Taylor & Francis
Taylor & Francis Group

Check for updates

REVIEW

Effects and mechanisms of tea on obesity

Xiao-Yu Xu[a,b], Cai-Ning Zhao[c], Bang-Yan Li[a], Guo-Yi Tang[b], Ao Shang[a,b], Ren-You Gan[d,e] (iD), Yi-Bin Feng[b] and Hua-Bin Li[a] (iD)

[a]Guangdong Provincial Key Laboratory of Food, Nutrition and Health, Department of Nutrition, School of Public Health, Sun Yat-Sen University, Guangzhou, China; [b]Li Ka Shing Faculty of Medicine, School of Chinese Medicine, The University of Hong Kong, China Hong Kong; [c]Li Ka Shing Faculty of Medicine, Department of Clinical Oncology, The University of Hong Kong, China Hong Kong; [d]Research Center for Plants and Human Health, Institute of Urban Agriculture, Chinese Academy of Agricultural Sciences, Chengdu, China; [e]Key Laboratory of Coarse Cereal Processing (Ministry of Agriculture and Rural Affairs), Sichuan Engineering & Technology Research Center of Coarse Cereal Industrialization, Chengdu University, Chengdu, China

ABSTRACT

Obesity has become a global health concern. It increases the risk of several diseases, such as type 2 diabetes mellitus, nonalcoholic fatty liver disease, and certain cancers, which threatens human health and increases social economic burden. As one of the most consumed beverages, tea contains various phytochemicals with potent bioactive properties and health-promoting effects, such as antioxidant, immune-regulation, cardiovascular protection and anticancer. Tea and its components are also considered as potential candidates for anti-obesity. Epidemiological studies indicate that regular consumption of tea is beneficial for reducing body fat. In addition, the experimental studies demonstrate that the potential anti-obesity mechanisms of tea are mainly involved in increasing energy expenditure and lipid catabolism, decreasing nutrient digestion and absorption as well as lipid synthesis, and regulating adipocytes, neuroendocrine system and gut microbiota. Moreover, most of clinical studies illustrate that the intake of green tea could reduce body weight and alleviate the obesity. In this review, we focus on the effect of tea and its components on obesity from epidemiological, experimental, and clinical studies, and discuss their potential mechanisms.

Introduction

Obesity has a high prevalence and becomes a global health problem affecting all ages and genders (Williams et al. 2015; Wang et al. 2021). According to data from WHO, body mass index (BMI) $\geq 25\,kg/m^2$ is defined as overweight, and BMI $\geq 30\,kg/m^2$ is defined as obesity for adults (World Health Organization 2021). Younger generations tend to experience obesity from earlier stages (Lee et al. 2010). Obesity is associated with multiple factors and complex interactions, including dietary patterns, lifestyle, genetic and environmental factors (Chang et al. 2008; Lettieri-Barbato, Giovannetti, and Aquilano 2016; Salas-Salvadó et al. 2018). The rapid development of modern society may lead to easier access for consumers to abundant food sources but less time to take exercise, and an unbalanced diet high in calories often cause the fat accumulation, which easily makes individuals overweight and obese (Ladabaum et al. 2014; Liberini et al. 2020). Obesity could increase the risks of several diseases, such as type 2 diabetes mellitus, nonalcoholic fatty liver disease, cardiovascular diseases and certain cancers, threatening the quality and expectancy of human life (Blüher 2019). Hence, it is essential to explore proper ways to prevent and treat obesity.

Although dietary regulation and physical exercise are common strategies for combating obesity, it is difficult to maintain a healthy lifestyle in a long term. FDA has approved several medications for anti-obesity therapy, such as phentermine and orlistat, but these drugs have shown some side effects for health (Pilitsi et al. 2019). Phentermine is the oral noradrenergic agonist that suppresses the appetite, and its common adverse events are dry mouth and insomnia (Kim et al. 2006). Orlistat inhibits the activities of gastrointestinal and pancreatic lipases, and reduces the fatty acid absorption, but it may cause steatorrhea and gastrointestinal side effects (Torgerson et al. 2004). On the other hand, numerous investigations show that some natural products could be beneficial for weight loss with less or even no side effects (Li, Huang, and Xie 2008; Trigueros et al. 2013; Xu, Li, et al. 2020).

Tea (*Camellia sinensis*) is a popular beverage and is generally divided into six categories based on processing and fermentation methods, including green tea, white tea, yellow tea, oolong tea, black tea and dark tea (Shevchuk et al. 2020). Tea contains abundant chemical compounds like polyphenols, polysaccharides, amino acids and alkaloids (Lin et al. 2003; Jiang et al. 2019; Tang et al. 2019; Zhao et al. 2019). Tea has shown multiple bioactivities, such as antioxidant, anti-inflammatory and immunoregulatory activity, and it also exerts various health benefits like protecting the liver and cardiovascular system as well as combating cancers, diabetes and obesity (Xu, Li, et al. 2020; Mao et al. 2021). Given that tea consumption is rarely reported the adverse effects, tea could be a potential candidate with high safety

CONTACT Ren-You Gan ✉ ganrenyou@caas.cn; Hua-Bin Li ✉ lihuabin@mail.sysu.edu.cn

and acceptability for anti-obesity management and prevention (Tang et al. 2019). This review summarizes the effects of tea and its components on obesity from epidemiological, experimental and clinical studies, and it also discusses the underlying mechanisms of action.

Epidemiological studies

Some epidemiological studies have revealed that the consumption of tea benefited the loss of body weight or lowered the incident of obesity occurrence. A pooled analysis of 6 human trials demonstrated that the intake of green tea catechins could reduce the total fat area, visceral fat area and subcutaneous fat area (Hibi et al. 2018). In addition, a meta-analysis including 16 randomized controlled trials (RCTs) with a total of 1090 subjects showed that tea extract consumption (green tea, black tea or oolong tea extract) was effective to reduce BMI and blood glucose and increase high-density lipoprotein (HDL) in the obese with metabolic syndrome, and thus, tea extract consumption was considered beneficial for promoting the weight loss and improving lipid and glucose metabolism (Li et al. 2020). In another meta-analysis of 26 RCTs including 1344 obese subjects, green tea consumption significantly reduced body weight and BMI (Lin et al. 2020). Moreover, a meta-analysis showed that the combination of catechin and caffeine increased the energy expenditure over 24 h and fat oxidation dose-dependently, and the mean increases were 0.53 kJ/mg and 0.02 g/mg, respectively (Hursel et al. 2011). Hence, tea, especially green tea, in combination with a balanced and healthy diet as well as regular physical exercise is considered to be an effective way in the management of obese patients. However, there are still inconsistent results of epidemiological studies about tea consumption and obesity. For example, a meta-analysis revealed no association between green tea product consumption and obesity in nondiabetic overweight and obese females, possibly owing to the heterogeneity in study, such as ethnicity, BMI, and age (Lee, Yacyshyn, et al. 2019).

Although most of epidemiological results showed the inverse correlation between the consumption of tea and obesity (Table 1), it is hard to draw a definitive conclusion regarding the effects of tea consumption on obesity, since there are still multiple factors affecting the results, including the dosage, types of tea, ethnicity and duration. The individual factors are also considered like living habit which the maintenance of exercise might accelerate the fat oxidation in response to the altered metabolic signals.

Experimental studies

Many experimental studies illustrate that tea influences body weight and body composition, which are mainly involved with the change in energy expenditure, nutrient digestion and absorption, lipid catabolism, lipid synthesis, adipocytes, neuroendocrine system and gut microbiota, and they will be below discussed in details.

Increasing energy expenditure

The long-term energy imbalance which energy intake exceeds the total expenditure leads to the occurrence of obesity (Spiegelman and Flier 2001). In addition to food intake control, increasing energy expenditure is an important strategy for the weight loss. There are two types of adipose tissues in human body, white adipose tissue (WAT) and brown adipose tissue (BAT) (Marlatt and Ravussin 2017). WAT stores the energy retaining triglycerides (TGs) and releases hormones and cytokines implicated in metabolism, inflammation and insulin resistance (Rosen and Spiegelman 2006). On the other hand, BAT dissipates certain energy to maintain body temperature through thermogenesis and heat regulation, and the activation of BAT is associated with the increased resting metabolic rate and enhances the energy expenditure in the form of heat, which BAT has become a trending target to treat obesity (Fenzl and Kiefer 2014; Scheele and Nielsen 2017).

The feeding with green tea extract prevented the body weight gain by increasing BAT thermogenesis through β-adrenoceptor activation in rats fed with a high-fat diet (HFD) (Choo 2003). Besides, the supplementation of green tea extract decreased the adiposity in both WAT and BAT as well as the whitening in BAT. It also induced the browning of WAT, which a BAT-like cellular and molecular program were stimulated in WAT (Neyrinck et al. 2017). Additionally, the browning of adipose tissue in visceral WAT was induced by decaffeinated green tea and voluntary exercise. The treatment increased the expression of genes related to adipose tissue browning, including peroxisome proliferator-activated receptor-gamma coactivator-1 alpha (PGC-1α), bone morphogenetic protein 4 (BMP4) and phosphatase and tensin homolog (PTEN) (Sae-Tan, Rogers, and Lambert 2015). Furthermore, BAT and browning of WAT increased the energy expenditure mainly through the uncoupled respiration mediated by uncoupling protein-1 (UCP-1) and AMP-activated protein kinase (AMPK) which is a crucial regulator of the browning process in inguinal WAT and maintains the energy homeostasis (Fenzl and Kiefer 2014; Wu et al. 2018). For instance, the oolong, black and Pu-erh tea induced the browning of WAT and activated the AMPK signaling pathway via increasing UCP-1 expression (Yamashita et al. 2014).

Overall, tea could increase the energy expenditure to dissipate the excessive stored energy. This effect was achieved through activation of BAT, induction of browning and upregulation of UCP-1 expression as well as AMPK signaling pathway, which might offer a safe and efficacious approach for anti-obesity. However, a study revealed that the green tea compounds negatively affected the basal UCP-1 gene expression in both brown and white primary adipocytes which were different from the results of adipogenic cell lines, suggesting that the epigenetic status of adipogenic cell lines were different from the genuine adipocytes. The differences should be considered in the investigation about the effects of tea on obesity via the browning process in vitro (Otton et al. 2021).

Table 1. The effects of tea and its components on obesity from epidemiological studies.

Study Type	Tea or its components	Participants	Dosage	Duration	Outcomes	References
Pooled analysis of 6 human trials	Green tea catechin	N = 921 (505 males and 416 females)	540-588 mg GTC/ beverage	12 weeks	The total fat area (EM, −17.7 cm²; 95% CI, −20.9 ~ −14.4), visceral fat area (EM, −7.5 cm²; 95% CI, −9.3 ~ −5.7), and subcutaneous fat area (EM, −10.2 cm²; 95% CI, −12.5 ~ −7.8) were reduced. The metabolic syndrome was improved (OR, 1.67; 95% CI, 1.08 ~ 2.57).	(Hibi et al. 2018)
Meta-analysis of 16 RCTs	Green tea, black tea, or oolong tea	N = 1090	NA	NA	BMI (SMD, −0.27; 95% CI, −0.40 ~ −0.15) and blood glucose (SMD, −0.22; 95% CI, −0.34 ~ −0.10) were reduced. HDL was increased (SMD, 0.18; 95% CI, 0.01 ~ 0.35). Blood pressure and other anthropometric, cholesterol and biochemical outcomes had non-significant changes.	(Li et al. 2020)
Meta-analysis of 26 RCTs	Green tea	N = 1344	NA	NA	BMI (WMD, −0.65 kg/m², 95% CI: −1.04 ~ −0.25) and body weight (WMD, −1.78 kg, 95% CI: −2.80 ~ −0.75) were reduced. The dose of green tea <500 mg/ day and duration of 12 weeks showed a more important reduction in body weight.	(Lin et al. 2020)
Meta-analysis	Green tea	N = 332 (females)	NA	NA	There was no association between green tea product consumption and obesity in nondiabetic overweight and obese females.	(Lee, Yacyshyn, et al. 2019)
Meta-analysis	Combination of catechin and caffeine	N = 107	NA	NA	The energy expenditure over 24 h (EM, 428.0 kJ/d; 95% CI, 252.7 ~ 603.4) and fat oxidation (EM, 12.2 g; 95% CI, 1.7 ~ 22.8) were increased	(Hursel et al. 2011)

BMI, Body Mass Index; EM, estimated mean; GTC, green tea catechin; OR, odds ratio; SMD, standardized mean difference; WMD, weighted mean difference. NA, not avaibale.

Decreasing nutrient digestion and absorption

As a public health concern, obesity is mainly caused by the imbalance of energy intake and expenditure, which the excessive intake and absorption of nutrients are major contributors. It could lead to the dysfunction of adipose tissue and trigger the disruption of other metabolic pathways like inflammation (Garcia-Barrado et al. 2020). Tea is reported to interfere with the process of nutrient digestion and absorption in the gastrointestinal tract, thereby decreasing the energy intake, which presents pharmacological functions beneficial to obesity (Wolfram, Wang, and Thielecke 2006).

After being broken down in the lumen of the intestine, the dietary lipid is absorbed by enterocytes, and then secreted into the lymphatic system. Targeting the molecules like lipase and uptake protein involved in the digestion and absorptive process could be helpful to treat the diet-induced obesity and its associated complications (Hussain 2014; Ko et al. 2020). Tea has shown anti-obesity effect which is associated with the reduction in fat digestion and lipid uptake. The treatment of epigallocatechin gallate (EGCG) reduced body weight gain and increased fecal lipid in mice fed with a high fat/Western-style diet, suggesting that EGCG

decreased the absorption of lipid from diet (Chen et al. 2011). Also, EGCG could decrease the incorporation of lipids into fat tissues, liver, and skeletal muscle by reducing the energy intake with the excretion of fat and nitrogen (Friedrich et al. 2012). Pancreatic lipase is known as a crucial enzyme for fat breakdown in the intestine, and the inhibition of its activity could be a target of treating obesity (Sun, Wu, and Chau 2016). Catechins with a galloyl moiety like EGCG and epicatechin gallate (ECG) could inhibit the activity of pancreatic lipase, resulting in the slowdown of dietary fat absorption in rats (Ikeda et al. 2005). Cellular studies showed that black tea extract suppressed pancreatic lipase activity and reduced fat digestion, and the in vivo study indicated that black tea extract inhibited the body weight gain and reduced the parametrial adipose tissue mass, which was attributed to the decreased intestinal lipid absorption (Uchiyama et al. 2011; Oi et al. 2012). Another in vitro assay showed that oolong tea extract and catechins exerted an inhibitory effect on pancreatic lipase, which might contribute to decreasing body weight and preventing hyperlipidemia (He et al. 2009). Besides, green tea extract reduced the lipid accumulation in mice fed with HFD by

downregulating mRNA expression of hepatic lipid uptake genes, such as cluster of differentiation 36 (CD36) (Li, Kek, et al. 2016).

Tea could also reduce the digestion and absorption of carbohydrates, and the effects are partly mediated by glucose transporter 4 (GLUT-4) and digestive enzymes like amylase (Ashida et al. 2004; Roberto et al. 2016). The stimulation of GLUT-4 translocation from the intracellular pool to the plasma membrane in skeletal muscle could increase the glucose uptake in skeletal muscle rather than in adipose tissues, contributing to the anti-obesity effect (Hajiaghaalipour, Khalilpourfarshbafi, and Arya 2015; Dinda et al. 2020). Three-week treatment of green tea effectively reduced the translocation of GLUT-4 and the uptake of glucose in adipose tissue, while it increased the uptake of glucose accompanied with GLUT-4 translocation in skeletal muscle (Ashida et al. 2004). The long-term treatment of green tea or black tea reduced the diet-induced deposition of WAT, and the translocation of GLUT-4 was stimulated to the plasma membrane in muscle, which maintained the GLUT-4-dependent glucose transport in muscle (Nishiumi et al. 2010).

In addition to the dietary lipid and carbohydrates, the digestion and absorption of protein could be negatively influenced by tea treatment. An in vivo study demonstrated that a high dose of green tea aqueous extract could negatively affect the availability of protein and reduce the accumulation of visceral fat by decreasing the digestion of protein in rats fed with HFD (Bajerska et al. 2011).

In short, the present data suggest that tea could reduce the digestion and absorption of fat by inhibiting the activity of pancreatic lipase and the expression of related lipid uptake genes, such as CD36. In addition, tea has efficacy of reducing digestion and absorption of carbohydrates mainly by regulating GLUT-4 translocation, and it could also negatively affect the availability of protein. However, an in vitro study concluded differently that the food stabilizing antioxidants might increase the availability of dietary lipids and carbohydrates and lead to higher risk of obesity development, especially the catechins which a low dose could increase the absorption of lipids and a high dose could decrease the absorption (Mika et al. 2017). Hence, the dose of tea and its compounds is an important and non-negligible factor in the investigation about the effects on obesity, and the anti-obesity effects of tea might need more consideration.

Increasing lipid catabolism

Tea is demonstrated to increase the lipid catabolism, including lipolysis and fatty acid oxidation, and accelerate the reduction of TGs and fat storage. The lipolysis is often mediated by various enzymes, such as hormone-sensitive lipase (HSL) and adipocyte triglyceride lipase (ATGL) (Langin et al. 2005). EGCG treatment could prevent obesity by significantly upregulating the mRNA levels of HSL and ATGL in WAT (Lee, Kim, and Kim 2009). In addition, Huangjinya green tea extract elevated the mRNA levels of HSL and ATGL, promoting WAT lipolysis and lipid breakdown (Li et al. 2020).

In addition to lipolysis, fatty acid oxidation is another main way of lipid catabolism to alleviate the abnormal increase of lipid (Lee et al. 2015). Proliferator-activated receptor alpha (PPARα) and PPARδ play essential roles in the fatty acid oxidation and utilization of TGs (Varga, Czimmerer, and Nagy 2011; Tong et al. 2019). PPARα commonly presents in tissues with substantial mitochondrial and peroxisomal β-oxidation, and its activation triggers fatty acid oxidation and reduces the circulating or cellular lipids. PPARδ also acts on the activation of oxidative metabolism (Escher et al. 2001; Poulsen, Siersbaek, and Mandrup 2012). Besides, carnitine palmitoyltransferase-1 (CPT-1) as the rate-limiting enzyme mediates the transport of fatty acid to mitochondria for oxidation, and thus, the increased CPT-1 activity could stimulate the fatty acid oxidation (Rupasinghe et al. 2016).

Green tea catechins upregulated PPARδ in subcutaneous WAT and visceral WAT and increased the expression of down-stream target genes of PPARδ, such as CPT-1, acyl-CoA oxidase (ACOX), and UCP-1, which contributed to the fatty acid oxidation (Yan, Zhao, and Zhao 2013). Additionally, Pu-erh tea exhibited lipid-lowering effects by increasing the expression of PPARα, CPT-1α, and ACOX-1 to enhance the fatty acid β-oxidation in the liver of HFD-induced obese mice (Huang, Wang, et al. 2019). Besides, the instant dark tea with higher contents of theabrownins and caffeine increased the gene expression of CPT1-α, promoting the lipid metabolism and reducing the lipid storage in adipose tissue (Sun et al. 2019). Also, the supplementation of tea catechins increased the mRNA expression of ACOX-1 and medium-chain acyl-CoA dehydrogenase (MCAD) which stimulated the fatty acid β-oxidation in the liver (Murase et al. 2002). Moreover, the green tea extract increased hepatic fatty acid oxidation both in the group with regular exercise and the group without exercise, and the green tea extract combined with exercises could also increase fatty acid oxidation in skeletal muscle and reduced more body weight gain in HFD-fed mice (Shimotoyodome et al. 2005). Furthermore, the combination of decaffeinated green tea extract and voluntary running exercise enhanced the fatty acid oxidation in mice liver by increasing the expression of PPARα and CPT-1α, and it was also stimulated in skeletal muscle by increasing NADH dehydrogenase 5, mitochondrial cytochrome b, and mitochondrial cytochrome c oxidase III (Sae-Tan, Rogers, and Lambert 2014).

AMPK is a major regulator of energy homeostasis in cells, and its activation promotes the expression of CPT-1, which further stimulates fatty acid oxidation to dissipate the excessively stored energy (Lopez 2018). Green tea activated AMPK in adipose tissue and reduced the lipid content in plasma and liver, suggesting that green tea ameliorated the obesity by stimulating fatty acid oxidation (Rocha et al. 2016). Besides, the aged oolong tea promoted mitochondrial fatty acid oxidation and reduced fat accumulation, which CPT-1 was upregulated via the AMPK/acetyl-CoA carboxylase (ACC) signaling pathway (Yuan et al. 2018). On the

other hand, the dose of aged oolong tea extract in this experiment reached up to 1000 mg/kg for mice. This dose was considered too high to reach in daily tea drinking if it is converted to human dose, unless the consumption of condensed oolong tea extract supplement, which the adverse effects of consuming tea extract might be a concern.

Overall, tea and its components stimulated the lipolysis by upregulating the expression of HSL and ATGL, and enhanced the fatty acid oxidation by regulating the levels of PPARα, PPARδ, CPT-1 and AMPK, which increased the lipid catabolism and prevent the obesity.

Inhibiting lipid synthesis

Dysregulations in lipid synthesis correlate with the development of obesity. Tea could inhibit lipid synthesis in adipose tissue by reducing the activity of lipogenic enzymes, such as fatty acid synthase (FAS), stearoyl-CoA desaturase (SCD) and ACC and decreasing the expression of lipogenic transcription factors like sterol regulatory element-binding protein-1c (SREBP-1c). For instance, the green tea extract could reduce the expression of SREBP-1c and its downstream targets FAS and SCD1, reducing body weight of mice (Li, Kek, et al. 2016). In addition, the decaffeinated green tea extract and voluntary running exercise exhibited a synergistic effect on the inhibition of lipogenesis by increasing the expression of SCD1 in the liver of HFD mice (Sae-Tan, Rogers, and Lambert 2014). Meanwhile, Huangjinya green tea extract administration resulted in the decreased lipogenic genes expression (FAS, ACC1) and the reduced lipid accumulation in WAT of HFD-fed mice (Li et al. 2020). Besides, Huangjinya black tea decreased the expression of lipogenic genes and increased the level of phosphorylation-ACC1, which eventually inhibited the lipid synthesis in HFD-fed mice (Xu, Li, et al. 2020). Moreover, the aged oolong tea inhibited fatty acid synthesis by downregulating the expression of FAS in HFD mice (Yuan et al. 2018). Fuzhuan brick tea decreased the genes expression of SREBP-1c, FAS, and CCAAT-enhancer-binding protein alpha (C/EBP-α) (Li et al. 2013). In addition, the instant dark tea exerted strong inhibitory effect on genes expression of SREBP-1 and FAS (Sun et al. 2019). Furthermore, the combination with other ingredients could potentiate the anti-obesity effect of tea. For instance, diallyl disulfide (DADS), a major organosulfur component in garlic, attenuated the increased phosphodiesterase 5 in adipose tissues of HFD-fed mice, which further upregulated the cyclic guanosine monophosphate (cGMP), an important regulator for the physiological effects of EGCG. Hence, the combination of green tea extract and DADS effectively suppressed the lipid synthesis-related molecules like SREBP-1, FAS and SCD and increased the expression of thermogenesis-related genes (Bae et al. 2019).

To sum up, tea and its components could decrease the lipid synthesis effectively by suppressing lipogenic enzymes (FAS, SCD and ACC), lipogenic transcription factors (SREBP-1c) and other related molecules. The combined treatment with other natural products or their bioactive components might mediate and potentiate the anti-obesity effect of tea.

Influencing adipocytes

The abnormal changes in adipocytes like the ever-increasing size and number may trigger obesity, and the adipocytes differentiation also plays an important role in the development of obesity. Tea is reported to suppress the increased size, number, and differentiation of adipocytes, contributing to the anti-obesity effect. The large yellow tea showed potent lipid-lowering efficacy by attenuating the enlargement of adipocytes and decreasing the number of adipose cells during the progression of obesity in mice (Xu et al. 2018). Based on histopathologic results, the aged oolong tea treatment could reduce the size of adipocytes in the epididymal fat in HFD mice accompanied with the reduction in body weight and fat accumulation (Yuan et al. 2018). Moreover, the long-term administration of strictinin isolated from Pu-erh tea could effectively reduce the size enlargement of adipocytes, body weight gain and epididymal fat weight in mice (Chen, Xie, Wan, et al. 2018).

Adipocyte differentiation consists of four main steps and the differentiation of preadipocytes into mature adipocytes is known as the final step of adipogenesis (Gregoire, Smas, and Sul 1998). The process of adipogenesis is tightly regulated by several intrinsic molecules, especially PPARγ and C/EBP (Schadinger et al. 2005; Ali et al. 2013). Preadipocyte factor 1 (Pref-1) and C/EBP-β and -δ induce PPARγ, and in turn, PPARγ particularly induces the expression of C/EBP-α, promoting the differentiation toward the mature adipocytes (MacDougald and Lane 1995; Rufino et al. 2021).

The treatment of green tea catechins reduced the level of PPARγ and inhibited fat accumulation in visceral WAT, whereas it increased the level of PPARγ in subcutaneous WAT, which promoted the lipid storage functions of subcutaneous WAT and prevented lipids from storing in other tissues like the liver (Yan, Zhao, and Zhao 2013). Additionally, EGCG supplements in diets resulted in the decreased mRNA levels of adipogenesis-related genes like PPARγ and C/EBP-α (Lee, Kim, and Kim 2009). Moreover, the long-term administration of green tea and black tea suppressed the differentiation of adipocytes in perirenal fat of rats by inhibiting the related genes. The green tea treatment decreased the expression of genes like Pref-1, C/EBP-β and PPAR-γ, while black tea only inhibited the expression of C/EBP-β (Chen et al. 2009). Different from other experiments, the model of this experiment is zebrafish which is usually used to investigate the signaling pathway and mechanism of human diseases. In the model of adult zebrafish pretreated with the green tea extract for two weeks before the induction of obesity, the extract reduced the visceral adiposity and the level of plasma TG, and the preventive treatment of the extract showed anti-obesity effects potentially through upregulation of signal transducer and activator of transcription (STAT) and downregulation of C/EBP signaling pathways (Zang et al. 2021). In addition, Huangjinya green tea extract reduced the expressions of adipogenic genes (C/EBP-α and

PPARγ) as well as the adipocyte size, which decreased WAT mass and prevented obesity (Li et al. 2020). Furthermore, a high dose of Huangjinya black tea reduced the levels of C/EBP-α and PPARγ to inhibit the adipogenesis and further alleviates the obesity in mice (Xu, Li, et al. 2020).

In short, the treatment of tea and its components were proved to reduce the size and number of adipocytes, and inhibit the adipogenesis through the regulation of PPARγ and C/EBP expressions.

Modulating neuroendocrine system

Obesity is also influenced by multiple and complex factors under the control of the neuroendocrine system (Paspala et al. 2012). Certain hormones regulate the appetite and development of obesity, such as leptin, adiponectin, ghrelin, galanin, and neuropeptide Y (Valassi, Scacchi, and Cavagnini 2008). A series of studies have suggested that tea could attenuate obesity by regulating neuroendocrine system. Green tea polyphenol supplementation decreased the percentage of fat mass and the levels of serum insulin-like growth factor I (IGF-1), leptin and adiponectin, which benefited body composition in obese rats with long-term HFD (Shen et al. 2012). In addition, the complex of polysaccharide and polyphenol of green tea had synergistic anti-obesity effects with a reduced level of serum leptin in HFD rats (Xu et al. 2015). Besides, the intake of the green tea extract reduced body weight and altered body composition with the mediation of neprilysin, a potent metallopeptidase modulating the metabolism of osteogenic peptides, and the extract increased the expression and activity of peripheral neprilysin, and downregulated the osteogenic peptides, such as galanin and neuropeptide Y in Berlin fat mice (Muenzner et al. 2016). Berlin fat mice is a mouse model for polygenic obesity and it could develop obesity under a standard diet at 6-week age instead of the diet-induced obesity (Arends et al. 2016). Furthermore, EGCG was found to control the appetite and decrease voluntary food intake, feeding frequency and meal size in HFD fed mice by regulating the expression of key appetite-related neuropeptide genes (AGRP, POMC and CART) and key circadian genes (Clock and Bmal1) in the hypothalamus (Li, Kek, et al. 2016).

Overall, tea and its bioactive compounds were effective to modulate certain hormones affected by obesity conditions and control the appetite. However, the regulation of some hormones by tea are still uncertain. As a hormone delivering signal to the hypothalamus to adjust food intake and regulate appetite, leptin tends to increase to control the development of obesity, but the above mentioned study detected a decreased level of leptin with anti-obesity effect after the treatment of tea compounds. It is suggested that the regulation of obesity-related hormones might depend on the obesity condition and the interaction of other endocrine molecules and genes. Moreover, most related articles focus on the correlation between green tea and the neuroendocrine system against obesity, and fewer studies are conducted on other types of tea.

Altering the gut microbiota

Gut microbiota is recognized as an essential "organ" of the human body with the function of regulating the host physiology and pathophysiology (Eckburg et al. 2005; Zhang et al. 2015). The alternations of its structure often present in metabolic disorders, such as diabetes, nonalcoholic liver disease and obesity (Torres-Fuentes et al. 2017; Abenavoli et al. 2019; Xu et al. 2021). There are increasing studies elucidating the intricate interaction of gut microbiota and host, which germ-free animals and fecal microbiota transplant are often used to demonstrate the causal role of gut microbiota in obesity and other metabolic disorders (Zhang et al. 2015; Cao et al. 2019; Lee, Yacyshyn, et al. 2019). Growing evidence suggests that tea and its metabolites could maintain gut health and attenuate obesity through exerting prebiotic-like effects and modulating the gut community structure (Guo et al. 2017). In obese mice, green tea extract, fermented green tea extract, green tea polyphenols, oolong tea polyphenols, Fuzhuan brick tea, ripened Pu-erh tea extract, decaffeinated green tea combined with black tea were observed to change the gut microbiota composition and ameliorate the dysbiosis mostly by decreasing the ratio of *Firmicutes* to *Bacteroidetes* (Seo et al. 2015; Chen, Xie, Wan, et al. 2018; Cheng et al. 2018; Henning et al. 2018; Zhang et al. 2018; Dey et al. 2019; Lu et al. 2019). Other microorganisms and related intestinal function are also affected by tea. For example, the green tea significantly reduced the body fat content and TG accumulation in the liver, which might be inversely correlated to the amount of *Akkermansia* in the intestine (Axling et al. 2012). In addition, the cold-water brewed green tea had anti-obesity effects on HFD-fed mice through modulating the gut microbiota, especially *Lachnospiraceae bacterium* DW67, *Blautia coccoide*s, *Parabacteroides merdae* and *Bacteroides_vulgatus* (Ma et al. 2020). Additionally, Fuzhuan brick tea alleviated obesity, hepatic steatosis, adipocyte hypertrophy and tissue inflammation, and it also improved the serum lipid parameters and blood glucose homeostasis. These beneficial effects were possibly induced by the change of gut microbiota composition and structure, which the abundance of beneficial bacteria (*Clostridiaceae*, *Bacteroidales* and *Lachnospiraceae*) was increased and the abundance of harmful bacteria (*Ruminococcaceae*, *Peptococcaceae*, *Peptostreptococcaceae* and *Erysipelotrichaceae*) was decreased (Liu et al. 2019). Besides, Fuzhuan brick tea could increase the relative abundance of *Bifidobacteriaceae* (Chen, Xie, Wan, et al. 2018). Its polysaccharides enhanced the phylogenetic diversity of HFD-induced microbiota and restored the increased relative abundance of *Erysipelotrichaceae*, *Coriobacteriaceae* and *Streptococcaceae* (Chen, Xie, Wan, et al. 2018). Moreover, black tea polyphenols enhanced the relative proportion of *Pseudobutyrivibrio* and short-chain fatty acids (SCFA) in intestine (Henning et al. 2018). Furthermore, the infusions of black tea, green tea, and oolong tea improved the diversity and structure of gut microbiota closely related to obesity, such as *Alistipes*, *Rikenella*, *Lachnospiraceae* and *Akkermansia* (Liu et al. 2016).

The green tea extract not only increased the gut microbial diversity but also improved the gut barrier function which inhibited the endotoxin translocation and reduced adipose Toll-like receptor 4 (TLR4)/nuclear factor kappa B (NF-κB) inflammation (Dey et al. 2019). In addition, the ripened Pu-erh tea extract reduced the weight gain and fat accumulation and increased the intestinal barrier integrity in obese mice. The fecal transplant trial revealed that the ripened Pu-erh tea extract could modulate the weight and metabolic syndrome in the recipient mice, demonstrating the important role of gut microbiota in the prevention of obesity (Lu et al. 2019).

To sum up, tea and its components could attenuate and prevent obesity by changing the gut microbiota composition, increasing the diversity of gut microbiota and improving the related host gut function. In turn, the gut microbiota could influence the metabolism of tea and further the biological activity of tea metabolites which are also considered as the main contributors for health benefits. Therefore, the interaction between tea and gut microbiota is notable for more investigations on treating or preventing metabolic disorders like obesity.

Experimental studies demonstrate that tea and its components exert a pronounced effect of anti-obesity through various pathways and mechanisms (Figure 1 and Table 2). The potential mechanisms of action are associated with the regulation of energy expenditure, nutrient digestion and absorption, lipid catabolism, lipid synthesis, adipocytes, neuroendocrine system and gut microbiota. Nevertheless, some studies demonstrated that the processing of tea like fermentation and roasting might significantly influence the chemical composition and drastically reduce the bioactivities and nutrition value, while other studies found that the processing posed no negative effects on the health benefits of tea, and even enhanced its benefits, which might be attributed to the biotransform of some chemical compounds. Hence, it is still possible to yield different outcomes of tea on obesity due to multiple factors like types of tea, intervention time and dosages (Chupeerach et al. 2021; Liu et al. 2022). It should be also pointed out that there has been an enormous amount of research about effect of tea on obesity, and some models are relevant, but some models are less relevant or irrelevant. In addition, some researches are done at such high concentrations, and it is very difficult to achieve such high concentration by drinking tea except the consumption of tea extract. Therefore, a special attention should be paid when the effect of drinking tea on obesity is interpreted, and more studies should be conducted on tea and obesity in the future.

Clinical studies

Numerous studies have shown the efficacy of tea on reducing body weight and alternating body composition in animal studies. Several clinical studies are also conducted to further confirm the anti-obesity effect of tea and its components in humans. For instance, a double-blind parallel multicenter
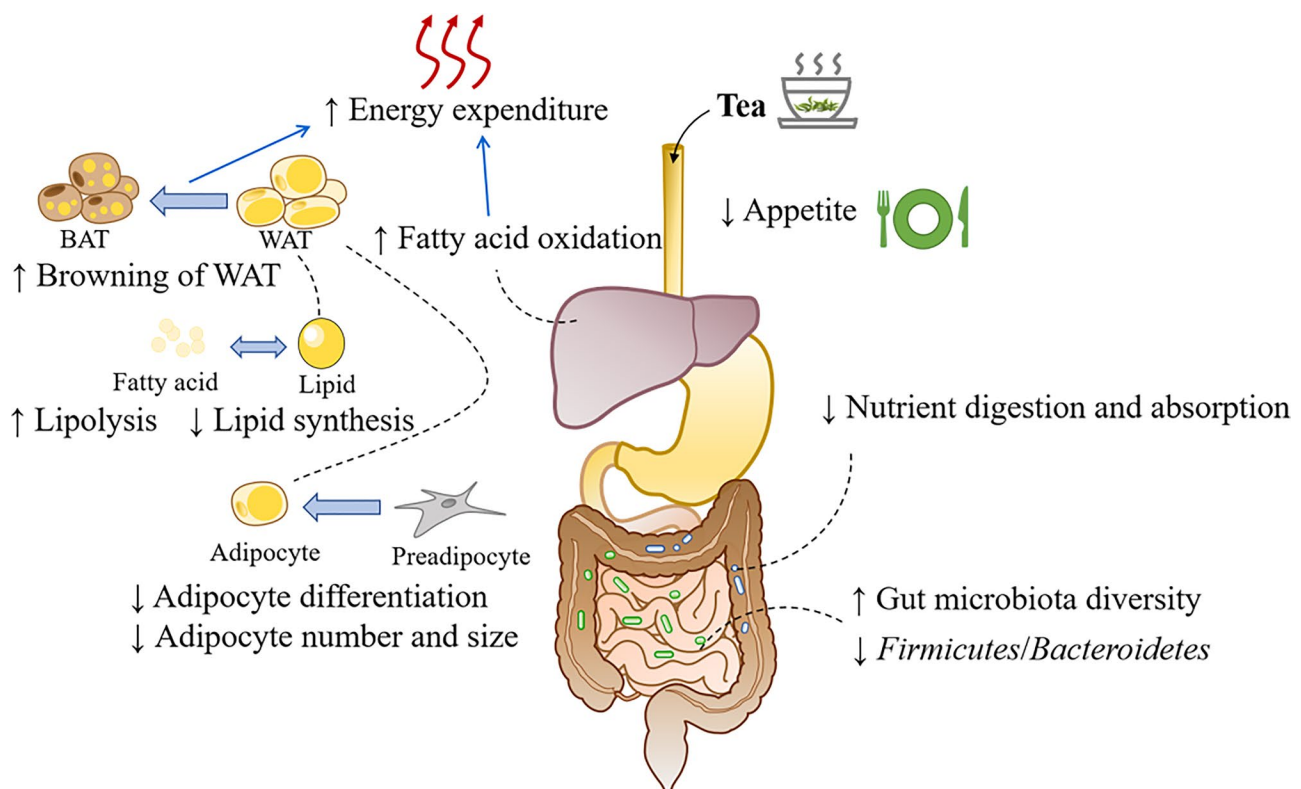
Figure 1. Anti-obesity effect and potential mechanisms of tea. The mechanisms of action are mainly involved with increasing energy expenditure, decreasing nutrient digestion and absorption, stimulating lipid catabolism, inhibiting lipid synthesis, and modulating adipocytes, neuroendocrine system, and gut microbiota. BAT, brown adipose tissue; WAT, white adipose tissue.

Table 2. The effects and mechanisms of tea and its components on obesity from experimental animal studies.

Tea or its components	Model	Dosage	Duration	Effects	Potential Mechanisms	References
Green tea						
Green tea	Male Wistar rats	1.1 and 2.0% in diet	56 days (8 weeks)	Decreased body weight gain Prevented visceral fat accumulation	↓ protein ingestion	(Bajerska et al. 2011)
Green tea	Male Wistar rats	500 mg/kg b.w.	60 days (12 weeks)	Reduced body weight, fat synthesis, and fat depots Decreased lipid content in plasma and liver	↑ AMPK in adipose tissue ↑ GLUT-4 ↑ fatty acid oxidation	(Rocha et al. 2016)
Green tea	Male Wistar rats	As drinking water	21 days (3 weeks)	Reduced adipose tissue weight	↑ GLUT-4 translocation in skeletal muscle ↓ GLUT-4 translocation in adipose tissue ↓ PPARα and SREBP-1	(Ashida et al. 2004)
Green tea	Male Sprague-Dawley rats	20 g/kg diet	14 days (2 weeks)	Prevented the body weight gain Increased the energy expenditure	↑ BAT thermogenesis through β-adrenoceptor activation	(Choo 2003)
Green tea	Male C57BL/6J mice	As drinking water	98 days (14 weeks)	Suppressed body weight again Reduced deposition of white adipose tissue	↑ GLUT-4 translocation in muscle	(Nishiumi et al. 2010)
Green tea	Male C57BL/6 mice	2% in diet	56 days (8 weeks)	Reduced lipid accumulation	↑ Nrf2 and NQO1 ↓ CD36 ↓ SREBP-1c, FAS and SCD1	(Li, Kek, et al. 2016)
Green tea	Male C57BL/6J mice	0.5% in diet	56 days (8 weeks)	Reduced obesity and fat mass expansion Decreased the adiposity in WAT and BAT	↑ browning of WAT ↓ whitening in BAT	(Neyrinck et al. 2017)
Green tea	Male C57BL/6J mice	2% in diet	56 days (8 weeks)	Attenuated the obesity Increased gut microbial diversity Improved intestinal barrier function	↑ ratio of Firmicutes to Bacteroidetes ↓ portal vein and circulating endotoxin	(Dey et al. 2019)
Green tea	Male C57BL/6J mice	4.0% in diet	154 days (22 weeks)	Reduced body fat content and hepatic triacylglycerol accumulation	↑ Akkermansia	(Axling et al. 2012)
Green tea	Male C57BL/6 mice	As drinking water	56 days (8 weeks)	Ameliorated obesity	↓ FAS and SREBP-1c ↑ PPARα and PGC-1 ↑ Lachnospiraceae bacterium DW67 and Blautia coccoides ↓ Parabacteroides merdae and Bacteroides_vulgatus	(Ma et al. 2020)
Green tea	Berlin fat mice	300 and 600 mg/kg b.w.	51 days (7.3 weeks)	Decreased body fat and food intake Prevented fat accumulation	↓ neprilysin ↑ galanin and neuropeptide Y	(Muenzner et al. 2016)
Green tea	Juvenile zebrafish	1 and 10 μg/mL	8–9 days	Decreased visceral adipose tissue accumulation in juvenile zebrafish	↑ STAT ↓ C/EBP signaling pathways	(Zang et al. 2021)
Green tea	Female adult zebrafish	250 μg/g b.w. 10% GTE-containing food	21 days (3 weeks)	Ameliorated visceral adiposity and plasma TG level in adult zebrafish		
Green tea combined with exercise	Male C57BL/6J mice	0.5% in diet	105 days (15 weeks)	Reduced body weight gain, visceral fat accumulation	↑ fatty acid oxidation	(Shimotoyodome et al. 2005)
Fermented green tea	Male C57BL/6 mice	500 mg/kg b.w.	56 days (8 weeks)	Reduced body weight gain and fat mass	↓ ratio of Firmicutes to Bacteroidetes ↓ ratio of Bacteroides to Prevotella	(Seo et al. 2015)
Huangjinya green tea	Male C57BL/6 mice	150 and 300 mg/kg b.w.	63 days (9 weeks)	Reduced hepatic lipid accumulation and liver steatosis Prevented white adipose tissue expansion	↑ HSL and ATGL in WAT ↑ PGC-1α and UCP-1 ↓ FAS and ACC1 ↓ C/EBP-α and PPARγ	(Li et al. 2020)

Table 2. (Continued)

Tea or its components	Model	Dosage	Duration	Effects	Potential Mechanisms	References
Decaffeinated green tea combined with exercise	C57BL/6J mice	7.7 g/kg in diet	112 days (16 weeks)	Induced the browning of adipose tissue in visceral WAT	↑ PGC-1α, BMP4 and PTEN ↑ HSL and PNPLA2 ↑ NADH dehydrogenase 5, cytochrome B and cytochrome C oxidase III	(Sae-Tan, Rogers, and Lambert 2015)
Green tea polyphenols	Female Sprague-Dawley rats	0.5% in diet	4 months (16 weeks)	Increased percentage of fat-free mass Decreased percentage of fat mass	↓ serum IGF-1, leptin and adiponectin	(Shen et al. 2012)
Green tea polyphenols	Male C57BL/6J mice	0.1% in diet	56 days (8 weeks)	Ameliorated the obesity-induced gut dysbiosis	↓ ratio of Firmicutes to Bacteroidetes	(Zhang et al. 2018)
Decaffeinated green tea polyphenols	Male C57BL/6J mice	0.25% in diet	28 days (4 weeks)	Induced weight loss	↓ ratio of Firmicutes to Bacteroidetes	(Henning et al. 2018)
Green tea polysaccharide combined with polyphenols	Male Sprague-Dawley rats	400 and 800 mg/kg b.w.	56 days (6 weeks)	Suppressed body weight gain Reduced fat accumulation	↓ serum leptin ↓ fatty acids absorption	(Xu et al. 2015)
Green tea catechins	Male Sprague-Dawley rats	100 mg/kg b.w.	45 days (6.4 weeks)	Reduced the body and liver weights Lowered TG levels in serum and liver	↑ PPARγ in subcutaneous WAT ↑ PPARδ in subcutaneous WAT, visceral WAT and brown adipose tissue ↑ CPT-1, ACOX and UCP-1 ↓ PPARγ in visceral WAT	(Yan, Zhao, and Zhao 2013)
Yellow tea						
Large yellow tea	Male C57BL/6 mice	0.5 and 2.5% in diet	84 days (12 weeks)	Reduced body, liver and adipose tissue weight Decreased the size and number of adipose cells	NA	(Xu et al. 2018)
Oolong tea						
Aged oolong tea	Male C57BL/6J mice	1000 mg/kg b.w.	42 days (6 weeks)	Decreased body weight, fat accumulation, and serum TG level Reduced the size of adipocytes in epididymal fat	↑ AMPK/ACC signaling pathway ↑ CPT-1 ↓ FAS	(Yuan et al. 2018)
Oolong tea polyphenols	Male C57BL/6J mice	0.1% in diet	28 days (4 weeks)	Increased bacterial biodiversity and the abundance of butyrate- and acetate-producing bacteria	↓ ratio of Firmicutes to Bacteroidetes	(Cheng et al. 2018)
Black tea						
Black tea	Male C57BL/6J mice	As drinking water	98 days (14 weeks)	Suppressed body weight again Reduced deposition of white adipose tissue	↑ GLUT-4 translocation to the plasma membrane in muscle	(Nishiumi et al. 2010)
Pu-erh tea	Female ddY mice	0.2 and 0.6% in diets	84 days (12 weeks)	Suppressed the body weight gain Reduced parametrial adipose tissue mass	↓ pancreatic lipase activity	(Oi et al. 2012)
Pu-erh tea	Male C57BL/6J mice	450 mg/kg b.w.	154 days (22 weeks)	Reduced body weight, liver weight, and adipose tissue weight	↑ PPARα, CPT-1α and ACOX-1 ↓ SREBP1c, CHREBP, ACC-1 and FAS	(Huang, Wang, et al. 2019)
Raw Pu-erh tea	Male Wistar rats	150 and 400 mg/kg b.w.	42 days (6 weeks)	Alleviated obesity Increased microbial diversity Altered cecal microbiota composition and function	↑ Akkermansia uciniphila ↓ ratio of Firmicutes to Bacteroidetes	(Xia et al. 2019)
Ripened Pu-erh tea	Male C57BL/6N mice	0.1, 0.2 and 0.4% in diet	56 days (8 weeks)	Decreased weight gain, fat accumulation, and adipose inflammation Improved intestinal barrier integrity	↓ ratio of Firmicutes to Bacteroidetes	(Lu et al. 2019)
Huangjinya black tea	Male C57BL/6 mice	150 and 300 mg/kg b.w.	63 days (9 weeks)	Decreased adipocyte expansion Alleviated the obesity	↓ HSL, ATGL and MGL ↑ PGC-1α and UCP-1 ↓ FAS, ACC-1 and SREBP-1	(Xu, Li, et al. 2020)
Black tea polyphenols	Female C57BL/6N mice	1%, 5% in diet	56 days (8 weeks)	Suppressed the body weight gain Reduced parametrial adipose tissue mass, and liver lipid content	↓ PPARγ and C/EBP-α ↓ intestinal lipid absorption	(Uchiyama et al. 2011)

Treatment	Animal model	Dose	Duration	Effects	Mechanism	Reference
Black tea polyphenols	Male C57BL/6J mice	0.25% in diet	28 days (4 weeks)	Induced weight loss	↑ *Pseudobutyrivibrio* ↑ SCFA ↓ ratio of *Firmicutes* to *Bacteroidetes*	(Henning et al. 2018)
Dark tea						
Instant dark tea	Male C57BL/6 mice	5 mg/mL infusion *ad libitum* feeding	56 days (8 weeks)	Inhibited body weight gain and visceral fat weights	↑ CPT1-α ↓ SREBP-1 and FAS	(Sun et al. 2019)
Fuzhuan brick tea	Male Sprague-Dawley rats	75 and 300 mg/kg b.w.	40 days (5.7 weeks)	Inhibited the increase of body weight and adipose tissue accumulation Reduced serum triacylglycerol	↑ PPARα and CPT1-α↓ SREBP-1c, FAS and C/EBP-α	(Li et al. 2013)
Fuzhuan brick tea	Male C57BL/6 mice	400 mg/kg b.w.	56 days (8 weeks)	Reduce the obesity Increased gut microbiota diversity	↑ *Bifidobacteriaceae* ↓ ratio of *Firmicutes* to *Bacteroidetes*	(Chen, Xie, Wan, et al. 2018)
Fuzhuan brick tea	Male C57BL/6 mice	100, 200, and 400 mg/kg b.w.	56 days (8 weeks)	Ameliorated obesity, serum lipid parameters, hepatic steatosis, and adipocyte hypertrophy	↑ *Clostridiaceae, Bacteroidales,* and *Lachnospiraceae* ↓ ratio of *Firmicutes* to *Bacteroidetes* ↓ *Ruminococcaceae, Peptococcaceae, Peptostreptococcaceae* and *Erysipelotrichaceae*	(Liu et al. 2019)
Fuzhuan brick tea polysaccharides	Male C57BL/6 mice	200, 400 and 800 mg/kg b.w.	56 days (8 weeks)	Attenuated metabolic syndrome Enhanced the phylogenetic diversity	↑ *Erysipelotrichaceae, Coriobacteriaceae,* and *Streptococcaceae*	(Chen, Xie, Xie, Wan, et al. 2018)
Components						
Catechins	Male C57BL/6J mice	0.1, 0.2, and 0.5% in diet	11 months (44 weeks)	Reduced body weight gain, visceral and liver fat accumulation	↑ ACOX and MCAD	(Murase et al. 2002)
EGCG	Male C57BL/6J mice	0.32% in diet	119 days (17 weeks)	Reduced body weight gain ncreased fecal lipids	↓ lipid absorption	(Chen et al. 2011)
EGCG	Male C57BL/6N mice	0.25%, 0.5% and 1% in diet	4-7 days	Increased fat and nitrogen excretion Increased lipid oxidation Reduced incorporation of dietary lipids into tissues	↓ CD36/FAT in intestinal mucosa ↓ ACC, FAS and SCD1	(Friedrich et al. 2012)
EGCG	Male C57BL/6J mice	0.2 and 0.5% in diet	56 days (8 weeks)	Reduced body weight and mass of various adipose tissues ecreased levels of lipids in plasma and liver	↑ CPT-1 ↑ UCP2 ↑ HSL and ATGL in WAT ↓ PPARγ and C/EBP-α ↓ SREBP-1c, aP2 and FAS	(Lee, Kim, and Kim 2009)
EGCG	Male C57BL/6J mice	0.5% in diet	3 months (12 weeks)	Reduced food intake, feeding frequency and meal size	Regulated the expression of genes AGRP, POMC and CART, and Clock and Bmal1	(Li, Kek, et al. 2016)
Strictinin	Male C57BL/6 mice	45 and 130 mg/kg b.w.	56 days (8 weeks)	Reduced body weight gain and epididymal fat weight Decreased the enlargement of adipocytes	NA	(Chen, Xie, Wan, et al. 2018)

ACC, acetyl-CoA carboxylase; ACOX, acyl-CoA oxidase; AMPK, AMP-activated protein kinase; aP2, adipocyte fatty acid-binding protein; ATGL, adipocyte triglyceride lipase; BAT, brown adipose tissue; BMP4, bone morphogenetic protein 4; CD36, cluster of differentiation 36; C/EBP-α, CCAAT-enhancer-binding protein alpha; CHREBP, carbohydrate responsive element-binding protein; CPT-1, carnitine palmitoyltransferase-1; FAS, fatty acid synthase; FAT, fatty acid translocase; GLUT-4, glucose transporter 4; HSL, hormone sensitive lipase; IGF-1, insulin-like growth factor I; MCAD, medium chain acyl-CoA dehydrogenase; MGL, monoacylglycerol lipase; NQO1, NADPH:quinone oxidoreductase 1; Nrf2, nuclear factor erythroid-2-related factor-2; PGC-1α, peroxisome proliferator-activated receptor-γ coactivator-1α; PNPLA2, patatin-like phospholipase domain-containing protein 2; PPAR, peroxisome proliferator activated receptor; PTEN, phosphatase and tensin homolog; SCD1, stearoyl-CoA desaturase 1; SREBP-1, sterol regulatory element binding protein-1; STAT, signal transducer and activator of transcription; UCP-1, uncoupling protein-1; WAT, white adipose tissue
NA, not applicable.

trial recruited 240 Japanese women and men with visceral fat-type obesity, and participants ingested green tea with 583 mg catechins or 96 mg catechins as control daily during 12 weeks. Results showed that the intake of green tea led to a significant decrease in body weight, BMI, body fat ratio, body fat mass, visceral fat area and subcutaneous fat area (Nagao, Hase, and Tokimitsu 2007). Besides, a 12-week clinical trial was performed with 120 healthy, overweight, and obese individuals and the treatment group received a green tea meal replacement formula product with 6 g green tea, which resulted in a significant body weight loss (Tsai et al. 2009). Additionally, a total of 104 Chinese adults with a high proportion of abdominal visceral fat were randomly consume a daily beverage with 609.3 mg catechins or a control beverage for 12 weeks, and the results showed that the consumption of beverage with catechin induced visceral fat loss and reduced body weight (Zhang et al. 2012). Moreover, 128 participants ingested 625 mg catechins or placebo for 12 weeks, and meanwhile, they were asked to maintain constant energy intake and perform exercises with moderate intensity. The intake of catechin reduced the total abdominal fat area, abdominal subcutaneous fat area and the concentrations of TG and FFA in serum, which improved the body composition and fat distribution in overweight adults (Maki et al. 2009). Furthermore, a total of 102 overweight or obese subjects daily ingested 8 g oolong tea for 6 weeks, and their body weight and plasma levels of TG and total cholesterol (TC) were decreased, indicating that the chronic consumption of oolong tea might prevent obesity and hyperlipidemia (He et al. 2009).

Although some clinical trials show that tea and its components could improve obesity-related indicators, such as fat oxidation, energy expenditure, serum lipid parameters and hormones, they exerted no significant change in the body weight. For instance, a 12-week study with 78 obese women randomly divide participants into treatment (receiving 491 mg catechins with 302 mg EGCG) and control groups. The consumption of catechins reduced the levels of low density-lipoprotein-cholesterol (LDL-c) and TG, and increased the levels of HDL-c, adiponectin and ghrelin, but there was no significant alternation in body weight, BMI and waist circumflex (Hsu et al. 2008). Besides, treatment with green tea extract for 6 weeks increased leptin and reduced LDL, but parameters associated with overweight had no significant changes in overweight and obese women (Huang et al. 2018). Moreover, the daily consumption of 580 mg decaffeinated green tea extract containing 400 mg EGCG, 50 mg quercetin and 150 mg α-lipoic acid for 8 weeks increased the maximal fat oxidation (MFO), accelerated the energy expenditure and decreased LDL-c, but the body composition and cardio-metabolic indexes were not significantly affected in overweight individuals who maintained regular physical activity (Roberts et al. 2021).

Some studies reported that tea consumption had no significant effects on body weight in obese or overweight individuals (Jurgens et al. 2012). For example, 60 Caucasian men and women consumed daily green tea extract (>0.56 g

epigallocatechin gallate and 0.28-0.45 g caffeine) or placebo capsules for 12 weeks. The results showed that there was no difference on the fecal energy and fat content of subjects between groups, and long-term green tea extract supplements had no significant effects on resting energy expenditure, respiratory quotient, and body composition in adults (Janssens, Hursel, and Westerterp-Plantenga 2015). Moreover, the low-energy diet with green tea had no contribution to the improvement of body weight and the significant reduction of resting energy expenditure in overweight women (Diepvens et al. 2005).

In summary, several clinical studies demonstrated that the intake of some tea benefited the weight loss in overweight and obese individuals, but in some cases, there is no significant effect of tea on weight loss. The detailed view of clinical data is presented in Table 3. This inconsistency may be attributed to intricate factors involved in clinical studies, the poor bioavailability of tea compounds which might not exert a significant effect in human body, and the inter-individual variability in response to the tea consumption. Moreover, the complication of obesity is another health concern and the individual treatment of tea might not enough to attenuate the disorder. Thus, further investigations are warranted considering the dose-response and longer-term effects as well as the combined effects with strategies, such as dietary habits and exercises.

Potential adverse effects and safety

Tea has shown great potential in combating obesity and improving obesity-related indicators based on in vitro and in vivo studies. Although tea might contain a little heavy metal, pesticide residue and mycotoxins from plantation, processing and storage, tea consumption is often safe to human (Cao et al. 2010; Haas et al. 2013; Brzezicha-Cirocka, Grembecka, and Szefer 2016; Chen et al. 2016; Tang et al. 2019; Y. Huang, Wang, et al. 2019; Kowalska 2021; Yu et al. 2021). On the other hand, a low dose of tea may have no significant effect, but a high dose of tea may trigger adverse effects. For instance, a high dose of green tea extract was found to cause hepatotoxicity and gastrointestinal disturbances like stomach damages, and EGCG was regarded as the main compound for theses adverse effects (Sarma et al. 2008; Isomura et al. 2016). Hence, some processing methods are explored to reduce the content of EGCG in tea extract to minimize the negative impacts, and our previous study has found that the combined treatment of tannase and ultrasound could reduce EGCG content in green tea extract (Xu et al. 2019).

In short, tea is a generally safe supplement for prevention and management of obesity though there are still some adverse effects in tea consumption, and it is crucial to control the quality of plantation, processing and storage to reduce the potential toxic factors in tea. In addition, a special attention should be paid to the duration and the adequate and effective dosages when green tea extract is used in prevention and management of obesity.

Table 3. The effects of tea and its components on obesity from clinical studies.

Types of Study	Subjects	Averages of BMI (Treatment group)	Tea and its components (Daily dosage)	Duration	Effects	References
Green tea						
Randomized, double-blind, controlled parallel multicenter trial	240 Japanese subjects with visceral fat-type obesity (140 males and 100 females)	$26.8 \pm 2.0\,kg/m^2$	Green tea (583 mg catechins)	12 weeks	Decreased body weight, BMI, body fat ratio, body fat mass, waist circumference, hip circumference, visceral fat area, and subcutaneous fat area	(Nagao, Hase, and Tokimitsu 2007)
Randomized controlled clinical trial	120 healthy, overweight and obese persons (25 males and 95 females)	$33.1 \pm 0.5\,kg/m^2$	Green tea (6 g)	12 weeks	Induced greater body weight loss Reduced more total body fat mass	(Tsai et al. 2009)
Randomized, double-blind, controlled clinical trial	104 Chinese adults with a high proportion of abdominal visceral fat (39 males and 65 females)	$30.5 \pm 3.0\,kg/m^2$	Green tea (609.3 mg catechins and 68.7 mg caffeine)	12 weeks	Induced visceral fat loss Reduced average visceral fat area, body weight, and body fat	(Zhang et al. 2012)
Randomized, double-blind, controlled clinical trial	128 healthy, normally sedentary persons (67 males and 61 females)	$32.2 \pm 0.5\,kg/m^2$	Green tea (625 mg catechins and 39 mg caffeine)	12 weeks	Reduced the total abdominal fat area, abdominal subcutaneous fat area, the concentrations of TG and FFA in serum	(Maki et al. 2009)
Randomized, double-blind, placebo-controlled, parallel trial	46 overweight women	$27.6 \pm 1.8\,kg/m^2$	Green tea (1125 mg catechins and 225 mg caffeine)	12 weeks	Not significantly reduced body weight, BMI, ratio of waist to hip, and resting energy expenditure	(Diepvens et al. 2005)
Randomized, placebo-controlled trial	60 healthy, normal-weight or overweight/obese Caucasian subjects (10 males and 50 females)	$23.3 \pm 4.4\,kg/m^2$	Green tea (>0.56 g EGCG and 0.28–0.45 g caffeine)	12 weeks	No difference on the fecal energy and fat content, resting energy expenditure, respiratory quotient, and body composition in adults	(Janssens, Hursel, and Westerterp-Plantenga 2015)
Randomized, double-blind, placebo-controlled clinical trial	78 healthy and obese women	$31.2 \pm 3.5\,kg/m^2$	Green tea (491 mg catechins containing 302 mg EGCG)	12 weeks	Reduced LDL-c and TG Increased HDL-c, adiponectin and ghrelin No significant change in body weight, BMI, and waist circumflex	(Hsu et al. 2008)
Randomized, double-blind, crossover, placebo-controlled clinical trial	73 overweight and obese women with high levels of LDL-c	$29.1 \pm 4.9\,kg/m^2$	Green tea (856.8 mg EGCG, 236.1 mg EGC, 115.5 mg EGC, 71.9 EC, and 63.7 mg GCG)	6 weeks	Increased leptin Reduced LDL No significant changes in other biochemical markers related to overweight	(Huang et al. 2018)
Randomized, repeated-measures, double-blinded, placebo-controlled trial	27 healthy, overweight subjects who maintained regular physical activity (7 males and 20 females)	$27.1 \pm 0.8\,kg/m^2$	Decaffeinated green tea (400 mg EGCG, 50 mg quercetin and 150 mg alpha-lipoic acid)	8 weeks	Increased maximal fat oxidation and energy expenditure Decreased LDL-c No significant changes in body composition and cardio-metabolic indexes	(Roberts et al. 2021)
Oolong tea						
Clinical trial	102 diet-induced overweight or obese Chinese subjects (42 males and 60 females)	NA	Oolong tea (8 g)	6 weeks	Decreased body weight Reduced the plasma levels of TG and TC	(He et al. 2009)

BMI, body mass index; EC, epicatechin; ECG, epicatechin gallate; EGC, epigallocatechin; EGCG, epigallocatechin gallate; GCG, gallocatechin gallate; HDL-c, high density-lipoprotein-cholesterol; LDL-c low density-lipoprotein-cholesterol; TC, total cholesterol; TG, triglyceride. NA, not applicable.

Conclusions

Tea has been widely investigated its effects on obesity in the cell, animal, and human studies. Several epidemiological studies showed that the consumption of tea is inversely correlated with the body weight and the risk of obesity, but there were also studies revealing no association. The experimental studies demonstrated the fat-lowering and anti-obesity effect of tea, and the action of mechanism is mainly involved in increasing energy expenditure, decreasing nutrient digestion and absorption, stimulating lipid catabolism, inhibiting lipid synthesis and modulating adipocytes, neuroendocrine system and gut microbiota. Given the significant anti-obesity effects of tea, it was considered as the potential candidate for the prevention and management of obesity. Most of clinical trials focus on the effects of green tea and its compounds like EGCG on body weight loss, and some of them confirmed that chronic consumption of green tea could decrease body weight and alter body composition, while other revealed that green tea failed to significantly reduce body weight, though it could improve obesity-related indicators. Furthermore, because green tea extract consumption at a high dose for a long time might cause liver injuries, a special attention should be paid to the dosage and duration of green tea extract intake. In the future, the methods of reducing adverse effects of tea extract should be explored, such as reducing the content of EGCG in the extract, or combination of the extract and other hepatoprotective natural products.

Abbreviations

ACC	acetyl-CoA carboxylase
ACOX	acyl-CoA oxidase
AMPK	AMP-activated protein kinase
ATGL	adipose triglyceride lipase
BAT	brown adipose tissue
BMI	body mass index
BMP4	bone morphogenetic protein 4
CD36	cluster of differentiation 36
C/EBP-α	CCAAT-enhancer-binding protein alpha
cGMP	cyclic guanosine monophosphate
CPT-1	carnitine palmitoyltransferase-1
DADS	diallyl disulfide
EGCG	epigallocatechin gallate
ECG	epicatechin gallate
FAS	fatty acid synthase
GLUT-4	glucose transporter 4
HDL	high-density lipoprotein
HFD	high- fat diet
HSL	hormone sensitive lipase
IGF-1	insulin-like growth factor I
LDL-c	low density-lipoprotein-cholesterol
MCAD	medium-chain acyl-CoA dehydrogenase
MFO	maximal fat oxidation
NF-κB	nuclear factor kappa B
PGC-1α	peroxisome proliferator-activated receptor-γ coactivator-1α
PPARα	proliferator-activated receptor alpha
Pref-1	preadipocyte factor 1
PTEN	phosphatase and tensin homolog
SCD	stearoyl-CoA desaturase
SCFA	short-chain fatty acids
SREBP-1c	sterol regulatory element-binding protein-1c
STAT	signal transducer and activator of transcription
TG	triglyceride
TLR4	Toll-like receptor 4
RCT	randomized controlled trial
UCP-1	uncoupling protein-1
WAT	white adipose tissue

Author contributions

Conceptualization, X.-Y.X., R.-Y.G. and H.-B.L.; Writing, original draft preparation, X.-Y.X., C.-N.Z., B.-Y.L., G.-Y.T. and A.S.; Writing, review and editing, R.-Y. G., Y.-B.F. and H.-B.L.; Supervision, R.-Y.G., Y.-B.F. and H.-B.L.; Funding acquisition, R.-Y.G. and H.-B.L.

Disclosure statement

The authors declare no conflict of interest.

Funding

ORCID

Hua-Bin Li http://orcid.org/0000-0003-2332-8554
Ren-You Gan http://orcid.org/0000-0002-4162-1511

References

Abenavoli, L., E. Scarpellini, C. Colica, L. Boccuto, B. Salehi, J. Sharifi-Rad, V. Aiello, B. Romano, A. De Lorenzo, A. A. Izzo, et al. 2019. Gut microbiota and obesity: A role for probiotics. *Nutrients* 11 (11):2690. doi: 10.3390/nu11112690.

Ali, A. T., W. E. Hochfeld, R. Myburgh, and M. S. Pepper. 2013. Adipocyte and adipogenesis. *European Journal of Cell Biology* 92 (6–7):229–36. doi: 10.1016/j.ejcb.2013.06.001.

Arends, D., S. Heise, S. Kärst, J. Trost, and G. A. Brockmann. 2016. Fine mapping a major obesity locus (*jObes1*) using a Berlin Fat Mouse × B6N advanced intercross population. *International Journal of Obesity (2005)* 40 (11):1784–8. doi: 10.1038/ijo.2016.150.

Ashida, H., T. Furuyashiki, H. Nagayasu, H. Bessho, H. Sakakibara, T. Hashimoto, and K. Kanazawa. 2004. Anti-obesity actions of green tea: Possible involvements in modulation of the glucose uptake system and suppression of the adipogenesis-related transcription factors. *BioFactors (Oxford, England)* 22 (1–4):135–40. doi: 10.1002/biof.5520220126.

Axling, U., C. Olsson, J. Xu, C. Fernandez, S. Larsson, K. Strom, S. Ahrne, C. Holm, G. Molin, and K. Berger. 2012. Green tea powder and Lactobacillus plantarum affect gut microbiota, lipid metabolism and inflammation in high-fat fed C57BL/6J mice. *Nutrition & Metabolism* 9 (1):105 doi: 10.1186/1743-7075-9-105.

Bae, J., M. Kumazoe, Y. Fujimura, and H. Tachibana. 2019. Diallyl disulfide potentiates anti-obesity effect of green tea in high-fat/high-sucrose diet-induced obesity. *Journal of Nutritional Biochemistry* 64:152–61. doi: 10.1016/j.jnutbio.2018.10.014.

Bajerska, J., M. Wozniewicz, J. Jeszka, S. Drzymala-Czyz, and J. Walkowiak. 2011. Green tea aqueous extract reduces visceral fat and decreases protein availability in rats fed with a high-fat diet. *Nutrition Research* 31 (2):157–64. doi: 10.1016/j.nutres.2011.01.005.

Blüher, M. 2019. Obesity: Global epidemiology and pathogenesis. *Nature Reviews. Endocrinology* 15 (5):288–98. doi: 10.1038/s41574-019-0176-8.

Brzezicha-Cirocka, J., M. Grembecka, and P. Szefer. 2016. Monitoring of essential and heavy metals in green tea from different geographical origins. *Environmental Monitoring and Assessment* 188 (3):183 doi: 10.1007/s10661-016-5157-y.

Cao, H., L. Qiao, H. Zhang, and J. Chen. 2010. Exposure and risk assessment for aluminium and heavy metals in Puerh tea. *Science of the Total Environment* 408 (14):2777–84. doi: 10.1016/j.scitotenv.2010.03.019.

Cao, S., C. Zhao, X. Xu, G. Tang, H. Corke, R. Gan, and H. Li. 2019. Dietary plants, gut microbiota, and obesity: Effects and mechanisms. *Trends in Food Science & Technology* 92:194–204. doi: 10.1016/j.tifs.2019.08.004.

Chang, Y. C., P. H. Liu, W. J. Lee, T. J. Chang, Y. D. Jiang, H. Y. Li, S. S. Kuo, K. C. Lee, and L. M. Chuang. 2008. Common variation in the fat mass and obesity-associated (FTO) gene confers risk of obesity and modulates BMI in the Chinese population. *Diabetes* 57 (8):2245–52. doi: 10.2337/db08-0377.

Chen, G. J., M. H. Xie, P. Wan, D. Chen, Z. Q. Dai, H. Ye, B. Hu, X. X. Zeng, and Z. H. Liu. 2018. Fuzhuan brick tea polysaccharides attenuate metabolic syndrome in High-Fat diet induced mice in association with modulation in the gut microbiota. *Journal of Agricultural and Food Chemistry* 66 (11):2783–95. doi: 10.1021/acs.jafc.8b00296.

Chen, G. J., M. H. Xie, Z. Q. Dai, P. Wan, H. Ye, X. X. Zeng, and Y. Sun. 2018. Kudingcha and Fuzhuan brick tea prevent obesity and modulate gut microbiota in high-fat diet fed mice. *Molecular Nutrition & Food Research* 62 (6):e1700485 doi: 10.1002/mnfr.201700485.

Chen, H. P., Z. X. Hao, Q. H. Wang, Y. Jiang, R. Pan, C. Wang, X. Liu, and C. Y. Lu. 2016. Occurrence and risk assessment of organophosphorus pesticide residues in Chinese tea. *Human and Ecological Risk Assessment: An International Journal* 22 (1):28–38. doi: 10.1080/10807039.2015.1046420.

Chen, N., R. Bezzina, E. Hinch, P. A. Lewandowski, D. Cameron-Smith, M. L. Mathai, M. Jois, A. J. Sinclair, D. P. Begg, J. D. Wark, et al. 2009. Green tea, black tea, and epigallocatechin modify body composition, improve glucose tolerance, and differentially alter metabolic gene expression in rats fed a high-fat diet. *Nutrition Research* 29 (11):784–93. doi: 10.1016/j.nutres.2009.10.003.

Chen, T. Y., M. Wang, S. K. Hsieh, M. H. Hsieh, W. Y. Chen, and J. Tzen. 2018. Pancreatic lipase inhibition of strictinin isolated from Pu'er tea (*Cammelia sinensis*) and its anti-obesity effects in C57BL6 mice. *Journal of Functional Foods* 48:1–8. doi: 10.1016/j.jff.2018.06.020.

Chen, Y. K., C. Cheung, K. R. Reuhl, A. B. Liu, M. J. Lee, Y. P. Lu, and C. S. Yang. 2011. Effects of green tea polyphenol (-)-epigallocatechin-3-gallate on newly developed high-fat/western-style diet-induced obesity and metabolic syndrome in mice. *Journal of Agricultural and Food Chemistry* 59 (21):11862–71. doi: 10.1021/jf2029016.

Cheng, M., X. Zhang, J. Y. Zhu, L. Cheng, J. X. Cao, Z. F. Wu, P. F. Weng, and X. J. Zheng. 2018. A metagenomics approach to the intestinal microbiome structure and function in high fat diet-induced obesity mice fed with oolong tea polyphenols. *Food & Function* 9 (2):1079–87. doi: 10.1039/c7fo01570d.

Choo, J. J. 2003. Green tea reduces body fat accretion caused by high-fat diet in rats through beta-adrenoceptor activation of thermogenesis in brown adipose tissue. *The Journal of Nutritional Biochemistry* 14 (11):671–6. doi: 10.1016/j.jnutbio.2003.08.005.

Chupeerach, C., A. Aursalung, T. Watcharachaisoponsiri, K. Whanmek, P. Thiyajai, K. Yosphan, V. Sritalahareuthai, Y. Sahasakul, C. Santivarangkna, and U. Suttisansanee. 2021. The effect of steaming and fermentation on nutritive values, antioxidant activities, and inhibitory properties of tea leaves. *Foods* 10 (1)177.117. doi: 10.3390/foods10010:.

Dey, P., G. Y. Sasaki, P. Wei, J. Li, L. Wang, J. Zhu, D. McTigue, Z. Yu, and R. S. Bruno. 2019. Green tea extract prevents obesity in male mice by alleviating gut dysbiosis in association with improved intestinal barrier function that limits endotoxin translocation and adipose inflammation. *The Journal of Nutritional Biochemistry* 67:78–89. doi: 10.1016/j.jnutbio.2019.01.017.

Diepvens, K., E. Kovacs, I. Nijs, N. Vogels, and M. S. Westerterp-Plantenga. 2005. Effect of green tea on resting energy expenditure and substrate oxidation during weight loss in overweight females. *British Journal of Nutrition* 94 (6):1026–34. doi: 10.1079/JBN20051580.

Dinda, B., M. Dinda, A. Roy, and S. Dinda. 2020. Dietary plant flavonoids in prevention of obesity and diabetes. *Advances in Protein Chemistry and Structural Biology* 120:159–235. doi: 10.1016/bs.apcsb.2019.08.006.

Eckburg, P. B., E. M. Bik, C. N. Bernstein, E. Purdom, L. Dethlefsen, M. Sargent, S. R. Gill, K. E. Nelson, and D. A. Relman. 2005. Diversity of the human intestinal microbial flora. *Science (New York, N.Y.)* 308 (5728):1635–8. doi: 10.1126/science.1110591.

Escher, P., O. Braissant, S. Basu-Modak, L. Michalik, W. Wahli, and B. Desvergne. 2001. Rat PPARs: Quantitative analysis in adult rat tissues and regulation in fasting and refeeding. *Endocrinology* 142 (10):4195–202. doi: 10.1210/endo.142.10.8458.

Fenzl, A., and F. W. Kiefer. 2014. Brown adipose tissue and thermogenesis. *Hormone Molecular Biology and Clinical Investigation* 19 (1):25–37. doi: 10.1515/hmbci-2014-0022.

Friedrich, M., K. J. Petzke, D. Raederstorff, S. Wolfram, and S. Klaus. 2012. Acute effects of epigallocatechin gallate from green tea on oxidation and tissue incorporation of dietary lipids in mice fed a high-fat diet. *International Journal of Obesity (2005)* 36 (5):735–43. doi: 10.1038/ijo.2011.136.

Garcia-Barrado, M. J., M. C. Iglesias-Osma, E. Perez-Garcia, S. Carrero, E. J. Blanco, M. Carretero-Hernandez, and J. Carretero. 2020. Role of flavonoids in the interactions among obesity, inflammation, and autophagy. *Pharmaceuticals* 13 (11):342. doi: 10.3390/ph13110342.

Gregoire, F. M., C. M. Smas, and H. S. Sul. 1998. Understanding adipocyte differentiation. *Physiological Reviews* 78 (3):783–809. doi: 10.1152/physrev.1998.78.3.783.

Guo, X. J., M. Cheng, X. Zhang, J. X. Cao, Z. F. Wu, and P. F. Weng. 2017. Green tea polyphenols reduce obesity in high-fat diet-induced mice by modulating intestinal microbiota composition. *International Journal of Food Science & Technology* 52 (8):1723–30. doi: 10.1111/ijfs.13479.

Haas, D., B. Pfeifer, C. Reiterich, R. Partenheimer, B. Reck, and W. Buzina. 2013. Identification and quantification of fungi and mycotoxins from Pu-erh tea. *International Journal of Food Microbiology* 166 (2):316–22. doi: 10.1016/j.ijfoodmicro.2013.07.024.

Hajiaghaalipour, F., M. Khalilpourfarshbafi, and A. Arya. 2015. Modulation of glucose transporter protein by dietary flavonoids in type 2 diabetes mellitus. *International Journal of Biological Sciences* 11 (5):508–24. doi: 10.7150/ijbs.11241.

He, R. R., L. Chen, B. H. Lin, Y. Matsui, X. S. Yao, and H. Kurihara. 2009. Beneficial effects of oolong tea consumption on diet-induced overweight and obese subjects. *Chinese Journal of Integrative Medicine* 15 (1):34–41. doi: 10.1007/s11655-009-0034-8.

Henning, S. M., J. P. Yang, M. Hsu, R. P. Lee, E. M. Grojean, A. Ly, C. H. Tseng, D. Heber, and Z. P. Li. 2018. Decaffeinated green and black tea polyphenols decrease weight gain and alter microbiome populations and function in diet-induced obese mice. *European Journal of Nutrition* 57 (8):2759–69. doi: 10.1007/s00394-017-1542-8.

Hibi, M., H. Takase, M. Iwasaki, N. Osaki, and Y. Katsuragi. 2018. Efficacy of tea catechin-rich beverages to reduce abdominal adiposity and metabolic syndrome risks in obese and overweight subjects: A pooled analysis of 6 human trials. *Nutrition Research (New York, N.Y.)* 55:1–10. doi: 10.1016/j.nuters.2018.03.012.

Hsu, C. H., T. H. Tsai, Y. H. Kao, K. C. Hwang, T. Y. Tseng, and P. Chou. 2008. Effect of green tea extract on obese women: A randomized, double-blind, placebo-controlled clinical trial. *Clinical Nutrition (Edinburgh, Scotland)* 27 (3):363–70. doi: 10.1016/j.clnu.2008.03.007.

Huang, F. J., S. L. Wang, A. H. Zhao, X. J. Zheng, Y. J. Zhang, S. Lei, K. Ge, C. Qu, Q. Zhao, C. Yan, et al. 2019. Pu-erh tea regulates

fatty acid metabolism in mice under High-Fat diet. *Frontiers in Pharmacology* 10:63 doi: 10.3389/fphar.2019.00063.

Huang, L. H., C. Y. Liu, L. Y. Wang, C. J. Huang, and C. H. Hsu. 2018. Effects of green tea extract on overweight and obese women with high levels of low density-lipoprotein-cholesterol (LDL-C): A randomised, double-blind, and cross-over placebo-controlled clinical trial. *BMC Complementary Medicine and Therapies* 18 (1):294 doi: 10.1186/s12906-018-2355-x.

Huang, Y., T. Shi, X. Luo, H. Xiong, F. Min, Y. Chen, S. Nie, and M. Xie. 2019. Determination of multi-pesticide residues in green tea with a modified QuEChERS protocol coupled to HPLC-MS/MS. *Food Chemistry* 275:255–64. doi: 10.1016/j.foodchem.2018.09.094.

Hursel, R., W. Viechtbauer, A. G. Dulloo, A. Tremblay, L. Tappy, W. Rumpler, and M. S. Westerterp-Plantenga. 2011. The effects of catechin rich teas and caffeine on energy expenditure and fat oxidation: A meta-analysis. *Obesity Reviews* 12 (7):E573–E581. doi: 10.1111/j.1467-789X.2011.00862.x.

Hussain, M. M. 2014. Intestinal lipid absorption and lipoprotein formation. *Current Opinion in Lipidology* 25 (3):200–6. doi: 10.1097/MOL.0000000000000084.

Ikeda, I., K. Tsuda, Y. Suzuki, M. Kobayashi, T. Unno, H. Tomoyori, H. Goto, Y. Kawata, K. Imaizumi, A. Nozawa, et al. 2005. Tea catechins with a galloyl moiety suppress postprandial hypertriacylglycerolemia by delaying lymphatic transport of dietary fat in rats. *The Journal of Nutrition* 135 (2):155–9. doi: 10.1093/jn/135.2.155.

Isomura, T., S. Suzuki, H. Origasa, A. Hosono, M. Suzuki, T. Sawada, S. Terao, Y. Muto, and T. Koga. 2016. Liver-related safety assessment of green tea extracts in humans: A systematic review of randomized controlled trials. *European Journal of Clinical Nutrition* 70 (11):1221–9. doi: 10.1038/ejcn.2016.78.

Janssens, P., R. Hursel, and M. S. Westerterp-Plantenga. 2015. Long-Term green tea extract supplementation does not affect fat absorption, resting energy expenditure, and body composition in adults. *The Journal of Nutrition* 145 (5):864–70. doi: 10.3945/jn.114.207829.

Jiang, H., F. Yu, L. Qin, N. Zhang, Q. Cao, W. Schwab, D. Li, and C. Song. 2019. Dynamic change in amino acids, catechins, alkaloids, and gallic acid in six types of tea processed from the same batch of fresh tea (*Camellia sinensis* L.) leaves. *Journal of Food Composition and Analysis* 77:28–38. doi: 10.1016/j.jfca.2019.01.005.

Jurgens, T. M., A. M. Whelan, L. Killian, S. Doucette, S. Kirk, and E. Foy. 2012. Green tea for weight loss and weight maintenance in overweight or obese adults. *The Cochrane Database of Systematic Reviews* 12:CD008650 doi: 10.1002/14651858.CD008650.pub2.

Kim, K. K., H. J. Cho, H. C. Kang, B. B. Youn, and K. R. Lee. 2006. Effects on weight reduction and safety of short-term phentermine administration in Korean obese people. *Yonsei Medical Journal* 47 (5):614–25. doi: 10.3349/ymj.2006.47.5.614.

Ko, C., J. Qu, D. D. Black, and P. Tso. 2020. Regulation of intestinal lipid metabolism: Current concepts and relevance to disease. *Nature Reviews Gastroenterology & Hepatology* 17 (3):169–83. doi: 10.1038/s41575-019-0250-7.

Kowalska, G. 2021. The safety assessment of toxic metals in commonly used herbs, spices, tea, and coffee in Poland. *International Journal of Environmental Research and Public Health* 18 (11):5779. doi: 10.3390/ijerph18115779.

Ladabaum, U., A. Mannalithara, P. A. Myer, and G. Singh. 2014. Obesity, abdominal obesity, physical activity, and caloric intake in US adults: 1988 to 2010. *The American Journal of Medicine* 127 (8):717–27. doi: 10.1016/j.amjmed.2014.02.026.

Langin, D., A. Dicker, G. Tavernier, J. Hoffstedt, A. Mairal, M. Rydén, E. Arner, A. Sicard, C. M. Jenkins, N. Viguerie, et al. 2005. Adipocyte lipases and defect of lipolysis in human obesity. *Diabetes* 54 (11):3190–doi: 10.2337. /diabetes.54.11.3190.

Lee, J. M., S. Pilli, A. Gebremariam, C. C. Keirns, M. M. Davis, S. Vijan, G. L. Freed, W. H. Herman, and J. G. Gurney. 2010. Getting heavier, younger: Trajectories of obesity over the life course. *International Journal of Obesity (2005)* 34 (4):614–23. doi: 10.1038/ijo.2009.235.

Lee, L. S., J. H. Choi, M. J. Sung, J. Y. Hur, H. J. Hur, J. D. Park, Y. C. Kim, E. J. Gu, B. Min, and H. J. Kim. 2015. Green tea changes serum and liver metabolomic profiles in mice with high-fat diet-induced obesity. *Molecular Nutrition & Food Research* 59 (4):784–94. doi: 10.1002/mnfr.201400470.

Lee, M. S., C. T. Kim, and Y. Kim. 2009. Green tea (-)-Epigallocatechin-3-Gallate reduces body weight with regulation of multiple genes expression in adipose tissue of diet-induced obese mice. *Annals of Nutrition & Metabolism* 54 (2):151–7. doi: 10.1159/000214834.

Lee, P., B. R. Yacyshyn, and M. B. Yacyshyn. 2019. Gut microbiota and obesity: An opportunity to alter obesity through faecal microbiota transplant (FMT). *Diabetes, Obesity & Metabolism* 21 (3):479–90. doi: 10.1111/dom.13561.

Lee, W., D. Lee, E. Han, and J. Choi. 2019. Intake of green tea products and obesity in nondiabetic overweight and obese females: A systematic review and meta-analysis. *Journal of Functional Foods* 58:330–7. doi: 10.1016/j.jff.2019.05.010.

Lettieri-Barbato, D., E. Giovannetti, and K. Aquilano. 2016. Effects of dietary restriction on adipose mass and biomarkers of healthy aging in human. *Aging* 8 (12):3341–55. doi: 10.18632/aging.101122.

Li, H. Y., H. C. Kek, J. Lim, R. W. Gelling, and W. P. Han. 2016. Green tea (-)-epigallocatechin-3-gallate counteracts daytime overeating induced by high-fat diet in mice. *Molecular Nutrition & Food Research* 60 (12):2565–75. doi: 10.1002/mnfr.201600162.

Li, J. H., T. N. Sapper, E. Mah, S. Rudraiah, K. E. Schill, C. Chitchumroonchokchai, M. V. Moller, J. D. McDonald, P. R. Rohrer, J. E. Manautou, et al. 2016. Green tea extract provides extensive Nrf2-independent protection against lipid accumulation and NFκB pro-inflammatory responses during nonalcoholic steatohepatitis in mice fed a high-fat diet. *Molecular Nutrition & Food Research* 60 (4):858–70. doi: 10.1002/mnfr.201500814.

Li, J. J., C. J. Huang, and D. Xie. 2008. Anti-obesity effects of conjugated linoleic acid, docosahexaenoic acid, and eicosapentaenoic acid. *Molecular Nutrition & Food Research* 52 (6):631–45. doi: 10.1002/mnfr.200700399.

Li, M., J. Xu, Y. Zhang, S. Chu, S. Sun, Y. Huo, J. Zhao, X. Hu, C. Wan, and L. Li. 2020. Comparative analysis of fecal metabolite profiles in HFD-induced obese mice after oral administration of Huangjinya green tea extract. *Food and Chemical Toxicology : An International Journal Published for the British Industrial Biological Research Association* 145:111744 doi: 10.1016/j.fct.2020.111744.

Li, Q., Z. H. Liu, J. A. Huang, G. A. Luo, Q. L. Liang, D. Wang, X. Y. Ye, C. B. Wu, L. L. Wang, and J. H. Hu. 2013. Anti-obesity and hypolipidemic effects of Fuzhuan brick tea water extract in high-fat diet-induced obese rats. *Journal of the Science of Food and Agriculture* 93 (6):1310–6. doi: 10.1002/jsfa.5887.

Li, X., W. Wang, L. M. Hou, H. H. Wu, Y. J. Wu, R. Xu, Y. Xiao, and X. M. Wang. 2020. Does tea extract supplementation benefit metabolic syndrome and obesity? A systematic review and meta-analysis. *Clinical Nutrition* 39 (4):1049–58. doi: 10.1016/j.clnu.2019.05.019.

Liberini, C. G., M. Ghidewon, T. Ling, R. Lhamo, N. Juntereal, L. M. Stein, and M. R. Hayes. 2020. Early life overnutrition impairs plasticity of non-neuronal brainstem cells and drives obesity in offspring across development in rats. *International Journal of Obesity (2005)* 44 (12):2405–18. doi: 10.1038/s41366-020-00658-5.

Lin, Y. S., Y. J. Tsai, J. S. Tsay, and J. K. Lin. 2003. Factors affecting the levels of tea polyphenols and caffeine in tea leaves. *Journal of Agricultural and Food Chemistry* 51 (7):1864–73. doi: 10.1021/jf021066b.

Lin, Y., D. Shi, B. Su, J. Wei, M. -A. Găman, M. Sedanur Macit, I. J. Borges do Nascimento, and N. S. Guimaraes. 2020. The effect of green tea supplementation on obesity: A systematic review and dose-response meta-analysis of randomized controlled trials. *Phytotherapy Research* 34 (10):2459–70. doi: 10.1002/ptr.6697.

Liu, D., J. Huang, Y. Luo, B. Wen, W. Wu, H. Zeng, and Z. Liu. 2019. Fuzhuan brick tea attenuates high-fat diet-induced obesity and associated metabolic disorders by shaping gut microbiota. *Journal of Agricultural and Food Chemistry* 67 (49):13589–604. doi: 10.1021/acs.jafc.9b05833.

Liu, Z. B., Z. C. Chen, H. W. Guo, D. P. He, H. R. Zhao, Z. Y. Wang, W. Zhang, L. Liao, C. Zhang, and L. Ni. 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):4869–79. doi: 10.1039/c6fo01439a.

Liu, Z., Q. Chen, C. Zhang, and L. Ni. 2022. Comparative study of the anti-obesity and gut microbiota modulation effects of green tea phenolics and their oxidation products in high-fat-induced obese mice. *Food Chemistry* 367:130735 doi: 10.1016/j.foodchem.2021.130735.

Lopez, M. 2018. Hypothalamic AMPK and energy balance. *European Journal of Clinical Investigation* 48 (9):e12996. doi: 10.1111/eci.12996.

Lu, X., J. Liu, N. Zhang, Y. Fu, Z. Zhang, Y. Li, W. Wang, Y. Li, P. Shen, and Y. Cao. 2019. Ripened pu-erh tea extract protects mice from obesity by modulating gut microbiota composition. *Journal of Agricultural and Food Chemistry* 67 (25):6978–94. doi: 10.1021/acs.jafc.8b04909.

Ma, H., B. Zhang, Y. Hu, X. Li, J. Wang, F. Yang, X. Ji, and S. Wang. 2020. The novel intervention effect of cold green tea beverage on high-fat diet induced obesity in mice. *Journal of Functional Foods* 75:104279. doi: 10.1016/j.jff.2020.104279.

MacDougald, O. A., and M. D. Lane. 1995. Adipocyte differentiation. When precursors are also regulators. *Current Biology : CB* 5 (6):618–21. doi: 10.1016/S0960-9822(95)00125-4.

Maki, K. C., M. S. Reeves, M. Farmer, K. Yasunaga, N. Matsuo, Y. Katsuragi, M. Komikado, I. Tokimitsu, D. Wilder, F. Jones, et al. 2009. Green tea catechin consumption enhances exercise-induced abdominal fat loss in overweight and obese adults. *The Journal of Nutrition* 139 (2):264–70. doi: 10.3945/jn.108.098293.

Mao, Q. Q., B. Y. Li, J. M. Meng, R. Y. Gan, X. Y. Xu, Y. Y. Gu, X. H. Wang, and H. B. Li. 2021. Effects of several tea extracts on nonalcoholic fatty liver disease in mice fed with a high-fat diet. *Food Science & Nutrition* 9 (6):2954–67. doi: 10.1002/fsn3.2255.

Marlatt, K. L., and E. Ravussin. 2017. Brown adipose tissue: An update on recent findings. *Current Obesity Reports* 6 (4):389–96. doi: 10.1007/s13679-017-0283-6.

Mika, M., A. Wikiera, A. Antończyk, and M. Grabacka. 2017. Food stabilizing antioxidants increase nutrient bioavailability in the in vitro model. *Journal of the American College of Nutrition* 36 (7):579–85. doi: 10.1080/07315724.2017.1333930.

Muenzner, M., N. Tappenbeck, F. Gembardt, R. Rulke, J. Furkert, M. F. Melzig, W. E. Siems, G. A. Brockmann, and T. Walther. 2016. Green tea reduces body fat via upregulation of neprilysin. *International Journal of Obesity* 40 (12):1850–5. doi: 10.1038/ijo.2016.172.

Murase, T., A. Nagasawa, J. Suzuki, T. Hase, and I. Tokimitsu. 2002. Beneficial effects of tea catechins on diet-induced obesity: Stimulation of lipid catabolism in the liver. *International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity* 26 (11):1459–64. doi: 10.1038/sj.ijo.0802141.

Nagao, T., T. Hase, and I. Tokimitsu. 2007. A green tea extract high in catechins reduces body fat and cardiovascular risks in humans. *Obesity (Silver Spring, Md.)* 15 (6):1473–83. doi: 10.1038/oby.2007.176.

Neyrinck, A. M., L. B. Bindels, L. Geurts, M. Van Hul, P. D. Cani, and N. M. Delzenne. 2017. A polyphenolic extract from green tea leaves activates fat browning in high-fat-diet-induced obese mice . *The Journal of Nutritional Biochemistry* 49:15–21. doi: 10.1016/j.jnutbio.2017.07.008.

Nishiumi, S., H. Bessyo, M. Kubo, Y. Aoki, A. Tanaka, K. Yoshida, and H. Ashida. 2010. Green and black tea suppress hyperglycemia and insulin resistance by retaining the expression of glucose transporter 4 in muscle of high-fat diet-fed C57BL/6J mice. *Journal of Agricultural and Food Chemistry* 58 (24):12916–23. doi: 10.1021/jf102840w.

Oi, Y., I. C. Hou, H. Fujita, and K. Yazawa. 2012. Antiobesity effects of Chinese black tea (Pu-erh tea) extract and gallic acid. *Phytotherapy Research : PTR* 26 (4):475–81. doi: 10.1002/ptr.3602.

Otton, R., N. Petrovic, B. Cannon, and J. Nedergaard. 2021. On the validity of adipogenic cell lines as model systems for browning processes: In authentic brown, brite/beige, and white preadipocytes, there is no cell-autonomous thermogenic recruitment by green tea compounds. *Frontiers in Nutrition* 8:715859 doi: 10.3389/fnut.2021.715859.

Paspala, I., N. Katsiki, D. Kapoukranidou, D. P. Mikhailidis, and A. Tsiligiroglou-Fachantidou. 2012. The role of psychobiological and neuroendocrine mechanisms in appetite regulation and obesity. *The Open Cardiovascular Medicine Journal* 6:147–55. doi: 10.2174/1874192401206010147.

Pilitsi, E., O. M. Farr, S. A. Polyzos, N. Perakakis, A. E. Papathanasiou, and C. S. Mantzoros. 2019. Pharmacotherapy of obesity: Available medications and drugs under investigation. *Metabolism: Clinical and Experimental* 92:170–92. doi: 10.1016/j.metabol.2018.10.010.

Poulsen, L. L. C., M. Siersbaek, and S. Mandrup. 2012. PPARs: Fatty acid sensors controlling metabolism. *Seminars in Cell & Developmental Biology* 23 (6):631–9. doi: 10.1016/j.semcdb.2012.01.003.

Roberto, B. S., G. A. Macedo, J. A. Macedo, I. M. Martins, V. M. Nakajima, J. W. Allwood, D. Stewart, and G. J. McDougall. 2016. Immobilized tannase treatment alters polyphenolic composition in teas and their potential anti-obesity and hypoglycemic activities in vitro. *Food & Function* 7 (9):3920–32. doi: 10.1039/c6fo00373g.

Roberts, J. D., A. G. B. Willmott, L. Beasley, M. Boal, R. Davies, L. Martin, H. Chichger, L. Gautam, and J. Del Coso. 2021. The impact of decaffeinated green tea extract on fat oxidation, body composition and cardio-metabolic health in overweight, recreationally active individuals. *Nutrients* 13 (3):764. doi: 10.3390/nu13030764.

Rocha, A., A. P. Bolin, C. Cardoso, and R. Otton. 2016. Green tea extract activates AMPK and ameliorates white adipose tissue metabolic dysfunction induced by obesity. *European Journal of Nutrition* 55 (7):2231–44. doi: 10.1007/s00394-015-1033-8.

Rosen, E. D., and B. M. Spiegelman. 2006. Adipocytes as regulators of energy balance and glucose homeostasis. *Nature* 444 (7121):847–53. doi: 10.1038/nature05483.

Rufino, A. T., V. M. Costa, F. Carvalho, and E. Fernandes. 2021. Flavonoids as antiobesity agents: A review. *Medicinal Research Reviews* 41 (1):556–85. doi: 10.1002/med.21740.

Rupasinghe, H. P. V., S. Sekhon-Loodu, T. Mantso, and M. I. Panayiotidis. 2016. Phytochemicals in regulating fatty acid β-oxidation: Potential underlying mechanisms and their involvement in obesity and weight loss. *Pharmacology & Therapeutics* 165:153–63. doi: 10.1016/j.pharmthera.2016.06.005.

Sae-Tan, S., C. J. Rogers, and J. D. Lambert. 2014. Voluntary exercise and green tea enhance the expression of genes related to energy utilization and attenuate metabolic syndrome in high fat fed mice. *Molecular Nutrition & Food Research* 58 (5):1156–9. doi: 10.1002/mnfr.201300621.

Sae-Tan, S., C. J. Rogers, and J. D. Lambert. 2015. Decaffeinated green tea and voluntary exercise induce gene changes related to beige adipocyte formation in high fat-fed obese mice. *Journal of Functional Foods* 14:210–4. doi: 10.1016/j.jff.2015.01.036.

Salas-Salvadó, J., A. Díaz-López, M. Ruiz-Canela, J. Basora, M. Fitó, D. Corella, L. Serra-Majem, J. Wärnberg, D. Romaguera, R. Estruch, et al. 2018. Effect of a lifestyle intervention program m with energy-restricted Mediterranean diet and exercise on weight loss and cardiovascular risk factors: One-Year results of the PREDIMED-Plus trial. *Diabetes Care* 42 (5):dc180836–788., doi: 10.2337/dc18-0836.

Sarma, D. N., M. L. Barrett, M. L. Chavez, P. Gardiner, R. Ko, G. B. Mahady, R. J. Marles, L. S. Pellicore, G. I. Giancaspro, and T. L. Dog. 2008. Safety of green tea extracts: A systematic review by the US Pharmacopeia. *Drug Safety* 31 (6):469–84. doi: 10.2165/00002018-200831060-00003.

Schadinger, S. E., N. Bucher, B. M. Schreiber, and S. R. Farmer. 2005. PPAR gamma 2 regulates lipogenesis and lipid accumulation in steatotic hepatocytes. *American Journal of Physiology. Endocrinology and Metabolism* 288 (6):E1195–1205. doi: 10.1152/ajpendo.00513.2004.

Scheele, C., and S. Nielsen. 2017. Metabolic regulation and the anti-obesity perspectives of human brown fat. *Redox Biology* 12:770–5. doi: 10.1016/j.redox.2017.04.011.

Seo, D. B., H. W. Jeong, D. Cho, B. J. Lee, J. H. Lee, J. Y. Choi, I. H. Bae, and S. J. Lee. 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):549–56. doi: 10.1089/jmf.2014.3265.

Shen, C. L., J. J. Cao, R. Y. Dagda, S. Chanjaplammootil, C. W. Lu, M. C. Chyu, W. M. Gao, J. S. Wang, and J. K. Yeh. 2012. Green tea polyphenols benefits body composition and improves bone quality in long-term high-fat diet-induced obese rats. *Nutrition Research (New York, N.Y.)* 32 (6):448–57. doi: 10.1016/j.nutres.2012.05.001.

Shevchuk, A., R. Megías-Pérez, Y. Zemedie, and N. Kuhnert. 2020. Evaluation of carbohydrates and quality parameters in six types of commercial teas by targeted statistical analysis. *Food Research International (Ottawa, Ont.)* 133:109122 doi: 10.1016/j.foodres.2020.109122.

Shimotoyodome, A., S. Haramizu, M. Inaba, T. Murase, and I. Tokimitsu. 2005. Exercise and green tea extract stimulate fat oxidation and prevent obesity in mice. *Medicine & Science in Sports & Exercise* 37 (11):1884–92. doi: 10.1249/01.mss.0000178062.66981.a8.

Spiegelman, B. M., and J. S. Flier. 2001. Obesity and the regulation of energy balance. *Cell* 104 (4):531–43. doi: 10.1016/S0092-8674(01)00240-9.

Sun, N. N., T. Y. Wu, and C. F. Chau. 2016. Natural dietary and herbal products in Anti-Obesity treatment. *Molecules* 21 (10):1351. doi: 10.3390/molecules21101351.

Sun, Y., Y. W. Wang, P. P. Song, H. S. Wang, N. Xu, Y. J. Wang, Z. Z. Zhang, P. X. Yue, and X. L. Gao. 2019. Anti-obesity effects of instant fermented teas in vitro and in mice with high-fat-diet-induced obesity. *Food & Function* 10 (6):3502–13. doi: 10.1039/C9FO00162J.

Tang, G. Y., X. Meng, R. Y. Gan, C. N. Zhao, Q. Liu, Y. B. Feng, S. Li, X. L. Wei, A. G. Atanasov, H. Corke, et al. 2019. Health functions and related molecular mechanisms of tea components: An update review. *International Journal of Molecular Sciences* 20 (24):6196. doi: 10.3390/ijms20246196.

Tong, L., L. Wang, S. S. Yao, L. N. Jin, J. Yang, Y. F. Zhang, G. Ning, and Z. G. Zhang. 2019. PPARδ attenuates hepatic steatosis through autophagy-mediated fatty acid oxidation . *Cell Death & Disease* 10 (3):197 doi: 10.1038/s41419-019-1458-8.

Torgerson, J. S., J. Hauptman, M. N. Boldrin, and L. Sjöström. 2004. XENical in the prevention of diabetes in obese subjects (XENDOS) study: A randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 27 (1):155–61. doi: 10.2337/diacare.27.1.155.

Torres-Fuentes, C., H. Schellekens, T. G. Dinan, and J. F. Cryan. 2017. The microbiota-gut-brain axis in obesity. *The Lancet. Gastroenterology & Hepatology* 2 (10):747–56. doi: 10.1016/S2468-1253(17)30147-4.

Trigueros, L., S. Peña, A. V. Ugidos, E. Sayas-Barberá, J. A. Pérez-Álvarez, and E. Sendra. 2013. Food ingredients as anti-obesity agents: A review. *Critical Reviews in Food Science and Nutrition* 53 (9):929–42. doi: 10.1080/10408398.2011.574215.

Tsai, C. H., W. C. Chiu, N. C. Yang, C. M. Ouyang, and Y. H. Yen. 2009. A novel green tea meal replacement formula for weight loss among obese individuals: A randomized controlled clinical trial. *International Journal of Food Sciences and Nutrition* 60 (sup6):151–9. 6: doi: 10.1080/09637480903136667.

Uchiyama, S., Y. Taniguchi, A. Saka, A. Yoshida, and H. Yajima. 2011. Prevention of diet-induced obesity by dietary black tea polyphenols extract in vitro and in vivo. *Nutrition* 27 (3):287–92. doi: 10.1016/j.nut.2010.01.019.

Valassi, E., M. Scacchi, and F. Cavagnini. 2008. Neuroendocrine control of food intake. *Nutrition, Metabolism, and Cardiovascular Diseases : NMCD* 18 (2):158–68. doi: 10.1016/j.numecd.2007.06.004.

Varga, T., Z. Czimmerer, and L. Nagy. 2011. PPARs are a unique set of fatty acid regulated transcription factors controlling both lipid metabolism and inflammation. *Biochimica et Biophysica Acta* 1812 (8):1007–22. doi: 10.1016/j.bbadis.2011.02.014.

Wang, L., B. Zhou, Z. Zhao, L. Yang, M. Zhang, Y. Jiang, Y. Li, M. Zhou, L. Wang, Z. Huang, et al. 2021. Body-mass index and obesity in urban and rural China: Findings from consecutive nationally representative surveys during 2004-18. *The Lancet* 398 (10294):53–63. doi: 10.1016/S0140-6736(21)00798-4.

Williams, E. P., M. Mesidor, K. Winters, P. M. Dubbert, and S. B. Wyatt. 2015. Overweight and obesity: Prevalence, consequences, and causes of a growing public health problem. *Current Obesity Reports* 4 (3):363–70. doi: 10.1007/s13679-015-0169-4.

Wolfram, S., Y. Wang, and F. Thielecke. 2006. Anti-obesity effects of green tea: From bedside to bench. *Molecular Nutrition & Food Research* 50 (2):176–87. doi: 10.1002/mnfr.200500102.

World Health Organization. 2021. Obesity and overweight. Last Modified June 9, 2021. Accessed June 20, 2021. https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight.

Wu, L., L. Zhang, B. Li, H. Jiang, Y. Duan, Z. Xie, L. Shuai, J. Li, and J. Li. 2018. AMP-Activated protein kinase (AMPK) regulates energy metabolism through modulating thermogenesis in adipose tissue. *Frontiers in Physiology* 9:122 doi: 10.3389/fphys.2018.00122.

Xia, Y., D. Tan, R. Akbary, J. Kong, R. Seviour, and Y. Kong. 2019. Aqueous raw and ripe Pu-erh tea extracts alleviate obesity and alter cecal microbiota composition and function in diet-induced obese rats. *Applied Microbiology and Biotechnology* 103 (4):1823–35. doi: 10.1007/s00253-018-09581-2.

Xu, J., M. Li, Y. Zhang, S. Chu, Y. Huo, J. Zhao, and C. Wan. 2020. Huangjinya black tea alleviates obesity and insulin resistance via modulating fecal metabolome in High-Fat Diet-Fed mice. *Molecular Nutrition & Food Research* 64 (22):e2000353 doi: 10.1002/mnfr.202000353.

Xu, N., J. Chu, M. Wang, L. Chen, L. Zhang, Z. W. Xie, J. S. Zhang, C. T. Ho, D. X. Li, and X. C. Wan. 2018. Large yellow tea attenuates macrophage-related chronic inflammation and metabolic syndrome in high-fat diet treated mice. *Journal of Agricultural and Food Chemistry* 66 (15):3823–32. doi: 10.1021/acs.jafc.8b00138.

Xu, X., C. Zhao, S. Cao, G. Tang, R. Gan, and H. Li. 2020. Effects and mechanisms of tea for the prevention and management of cancers: An updated review. *Critical Reviews in Food Science and Nutrition* 60 (10):1693–705. doi: 10.1080/10408398.2019.1588223.

Xu, X.-Y., J.-M. Meng, Q.-Q. Mao, A. Shang, B.-Y. Li, C.-N. Zhao, G.-Y. Tang, S.-Y. Cao, X.-L. Wei, R.-Y. Gan, et al. 2019. Effects of tannase and ultrasound treatment on the bioactive compounds and antioxidant activity of green tea extract. *Antioxidants* 8 (9):362. doi: 10.3390/antiox8090362.

Xu, Y., M. Zhang, T. Wu, S. D. Dai, J. L. Xu, and Z. K. Zhou. 2015. The anti-obesity effect of green tea polysaccharides, polyphenols and caffeine in rats fed with a high-fat diet. *Food & Function* 6 (1):297–304. doi: 10.1039/c4fo00970c.

Xu, Y., N. Wang, H. Y. Tan, S. Li, C. Zhang, and Y. Feng. 2021. Gut-liver axis modulation of Panax notoginseng saponins in non-alcoholic fatty liver disease. *Hepatology International* 15 (2):350–65. doi: 10.1007/s12072-021-10138-1.

Xu, Y., N. Wang, H. Y. Tan, S. Li, C. Zhang, Z. Zhang, and Y. Feng. 2020. Panax notoginseng saponins modulate the gut microbiota to promote thermogenesis and beige adipocyte reconstruction via leptin-mediated AMPKα/STAT3 signaling in diet-induced obesity. *Theranostics* 10 (24):11302–23. doi: 10.7150/thno.47746.

Yamashita, Y., L. Q. Wang, L. H. Wang, Y. Tanaka, T. S. Zhang, and H. Ashida. 2014. Oolong, black and Pu-erh tea suppresses adiposity in mice via activation of AMP-activated protein kinase. *Food & Function* 5 (10):2420–9. doi: 10.1039/c4fo00095a.

Yan, J. Q., Y. Zhao, and B. L. Zhao. 2013. Green tea catechins prevent obesity through modulation of peroxisome proliferator-activated receptors. *Science China. Life Sciences* 56 (9):804–10. doi: 10.1007/s11427-013-4512-2.

Yu, H., H. Z. Sun, X. R. Wang, Y. Liang, M. M. Guo, J. W. Yu, M. Yang, X. Z. Zhang, F. J. Luo, and L. Zhou. 2021. Residue behavior and safety evaluation of pymetrozine in tea. *Journal of the Science of Food and Agriculture* 101 (10):4118–24. doi: 10.1002/jsfa.11047.

Yuan, E. D., X. F. Duan, L. M. Xiang, J. Y. Ren, X. F. Lai, Q. H. Li, L. L. Sun, and S. L. Sun. 2018. Aged oolong tea reduces high-fat diet-induced fat accumulation and dyslipidemia by regulating the AMPK/ACC signaling pathway. *Nutrients* 10 (2):187. doi: 10.3390/nu10020187.

Zang, L., Y. Shimada, H. Nakayama, H. Katsuzaki, Y. Kim, D. Chu, L. R. Juneja, J. Kuroyanagi, and N. Nishimura. 2021. Preventive effects of green tea extract against obesity development in zebrafish. *Molecules* 26 (9):2627. doi: 10.3390/molecules26092627.

Zhang, X., M. Zhang, C. T. Ho, X. J. Guo, Z. F. Wu, P. F. Weng, M. D. Yan, and J. X. Cao. 2018. Metagenomics analysis of gut microbiota modulatory effect of green tea polyphenols by high fat

diet-induced obesity mice model. *Journal of Functional Foods* 46:268–77. doi: 10.1016/j.jff.2018.05.003.

Zhang, Y., S. Li, R. Gan, T. Zhou, D. Xu, and H. Li. 2015. Impacts of gut bacteria on human health and diseases. *International Journal of Molecular Sciences* 16 (4):7493–519. doi: 10.3390/ijms16047493.

Zhang, Y., Y. J. Yu, X. Li, S. Meguro, S. Hayashi, M. Katashima, T. Yasumasu, J. Z. Wang, and K. J. Li. 2012. Effects of catechin-enriched green tea beverage on visceral fat loss in adults with a high proportion of visceral fat: A double-blind, placebo-controlled, randomized trial. *Journal of Functional Foods* 4 (1):315–22. doi: 10.1016/j.jff.2011.12.010.

Zhao, C. N., G. Y. Tang, S. Y. Cao, X. Y. Xu, R. Y. Gan, Q. Liu, Q. Q. Mao, A. Shang, and H. B. Li. 2019. Phenolic profiles and antioxidant activities of 30 Tea infusions from green, black, oolong, white, yellow and dark Teas. *Antioxidants* 8 (7):215. doi: 10.3390/antiox8070215.