another study showed that apigenin could ameliorate obesity in HFD-fed C57BL/6J mice via attenuating insulin resistance and suppressing low-grade inflammation by increasing genera *Akkermansia* and *Incertae_Sedis*, and decreasing genera *Faecalibaculum* and *Dubosiella* [24]. Additionally, red cabbage could reduce body weight gain, and alter cholesterol metabolism in HFD-fed C57BL/6NCr mice, which might be positively correlated to the abundance of genus *AF12* [25]. Besides, red cabbage microgreen altered the gut microbiota in HFD-fed C57BL/6NCr obese mice. The abundance of genus *AF12* was reduced, which showed a positive correlation with fecal bile acid and body weight gain [26].

In brief, several vegetables and their components, such as *Brassica oleracea* var. *acephala*, red cabbage and apigenin, could attenuate obesity, which could alter cholesterol metabolism, alleviate insulin resistance, and suppress inflammation by regulating the gut microbiota.

2.3. Grains

Grains are the main source of dietary nutrients at the basis of daily diet, and are rich in various bioactive phytochemicals, such as phenolic compounds, dietary fiber, phytosterols and phytic acid, which are beneficial to human health [27, 28]. Several studies have revealed that grains exhibited anti-obesity effects. For instance, zeaxanthin could attenuate obesity in HFD-fed C57BL/6N mice through reducing fat weight and liver weight, decreasing adipocyte hypertrophy and lipid deposition, and improving insulin resistance and glucose intolerance by stimulating iWAT thermogenesis, enriching phylum *Firmicutes* and class *Clostridia*, and decreasing phylum *Proteobacteria* and genus *Desulfovibrio* [29]. Additionally, whole grain Qingke could reduce body weight gain, serum lipid levels and glucose tolerance in HFD-fed C57BL/6J mice by increasing genera *Akkermansia*, *Candidatus_Saccharimonas*, *Bifidobacterium* and *Lactobacillus*, and decreasing phylum *Firmicutes* [30]. Another study revealed that total saponins from *Chenopodium quinoa* Willd. bran could ameliorate body weight gain, decrease visceral fat accumulation, and improve glucose intolerance and insulin resistance in HFD-fed Sprague Dawley (SD) obese rats by increasing phylum *Bacteroidetes*, class *Bacilli* and genus *Lactobacillus*, and reducing phylum *Proteobacteria* and genus *Desulfovibrio* [31]. Furthermore, refined *Hordeum vulgare* L. var. *nudum* Hook. f. could prevent obesity via improving insulin resistance, decreasing inflammation, increasing the intestinal mucosal barrier, and enhancing the levels of butyric acid, isobutyric acid, valeric acid and propionic acid through enriching genera *Akkermansia*, *Alloprevotella*, *Bifidobacterium*, *Lachnospiraceae_UCG-001* and *Lachnospiraceae_NK4A136_group*, and reducing phylum *Firmicutes*/phylum *Bacteroidetes* ratio in HFD-fed C57BL/6J mice [32].

In summary, several grains and their components, such as whole grain Qingke, refined *Hordeum vulgare* L. var. *nudum* Hook. f. and total saponins from *Chenopodium quinoa* Willd. bran, could alleviate obesity,

which could inhibit inflammation and visceral fat accumulation, improve insulin resistance and glucose intolerance, and enhance SCFAs production via regulating gut microbiota.

2.4. Teas

Tea is the most widely consumed beverage in the world, second only to water^[33]. It is rich in polyphenols, polysaccharides, amino acids and alkaloids, which have been shown to alleviate obesity^[9, 34]. For example, Pu-erh tea extract could decrease body weight gain, inhibit fat accumulation, and improve glucose tolerance in HFD-fed C57BL/6 mice through increasing families *Bacteroidaceae*, *Muribaculaceae*, *Lachnospiraceae*, *Ruminococcaceae* and *Rikenellaceae*, and decreasing families *Erysipelotrichaceae* and *Lactobacillaceae*^[35]. Additionally, polysaccharides from Fu brick tea could ameliorate obesity in HFD-fed C57BL/6J mice via promoting adipocyte browning and thermogenesis, and enhancing the levels of acetate, propionate and butyrate through enriching genera *Lactobacillus*, *Bifidobacterium*, *Roseburia*, *Parabacteroides* and *Akkermansia*^[36]. Moreover, Junshanyinzhen tea extract could decrease body weight gain and fat accumulation, and reduce blood lipid levels by reducing families *Erysipelotrichaceae* and *Desulfovibrionaceae*, and increasing families *Bacteroidaceae*, *Bifidobacteriaceae*, genera *Clostridium* and *Akkermansia*^[37]. Furthermore, theabrownin from dark tea could attenuate obesity in HFD-fed C57BL/6J mice through enriching genera *Akkermansia*, *Parabacteroides* and *Bacteroides*^[38]. In addition, epigallocatechin-3-gallate (EGCG) could decrease body weight gain and inhibit fat accumulation in HFD-fed C57BL/6 mice by enriching genera *Dubosiella* and *Akkermansia*^[39].

In summary, some teas and their components, such as Pu-erh tea, Junshanyinzhen tea, Fu brick tea, theabrownin from dark tea and EGCG, could prevent obesity, which could promote adipocyte browning and thermogenesis, and reduce fat accumulation by modulating gut microbiota.

2.5. Herbs

Herbs are gaining more and more attention and are often used to treat some diseases, such as cancer and Alzheimer's disease^[40-41]. Some studies have revealed that herbs could reduce obesity. For instance, polysaccharides from *Platycodon grandifloras* could reduce body weight, and suppress fat accumulation in HFD-fed obese C57BL/6 mice by enriching family *Muribaculaceae*, genera *Faecalibaculum*, *Akkermansia*, and decreasing families *Lachnospiraceae*, *Oscillospiraceae* and genus *Dubosiella*^[42]. Additionally, polysaccharide from unripe fruits of *Rubus chingii* Hu could reduce fat accumulation and body weight gain, inhibit hyperlipidemia and inflammation, and enhance the levels of acetate, propionate and butyrate in HFD-fed C57BL/6 mice through increasing genus *Turicibacter*, species *Ruminococcaceae_UCG-014*, *Bifidobacterium_pseudolongum* and *Lactobacillus_taiwanensis*, and reducing genera *Parasutterella*, *Olsenella*, *Enterorhabdus*, species *Paramuribaculum_intestinale*, *Prevotellaceae_UCG-001*, and *Ruminiclostridium_9*^[43]. Another study showed that enzymatic saccharifying extracts from *Polygonatum kingianum* Coll. et Hemsl could attenuate obesity in HFD-fed C57BL/6J mice via inhibiting hepatic fat deposition and lipid degeneration, and enhancing the levels of isobutyric acid, acetic acid and butyric acid

through increasing genera *Akkermansia*, *Bifidobacterium* and *Lactobacillus*, and decreasing genera *Desulfovibrio*, *Dubosiella* and *Acinetobacter* ^[44]. Furthermore, bavachin from *Psoralea corylifolia* L. could alleviate obesity in HFD-fed C57BL/6 mice by alleviating lipid accumulation in BAT, activating BAT thermogenesis and WAT browning, reducing blood glucose/lipid levels, and growing the levels of acetate, propionate and butyrate through increasing genera *Akkermansia*, *Lactobacillus*, *Romboutsia*, *Bilophila*, *unidentified_Clostridia* and *Tyzzzeria* ^[45]. Besides, Hawk tea extract could prevent obesity in HFD-fed C57BL/6J mice via activating the AMP-activated protein kinase (AMPK)/acetyl-CoA carboxylase (ACC)/sterol regulatory element-binding protein 1c (SREBP1c) signaling pathways, enriching species *Faecalibaculum_rodentium*, *Bacteroides_vulgatus* and *Akkermansia_muciniphila*, and reducing phylum *Firmicutes*/phylum *Bacteroidetes* ratio, families *Lachnospiraceae* and *Desulfovibrionaceae* ^[46].

In general, some herbs and their components, such as polysaccharide from unripe fruits of *Rubus chingii* Hu, bavachin from *Psoralea corylifolia* L., polysaccharides from *Platycodon grandifloras* and enzymatic saccharifying extracts from *Polygonatum kingianum* Coll. et Hemsl, could reduce obesity, which could reduce fat accumulation, promote BAT thermogenesis and WAT browning, alleviate lipid accumulation, increase SCFAs levels and inhibit inflammation through regulating gut microbiota.

2.6. Seafoods

Seafoods are an important source of nutrients, such as calcium, eicosapentaenoic acid (EPA), zinc and docosahexaenoic acid (DHA), all of which contribute to human health ^[47]. Several studies have revealed that seafoods could ameliorate obesity. For instance, polysaccharide from *Crassostrea gigas* could prevent HFD-induced obesity in C57BL/6 mice by increasing genera *Lactobacillus*, *Bifidobacterium*, *Faecalibaculum* and *Dubosiella*, and reducing genera *Mucispirillum*, *Helicobacter* and *Erysipelatoclostridium* ^[48]. In addition, Tuna oil could alleviate obesity and lipid metabolism in HFD-fed ICR mice by enriching genera *Bifidobacterium*, *Muribaculum* and *Parabacteroides*, and decreasing genera *Terrisporobacter*, *Anaerobacterium*, *Millionella*, *Desulfovibrio*, *Paraeggerthella*, *Ruminiclostridium* and *Lachnoclostridium* ^[49]. Furthermore, egg oil from *Portunus trituberculatus* could prevent obesity in HFD-fed C57BL/6J mice via decreasing adipose weight, inhibiting epididymal adipose cell size, reducing circulatory cytokines and lipid accumulation, and enhancing the levels of acetate, propionate and butyrate through increasing phylum *Verrucomicrobia* and class *Bacteroidia*, and decreasing phyla *Proteobacteria* and *Actinobacteria*, and class *Epsilonproteobacteria* ^[50]. Moreover, fish oil from *Coregonus peled* could decrease body weight gain and glucose tolerance by reducing phylum *Firmicutes*, order *Clostridiales*, genera *Clostridium* and *Prevotella*, and enriching order *Coriobacteriales*, genera *Bifidobacterium* and *Adlercreutzia* in HFD-fed C57BL/6J mice ^[51].

In summary, several seafoods and their components, such as Tuna oil, fish oil from *Coregonus peled*, polysaccharide from *Crassostrea gigas* and egg oil from *Portunus trituberculatus*, exerted anti-obesity effects, which could ameliorate lipid metabolism, reduce glucose tolerance and lipid accumulation, and increase SCFAs levels by modulating gut microbiota.

2.7. Algae

Algae are abundant in essential nutrients, such as fatty acids, dietary fiber, minerals and vitamins, and have garnered growing attention in the fields of food applications and nutraceuticals [52]. Several studies have shown that algae could attenuate obesity. For example, polysaccharides from *Chlorella pyrenoidosa* and *Spirulina platensis* could alleviate obesity in HFD-fed C57BL/6 mice through ameliorating glucose tolerance impairment, reducing dyslipidemia and fat deposition, suppressing systemic inflammation, and increasing the levels of acetate, butyrate and propionate by enriching classes *Clostridia*, *Mollicutes* and *Bacteroidia*, and reducing phyla *Actinobacteria* and *Verrucomicrobia* [53]. Furthermore, low-molecular alginate from *Laminaria japonica* could decrease weight gain, inhibit lipid abnormality and inflammation, reduce fat accumulation in the liver and epididymal adipose tissue, and enhance the levels of acetate, butyrate and propionate in HFD-fed BALB/c mice through increasing order *Bacteroidales*, and decreasing order *Clostridiales* [54]. Besides, astaxanthin from *Haematococcus pluvialis* could reduce body weight, decrease lipid droplet accumulation in the liver, and modulate lipid metabolism by enriching phylum *Bacteroidetes*, order *Coriobacteriales*, families *Rikenellaceae* and *S24-7*, genera *Olsenella*, and reducing phylum *Firmicutes* in HFD-fed C57BL/6 mice [55].

In a word, some algae and their components, such as astaxanthin from *Haematococcus pluvialis*, low-molecular alginate from *Laminaria japonica*, polysaccharides from *Chlorella pyrenoidosa* and *Spirulina platensis*, could alleviate obesity, which could modulate lipid metabolism, ameliorate glucose tolerance impairment, reduce systemic inflammation, and increase SCFAs levels via regulating gut microbiota.

2.8. Macrofungi

Edible macrofungi have always been regarded as healthy foods with health benefits. They are rich in protein, polyunsaturated fatty acids, vitamins, dietary fiber and minerals [56]. Some studies have demonstrated that macrofungi could ameliorate obesity. For instance, polysaccharide from sporoderm-broken spore of *Ganoderma lucidum* could prevent obesity, fat accumulation and hyperlipidemia in HFD-fed C57BL/6 mice. These beneficial effects were possibly induced through enriching genera *Allobaculum*, *Christensenellaceae_R-7_group* and *Bifidobacterium*, and reducing species *Alistipes_sp._627*, *Clostridium_leptum* and *Firmicutes_bacterium_ASF500* [57]. Additionally, ethanolic extract from *Cordyceps guangdongensis* could improve glucose tolerance and hyperlipidemia, inhibit fat accumulation, decrease body weight gain, and increase butyric acid level in HFD-fed C57BL/6J mice through enhancing species *Bifidobacterium animalis* and *Akkermansia muciniphila* [58]. Moreover, polysaccharides from *Auricularia auricula-judae* (Bull.) could attenuate obesity, improve glucose and lipid metabolism, and enhance the levels of isobutyric acid, butyric acid, isovaleric acid, acetic acid and propionic acid in HFD-fed C57BL/6J mice by increasing genera *Lactobacillus*, *Allobaculum*, *Bacteroides*, *Lactococcus* and *Parabacteroides*, and decreasing phylum *Firmicutes*/phylum *Bacteroidetes* ratio, genera *Bilophila*, *Desulfovibrio* and *Streptococcus* [59]. Besides, *Pleurotus eryngii* could reduce obesity in HFD-fed C57BL/6J mice through enriching genera

Bifidobacterium, *Sutterella*, *Akkermansia* and *Lactobacillus*, and reducing genera *Dorea*, *Ruminococcus*, *Coprococcus*, *rc4-4* and *Oscillospira*, which could inhibit the abnormal gain of body weight and adipose tissue weight, and improve glucose tolerance [60].

Overall, some edible macrofungi and their components, such as polysaccharides from *Auricularia auricula-judae* (Bull.), *Pleurotus eryngii*, polysaccharide from sporoderm-broken spore of *Ganoderma lucidum* and ethanolic extract from *Cordyceps guangdongensis*, could prevent obesity, reduce fat accumulation, improve glucose and lipid metabolism, and increase SCFAs through regulating gut microbiota.

2.9. Spices

Spices are not only used for cooking but also have medicinal value, and possess some biological activities, such as antioxidant, anti-inflammatory and antibacterial properties [61, 62]. Several studies have indicated that spices could ameliorate obesity. For example, one study showed that capsaicin from chili could attenuate obesity in HFD-fed C57BL/6J mice through enriching genera *Bacteroides*, *Akkermansia*, *Allobaculum*, *Prevotella*, *Coprococcus* and *Odoribacter*, and reducing genera *Escherichia*, *Helicobacter*, *Desulfovibrio* and *Sutterella* [63]. In another study, ginger could reduce body weight, decrease liver steatosis, ameliorate insulin resistance, and enhance the levels of butyric acid, acetic acid and valeric acid in HFD-fed C57BL/6J mice. These beneficial effects were possibly induced via modulating the gut microbiota composition, and increasing genera *Alloprevotella*, *Faecalibaculum*, *Bifidobacterium*, *Allobaculum* and *Parasutterella* [64].

In general, several spices and their components, such as capsaicin from chili and ginger, could alleviate obesity, which could reduce liver steatosis, improve insulin resistance, and increase SCFAs levels via regulating gut microbiota.

2.10. Legumes and nuts

Legumes and nuts are an important part of the diet, providing various health benefits, including a reduced risk of cardiovascular disease [65]. Several studies have revealed that legumes and nuts could prevent obesity. For instance, 3'-hydroxydaidzein from fermented soybean products could decrease body weight, reduce inguinal fat, and stimulate browning of the white adipose tissue in HFD-fed C57BL/6 mice through modulating gut microbiota, and reduce genera *Lachnospira* and *GCA_900066225* [66]. Another study suggested that insoluble dietary fiber from soybean could ameliorate obesity in HFD-fed C57BL/6J mice through enhancing order *Lactobacillales*, genera *Lactobacillus* and *Lachnospirace_Nk4A136_group*, and reducing family *Lachnospiraceae* and species *Bacteroides_acidifaciens* [67]. Besides, Chinese *Torreya grandis* cv. *Merrillii* seed oil could decrease the fat and liver indices, change the fatty acid composition, and decrease triglycerides, total cholesterol and low-density lipoprotein cholesterol in HFD-fed ICR mice through rising genera *Lactobacillus*, *Allobaculum*, *Faecalibaculum* and *Bifidobacterium* [68].

In a word, several legumes, nuts and their components, such as insoluble dietary fiber from soybean, 3'-hydroxydaidzein from fermented soybean products and Chinese *Torreya grandis* cv. *Merrillii* seed oil, have anti-obesity effects through regulating gut microbiota.

2.11. Probiotics

Probiotics have become one of the most important ingredients in the era of functional foods, with a variety of health benefits, including preventing and managing cancer, hypertension and gastrointestinal diseases [69]. Several studies have reported that probiotics could reduce obesity. For example, *Ligilactobacillus Salivarius* LCK11 could attenuate obesity in HFD-fed C57BL/6J mice through suppressing appetite via promoting peptide YY secretion, increasing phylum *Bacteroidetes*, orders *Verrucomicrobiales*, *Bacteroidales* and *Coriobacteriales*, and reducing phylum *Firmicutes*/phylum *Bacteroidetes* ratio, orders *Clostridiales*, *Desulfovibrionales* and *Deferribacterales* [70]. Moreover, *Lactobacillus plantarum* FRT4 could decrease weight gain, fat weight and liver weight, reduce the levels of serum cholesterol and triglyceride, decline liver alanine aminotransferase levels, and regulate liver metabolome by increasing genera *Bacteroides*, *Butyricimonas*, *Intestinimonas*, *Anaerotruncus*, *Alistipes*, *Butyricoccus* and *Parabacteroides* in HFD-fed Kunming mice [71]. In addition, *Eurotium cristatum* could ameliorate obesity in HFD-fed C57BL/6J mice through modulating energy and lipid metabolism, increasing the levels of acetic acid, propionic acid, isobutyric acid and butyric acid, enriching genus *Akkermansia*, and lessening phylum *Firmicutes*/phylum *Bacteroidetes* ratio [72]. Furthermore, *Lacticaseibacillus paracasei* AO356 could attenuate obesity in HFD-fed C57BL/6J mice through rising genera *Lactobacillus*, *Oscillospira*, *Ruminococcus* and *Allobaculum*, and reducing genus *Bacteroides* [73].

In brief, some probiotics, such as *Lacticaseibacillus paracasei* AO356, *Ligilactobacillus Salivarius* LCK11, *Eurotium cristatum* and *Lactobacillus plantarum* FRT4, could prevent obesity through modulating gut microbiota.

2.12. Prebiotics

Prebiotics can help maintain a beneficial microbiome, promoting the growth of good bacteria while inhibiting the proliferation of potentially dangerous species [74]. Prebiotics have health benefits, such as anti-diabetic, anti-bacterial, cholesterol-lowering and anti-cancer [75]. Some studies have found that prebiotics could alleviate obesity. For instance, type 4 resistant starch from tapioca could reduce body weight and adipose tissue accumulation, decrease fatty liver, and improve glucose tolerance in HFD-fed mice through rising genera *Bacteroides*, *Lactobacillus*, *Bifidobacterium* and *Parabacteroides*, and lowering genera *[Eubacterium]_xylanophilum_group*, *Dubosiella*, *Clostridia_UCG-014* and *Allobaculum* [76]. In another study, insoluble yeast β -glucan could reduce weight gain, inhibit systemic inflammation, decrease dyslipidemia, improve glucose intolerance and insulin resistance, reduce gut permeability in HFD-fed SD rats by growing genera *Bacteroides*, *Erysipelotrichaceae*, *Romboutsia*, *Turicibacter*, *Parasutterella*, *Holdemanella*, *Helicobacter*, *Peptostreptococcaceae*, *Anaerovorax*, *Eggerthellaceae*, *Sutterella*, *Peptococcaceae*, *Faecalibacterium*, *Parvibacter* and *Anaerofilum*, and declining genera *Erysipelatoclostridium* and *Candidatus_Soleaferrea* [77]. Additionally, 2'-fucosyllactose could decrease body weight gain, increase energy expenditure, promote browning of iWAT, enhance adaptive thermogenesis, and improve serum lipid profiles

by lowering family *Lachnospiraceae*, and rising *Bacteroides/Firmicutes* ratio and genus *Bifidobacterium* [78]. Moreover, stachyose could prevent obesity in HFD-fed C57BL/6J mice through improving the integrity of the intestinal epithelial barrier, increasing genera *Limosilactobacillus*, *Phocaeicola* and *Faecalibaculum* *Phocaeicola vulgatus*, species *Faecalibaculum rodentium*, *Limosilactobacillus reuteri*, *Parabacteroides distasonis*, and decreasing genera *Erysipelatoclostridium*, *Enterocloster* and *Mucispirillum* [79].

In general, some prebiotics, such as type 4 resistant starch from tapioca, stachyose, 2'-fucosyllactose and insoluble yeast β -glucan, exerted anti-obesity effects by regulating gut microbiota.

2.13. Synbiotics and Postbiotics

Synbiotics and prebiotics are current research hotspots. Synbiotics can regulate immunity and improve gastrointestinal health, while postbiotics have good anti-bacterial and anti-inflammatory properties [80, 81]. Several studies have reported that synbiotics and postbiotics could ameliorate obesity. For example, *Cudrania tricuspidata* and *Lacticaseibacillus rhamnosus* as synbiotics could decrease the percent of fat mass, reduce the levels of serum triglyceride and alanine aminotransferase activity in HFD-fed mice through enriching genera *Desulfovibrio*, *Adlercreutzia*, *Allobaculum*, *Coprococcus*, *Lactococcus*, *Lactobacillus* and *Dorea* [82]. Besides, rice kefir as postbiotics could decrease body weight gain, decrease liver fat accumulation, improve insulin resistance, and enhance acetate in HFD-fed C57BL/6J mice via increasing genera *Bacteroides* and *Alistipes*, and reducing family *Lachnospiraceae* and genus *Lachnoclostridium* [83].

In short, several synbiotics and postbiotics, such as *Cudrania tricuspidata* and *Lacticaseibacillus rhamnosus*, and rice kefir, could attenuate obesity by regulating gut microbiota and SCFAs.

2.14. Comparison and mechanisms of different dietary natural products

Different dietary natural products, such as some fruits, vegetables, grains, teas, herbs, seafoods, edible macrofungi, algae, spices, legumes, nuts, probiotics, prebiotics, synbiotics and postbiotics, could reduce obesity. Several kinds of dietary natural products, such as, green tea, dark tea, mulberry leaf, *Ganoderma lucidum*, *Spirulina platensis*, chili, resistant starch and β -glucan, should be paid to special attention in future research and development of functional foods because they have good anti-obesity effects and safety. Furthermore, this paper focused on the anti-obesity effects of dietary natural products by targeting gut microbiota (Fig. 2). Some dietary natural products could reduce phylum *Firmicutes*/phylum *Bacteroidetes* ratios. Furthermore, dietary natural products could enrich specific beneficial bacteria, most notably genera *Akkermansia*, *Bifidobacterium* and *Lactobacillus*. In addition, dietary natural products also could persistently suppress the abundance of opportunistic pathogens and inflammation-associated bacteria, such as phylum *Proteobacteria* and genus *Desulfovibrio*. Moreover, some dietary natural products could serve as fermentation substrates, promoting the production of SCFAs, such as acetic acid, propionic acid and butyric acid. Some gut microbiota and SCFAs could enhance the expression of tight junction proteins, thereby reducing intestinal permeability. This strengthening of the intestinal barrier prevents inflammatory factors from entering the bloodstream, thus suppressing systemic inflammation and improving insulin sensitivity. Besides, SCFAs

could regulate energy expenditure and appetite. Additionally, dietary natural products alleviated obesity by modulating key signaling pathways involved in lipid synthesis, particularly in the liver and adipose tissue, such as regulating the AMPK/PPAR signaling pathway. Dietary natural products could stimulate browning of WAT and enhance the thermogenic activity of BAT through regulating gut microbiota and SCFAs.

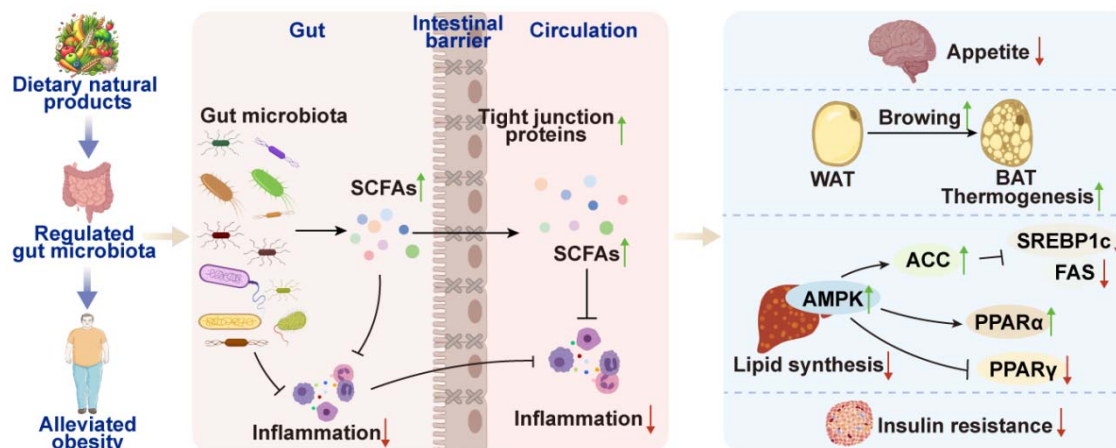


Fig. 2. Dietary natural products could reduce obesity by regulating gut microbiota. Some dietary natural products could enrich specific beneficial bacteria, inhibit the abundance of opportunistic pathogens and inflammation-associated bacteria, and promote the production of SCFAs. Then, some gut microbiota and SCFAs could enhance the expression of tight junction proteins, prevent inflammatory factors from entering the bloodstream, regulate appetite, promote browning of WAT, enhance the thermic activity of BAT, improve insulin sensitivity, and regulate the AMPK/PPAR signaling pathway and reduce lipid synthesis. Abbreviations: ACC, acetyl-CoA carboxylase; AMPK, AMP-activated protein kinase; BAT, brown adipose tissue; FAS, fatty acid synthetase; PPAR, peroxisome proliferator activated receptor; SCFAs, short-chain fatty acids; SREBP1c, sterol regulatory element-binding protein 1c; WAT, white adipose tissues.

3. Effects of dietary natural products on obesity through modulating gut microbiota from clinical trials

Some clinical trials have revealed that several dietary natural products could reduce obesity (Table 2). For instance, based on a double-blind, parallel-group and placebo-controlled trial among 38 obese-prone volunteers found that a prebiotic 1-Kestose supplementation (5 g twice per day for 12 weeks) could decrease the level of fasting serum insulin through enriching genus *Bifidobacterium*. The limitation of this study was its small sample size [84]. Moreover, based on a randomized, double-blind, placebo-controlled trial revealed that supplementation of prebiotic inulin for 6 months in 165 children (aged 7-15) with obesity could modulate proteasome and riboflavin metabolism by enriching genera *Bifidobacterium*, *Megasphaera*, *Blautia*, *Subdoligranulum*, *Eubacterium coprostanoligenes* and *Agathobacter*, which are related to obesity-related inflammation. The limitation of this study was that it only detected fecal SCFAs, and the results of fecal SCFA detection might not be able to distinguish differences between different groups and might not be able to explain the entire process of metabolic changes [85]. Furthermore, a randomized placebo-controlled intervention clinical trial revealed that synbiotics (contained *Bifidobacterium longum*, *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, *Bifidobacterium lactis*, and a galactooligosaccharide mixture) supplement daily for 3 months could increase genera *Bifidobacterium* and *Lactobacillus* in 20 new weight-loss participants with overweight/obesity, and a decrease in blood glucose over time was associated with an increase in the abundance of *Lactobacillus*, while, a decrease in weight, waist circumference, body mass index and body fat

over time was related to a reduction in the abundance of *Bifidobacterium*. The limitation of this study was its small size [86].

Table 2. The effects of dietary natural products on obesity from clinical studies

Name	Study type	Subject	Methods	Alterations of gut microbiota	Ref.
Prebiotics					
1-Kestose	Randomized, double-blind, parallel-group and placebo-controlled trial	38 obese-prone volunteers	5 g twice per day for 12 weeks	↑Genus <i>Bifidobacterium</i>	[84]
Inulin	Randomized, double-blinded, placebo-controlled trial	165 children with obesity aged 7-15 years	About 30 minutes before dinner every day for 6 months	↑Genera <i>Bifidobacterium</i> , <i>Megasphaera</i> , <i>Blautia</i> , <i>Subdoligranulum</i> , <i>Eubacterium</i> , <i>Coprostanoligenes</i> and <i>Agathobacter</i>	[85]
Synbiotics					
Synbiotic (probiotic: <i>Bifidobacterium lactis</i> , <i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> and <i>Bifidobacterium longum</i> ; prebiotic: a galactooligosaccharide mixture)	Randomized placebo-controlled intervention clinical trial	20 new weight-loss participants with overweight/obesity	Synbiotic supplement daily for 3 months	↑Genera <i>Bifidobacterium</i> and <i>Lactobacillus</i>	[86]

In general, several dietary natural products, such as inulin and 1-Kestose, could reduce body weight, waist circumference, body mass index and body fat, as well as gut microbiota dysbiosis in people with obesity. In the future, larger-scale, high-quality clinical trials should be carried out to investigate the effects of more dietary natural products on obesity.

4. Strategies to enhance the effects of dietary natural products on obesity

Some strategies have been explored to improve anti-obesity effects of dietary natural products. For instance, combining different dietary natural products could enhance anti-obesity effects. For example, the combination of low-dose EGCG and caffeine could show a synergistic effect against obesity in HFD-fed C57BL/6J mice via declining phylum *Firmicutes*, and increasing genus *Bifidobacterium*, acetic acid and propionic acid [87]. In another study, the combination of *Lactiplantibacillus plantarum* BLP53 and *Lactiacaseibacillus paracasei* BEPC22 exhibited a synergistic anti-obesity effect in HFD-fed C57BL/6J mice, which could reduce body weight gain and adipocyte size, decrease adipose tissue volume, lower food efficiency ratio, and enrich genera *Akkermansia*, *Ruminococcus* and *Alistipes* [88].

Microbial fermentation of dietary natural products could also enhance their anti-obesity effect. For instance, tartary buckwheat fermented with *Aspergillus niger* has increased soluble dietary fiber content, and exhibited anti-obesity activity in HFD-fed C57BL/6J mice by regulating gut microbiota dysbiosis, increasing genera *Lactobacillus*, and decreasing order *Clostridiales* [89]. Besides, the bioaccessibility of polyphenols in quinoa was increased after fermentation by *Monascus anka*. Fermented quinoa polyphenols could alleviate

obesity and relieve gut microbiota disorder, lessen phylum *Firmicutes*/phylum *Bacteroidetes* ratio, and enhance genera *Lactobacillus* and *Colidextribacter* in HFD-fed C57BL/6J mice^[90].

Preparation of superabsorbent hydrogels presents a promising strategy for obesity treatment. A study reported that β -glucan-based superabsorbent hydrogel, prepared by sodium carboxymethylcellulose, malic acid and β -glucan, could prevent obesity in HFD-fed C57BL/6J mice, with better efficacy than β -glucan or sodium carboxymethylcellulose. It could decrease fat accumulation, reduce body weight, and improve blood glucose by enhancing genera *norank_f_Muribaculaceae*, *Akkermansia*, *Faecalibaculum*, acetate, butyrate, propionate and total SCFAs^[91].

Preparation of microspheres with chitosan could enhance anti-obesity effects. It has been demonstrated that compared with high-amylose maize starch, starch-entrapped microspheres could more effectively reduce adipose tissue and body weight in HFD-fed C57BL/6 mice, and have a synergistic effect in ameliorating obesity. Starch-entrapped microspheres intervention enhanced phylum *Firmicutes*, genera *Streptococcaceae*, *unclassified Clostridiales*, *Bacilli*, butyrate and propionate^[92].

In a word, some strategies, such as combination, fermentation, and the preparation of hydrogels and microspheres, can enhance the anti-obesity effects of dietary natural products.

5. Safety of dietary natural products possessing anti-obesity effects

The safety assessment of dietary natural products is essential to ensure their safe use in preventing and managing obesity. Safety concerns can be broadly categorized into two distinct aspects: exogenous contamination and intrinsic dosage-dependent toxicity.

First, potential safety risks may arise from exogenous contaminants introduced during cultivation or processing. These pollutants include heavy metals (e.g., cadmium, lead, mercury and arsenic), pesticide residues (e.g., organophosphate pesticides, pyrethroids and carbamates), microbial pathogens (e.g., *Salmonella* spp. and *Bacillus cereus*), parasites (e.g., protozoa, roundworms and flatworms), biotoxins (e.g., marine toxins, bacterial food toxins and mycotoxins)^[93-95].

Second, distinct from external contamination, specific risks relate to the high concentration of the natural products. Toxicity in this context often depends on the exposure dose and duration. For example, high concentrations of green tea extract could cause liver damage. When green tea extract is consumed in the form of a beverage, the safe intake of EGCG is 704 mg/day^[96]. Moreover, 1,2-unsaturated pyrrolizidine alkaloids (PAs), mainly present in herbal teas and teas, are associated with hepatotoxicity and genotoxicity^[97]. Furthermore, saponins, naturally occurring in legumes, grains, and certain herbs, may also cause gastrointestinal irritation and mucosal damage at high concentrations^[98]. Besides, excessive amounts of *Akkermansia muciniphila* may deplete mucus and lead to damage to the gut-barrier integrity^[99]. Additionally, pasteurized *Akkermansia muciniphila* has been reported to facilitate *Salmonella* infection^[100].

In summary, although dietary natural products offer potential benefits in obesity management, their safety issue must not be overlooked. A comprehensive evaluation of contaminants' effects and dosage-related side effects is necessary to ensure safe and effective application.

6. Current challenges and future perspectives

At present, there are still some challenges in alleviating obesity with dietary natural products. First, most studies are conducted using animal models, and the experimental results should be confirmed through human studies. In the future, more clinical studies should be conducted, with a particular focus on the long-term safety of dietary natural products. Secondly, the dose-effect relationship between dietary natural products and anti-obesity remains unclear, and they should be studied in the future. Third, there are also challenges with delivery systems, such as insufficient efficiency, indicating the need for the development of more advanced delivery systems to improve stability, enhance bioavailability, and target specific tissues (e.g., adipose tissue) or gut regions. Fourth, individual variability significantly influences the efficacy of dietary natural products on obesity. The heterogeneity in host genetics and gut microbiota composition often leads to inconsistent responses (i.e., responders vs. non-responders) to the same dietary natural product. This challenge necessitates a shift towards personalized nutrition driven by multi-omics and artificial intelligence. For instance, genomics can help identify genetic variants that affect nutrient metabolism, and metabolomics can trace metabolic flux to predict individual responsiveness. Integrating these high-dimensional datasets via AI algorithms will enable the formulation of precision nutrition strategies tailored to an individual's unique biological profile. Finally, there are bottlenecks in the large-scale production of dietary ingredients possessing anti-obesity effects. More advanced processes (such as synthetic biology) should be developed and integrated to innovate and apply these technologies in product development, and also maximize the use of by-products during the processing phase.

7. Conclusion

Obesity has become one of the global public health problems. Gut microbiota is closely related to obesity. Many studies have reported that some dietary natural products, such as fruits (e.g., guava and *Prunus salicina* L.), vegetables (e.g., red cabbage and *Brassica oleracea* var. *acephala*), grains (e.g., refined highland barley and *Chenopodium quinoa* Willd.), teas (e.g., Fu brick tea and Black tea), herbs (e.g., *Rosa davurica* Pall. and *Polygonatum kingianum* Coll. et Hemsl), seafoods (e.g., *Coregonus peled* and *Crassostrea gigas*), edible macrofungi (e.g., *Agrocybe cylindracea* and *Cordyceps guangdongensis*), algae (e.g., *Haematococcus pluvialis* and *Laminaria japonica*), spices (e.g., chili and ginger), legumes (e.g., soybean), nuts (e.g., *Torreya grandis* cv. *Merrilli* seed), probiotics (e.g., *Ligilactobacillus salivarius* LCK11 and *Lacticaseibacillus paracasei* AO356), prebiotics (e.g., resistant starch, inulin and insoluble yeast β -glucan), synbiotics (e.g., *Cudrania tricuspidata* and *Lacticaseibacillus rhamnosus*) and postbiotics (e.g., rice kefir), could attenuate obesity by modulating gut microbiota.

Some dietary natural products could inhibit obesity in multiple ways, such as reducing fat and lipid accumulation, improving insulin resistance and glucose intolerance, enhancing BAT thermogenesis, stimulating iWAT browning, alleviating inflammation, altering cholesterol and lipids metabolism, and increasing SCFAs levels by regulating gut microbiota. In the future, more focus should be placed on exploring

the mechanisms by which gut microbiota influence obesity. Additionally, attention should be paid to the active ingredients in by-products during food processing, ensuring their full utilization. Currently, methods such as fermentation, the preparation of hydrogels and microspheres have been used to enhance the anti-obesity effects of dietary natural products, and future research should explore additional techniques (such as nano-materials). Furthermore, personalized and precision nutrition should be prioritized to alleviate obesity. In addition, special consideration should also be given to the dose-effect relationship and long-term safety of dietary natural products possessing anti-obesity effects. Moreover, high-quality clinical trials are essential to validate their anti-obesity effects. This review may assist the public in selecting dietary natural products to against obesity, and could also help develop dietary natural products into functional foods for the prevention and treatment of obesity.

Conflict of interest

The authors declare that they have no conflicts of interest.

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