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Review

The effects of green tea on lipid metabolism and its potential applications for obesity and related metabolic disorders - An existing update

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ABSTRACT

Obesity is one of the top global issues, which induces several serious health consequences both physically and mentally, such as type 2 diabetes, cardiovascular diseases, dyslipidemia, eating disorders, depression and stress. However, the effective therapy to prevent and treat obesity and overweight, up to now, cannot be found nowadays. Several methods/medicines namely diet control, energy balance, environmental changes, genetic and stem cell therapies, new drugs/chemicals have been extensively studied to enhance the ability to control bodyweight and prevent obesity. Of all the aforementioned methods, green tea, used as a daily beverage, has shown beneficial impacts for the health, especially its anti-obesity effects. Available evidence shows that green tea can interrupt lipid emulsification, reduce adipocyte differentiation, increase thermogenesis, and reduce food intake, thus green tea improves the systemic metabolism and decreases fat mass. Here, we highlight and sum up the update investigations of anti-obesity effect of green tea as well as discuss the potential application of them for preventing obesity and its related metabolic disorders.

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1. Introduction

Obesity is one of the top problems in global health inducing several health consequences [1,2]. There has been recorded that more than 1.9 billion adults aged 18 years and older were overweight, including 650 million obese people, in 2016 (according to WHO). It was also estimated about 13% of the adult global population and 20% of US children and adolescents suffered from obesity in that same year. Body mass index (BMI) (weight/height^2) is generally used to define overweight and obesity. The BMI range is 18.5–24.9 kg/m^2 for healthy, from 25 to 29.9 kg/m^2 for overweight, and over 30 kg/m^2 for obesity [3].

Obesity is not a single disorder, but combination of genetic, metabolic, food habit, environmental, physical activity, social and culture factors [4,5]. It leads to imbalance energy and storage of excessive amount of lipids in adipose tissue which result in obesity [6]. Leptin, as a the energy regulation hormone in adipose cells, is considered as a player in lipid metabolism and food intake. Mutation of *ob* gene leads to obesity [7]. Recently, about 200 genes associated with obesity have been identified [8].

Obesity and overweight cause serious impacts on health, including type 2 diabetes, hypertension, dyslipidemia, cardiovascular diseases, musculoskeletal disorders, aging and cancers [1,9–11]. Overweight and obesity also influence variety of mood disorders including depressive disorders, bipolar disorders, anxiety disorders, posttraumatic stress disorders, and dementia, sleep disturbances [2,12,13]. Waist circumference (WC), an indicators for body fat, was found to be correlated with blood pressure in a study group in Vietnam [14]. Obesity and its health consequences are related and increased during aging [15].

Overweight and obesity are the results of energy imbalance by eating more calories than demand. The risk of obesity-related diseases is higher depending on the period and level of obesity. It is the fact that obesity and its related diseases are difficult to treat and prevent. The treatment method depends on the level of obesity, health status and patient's motivation to lose weight and cut down the weight regained. The lack of physical activity and poor eating habit are generally the main reasons for obesity in young people. Therefore, the appetite regulation and regular physical activity are the most efficient methods to control the weight gain. Several treatment strategies have been studied and tried to prevent obesity and overweight [2,16–18], but there has not been any optimal solution for this metabolic disorder.

2. Green tea and its health effects

Green tea, named *Camellia sinensis,* is a type of tea plant in *Theaceace* family. Tea is one of the most popular non-alcoholic beverages in the world, and over three million tones are grown annually. *Camellia sinensis* grows mainly in tropical and subtropical climates. Tea plant is cultured from seed which needs 7–10 years to get ready for harvesting. Two varieties of tea have been found namely *Camellia sinensis* var. *sinensis* used in China and Japan and *C.s. var. assamica* used in India. Among these countries, tea leaves are processed to green tea; however, in India and Turkey, they were made to red or black tea.

Green tea possesses a great amount of bioactive components including free amino acids, caffeine and polyphenols. Especially, catechins, which is the major class of polyphenols, have shown high biological activity. Generally, the amount of catechin and its derivatives were qualitied in the green tea infusion, including (−)-epigallocatechin gallate (EGCG), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), (−)-epicatechin (EC) and (+)-catechin (C), which were 117–442 mg/l, 203–471 mg/l, 16.9–150 mg/l, 25–81 mg/l and 9.03–115 mg/l, respectively [19]. Hydroxyl groups in catechins are highly associated with the antioxidant properties of green tea, that will bind and react with free radicals in the bloodstream [20]. In green tea infusions, caffeine contents varied from 141 to 338 mg/l [19]. Other components included in green tea infusion are flavonoids (<10% of total polyphenols), known as kaempferol, quercetin, and myricetin [21], which are potent antioxidants. Besides, green tea also contains many nutritional components such as vitamins and minerals, amino acids, lipids, carbohydrates and pigments. There are a huge number of metal found in green tea extract as potassium (92–151 mg/l), sodium (35–69 mg/l), calcium (1.9–3.5 mg/l), fluoride (0.80–2.0 mg/l), aluminum (1.0–2.2 mg/l), manganese (0.52–1.9 mg/l), and iron (0.020–0.128 mg/l) [19].

There are several investigations about beneficial effects of green tea, including antioxidative, anti-inflammatory, antibacterial, antiviral, anti-angiogenic effects and against cancer, obesity, diabetes and cardiovascular diseases [22]. Green tea has been investigated to prevent many types of cancer such as lung, colon, stomach, liver and prostate cancer. EGCG, the main green tea catechin, inhibits proliferative activity in hematoma cells and suppresses lipidemic activity in hematoma-treated rats, regulates immune activity and cancer post-initiation [23]. Green tea (0.1–2.0% of diet) suppressed the tumor and the DMH-induced expression of ras p21 - a marker of genetic alteration in colon cancer [24,25]. EGCG is also considered as an anticancer agent and as a compound that can improve functions of immune system in lung cancer [26].

Green tea catechins increased directly or indirectly total plasma antioxidant activity, as well as inhibited LDL oxidation, and decreased HDL cholesterol [27,28]. A randomized controlled trial reported that total blood cholesterol was significantly reduced after 4 weeks of use of green tea extract comparing to the control group of postmenopausal women [29].

Green tea has been used as a treatment for diarrhea and typhoid for a long time in Asia. Catechins are used to treat *Helicobacter pylori* infection [30] and a variety of viruses known as influenza A, hepatitis B and C, herpes simplex and adenovirus. Especially, the antibacterial effects of EGCG alone and in combination with different antibiotic against multidrug-resistant strain *Staphylococcus aureus* and *Pseudomonas aeruginosa* have also been demonstrated [31,32]. Furthermore, EGCG has shown the antifungal activity like *Candida albicans* infection in human [31].

There has been evidence presenting that it is possible for green tea to be used for the prevention and treatment of obesity and type 2 diabetic. Catechins in green tea decreased serum glucose levels [33], specially EGCG could mimic action of insulin and improve insulin resistance [34,35]. Additionally, catechins reduced the absorption of triglycerides, cholesterol and regulate lipid and glucose metabolism in high-fat diet (HFD) mouse model [23,35,36].

Moreover, feeding 0.5% green tea catechins for 4 months prevented muscle atrophy in HDF SAMP8 mice, which correlated with insulin resistance and anti-obesity effects of green tea [37].

Nonetheless, green tea has some negative health effects which are found on excessive consumption of green tea. Possible side effects include nausea, vomiting, dehydration, lethargy, central nervous system stimulation, heart rate irregularities. Polyphones present in green tea may also stain the teeth.

3. The effect of green tea on lipid metabolism

Lipid accumulation, which is one of the clear evidence resulting in overweight and obesity, is related to insulin resistance in muscle and liver and a well-known factor in the development of type 2 diabetes [38,39]. Lipid accumulation is the consequence of either increasing lipogenesis, fatty acid uptake, or reducing fatty acid oxidation [40].

Green tea catechins have been investigated recently in the modulation of serum lipid homeostasis. Mak-Soon Lee et al. observed that lipid droplets in 3T3-L1 adipocytes were suppressed after 24 h of incubation with 10 μM green tea catechins without any side effects on cell viability during differentiation [41]. Another study, which was conducted by Furuyashiki et al. also found the attenuation of lipid accumulation of green tea components in 3T3-L1. CG and ECG reducing the number of lipid droplets from day 3 and 50% suppression in day 8, suggests that green tea possesses the effects in early and late stage of differentiation process [42]. Similar results after treatment with green tea were found in the mouse experiments and human trials. It was clear that lipid accumulation in hepatocytes decreased after treatment 3.2 g EGCG/kg in 16 weeks in HDF mice [43]. In human, body weight and abdominal fat were significantly decreased comparing to control group (lower green tea catechin diet) [44]. Both green tea catechins and caffeine regulated lipid accumulation. The combination of high concentration of catechins, EGCG or caffeine had stronger anti-obesity effects than EGCG, green tea extract or caffeine alone [45,46], which can lower body weight and lipid accumulation.

Green tea catechins and caffeine reduce lipid accumulation by the inhibition of synthesis and the up-regulation of β-oxidation of fatty acids in the mouse liver [45]. Catechins reduced significantly lipogenesis genes as acyl-CoA oxidase and dehydrogenase, sterol regulatory element-binding protein-1c (SREBP-1c) and FAS, but induced oxidative genes as peroxisome proliferator-activated receptor γ2 PPAR2 and C/EBP mRNA level [44], carnitine palmitoyltransferase-I (CPT-I) and uncoupling protein 2 (UCP2) expression [47] or reduced ROS formation [48,49].

Furuyashiki et al. [33] demonstrated that catechin, CG, EGC, ECG, and EGCG at 5 lM suppressed lipid accumulation induced by the same mixture in another adipocyte model, 3T3-L1 cells. In a time-course experiment, CG and EGC attenuated lipid accumulation starting from day 3 and the amount of lipid was reduced to 50% compared to the control at day 8, suggesting that catechins inhibit both early-stage and late-stage differentiation programs Furuyashiki et al. [33] demonstrated that catechin, CG, EGC, ECG, and EGCG at 5 lM suppressed lipid accumulation induced by the same mixture in another adipocyte model, 3T3-L1 cells. In a time-course experiment, CG and EGC attenuated lipid accumulation starting from day 3 and the amount of lipid was reduced to 50% compared to the control at day 8, suggesting that catechins inhibit both early-stage and late-stage differentiation programs Furuyashiki et al. [33] demonstrated that catechin, CG, EGC, ECG, and EGCG at 5 lM suppressed lipid accumulation induced by the same mixture in another adipocyte model, 3T3-L1 cells. In a time-course experiment, CG and EGC attenuated lipid accumulation starting from day 3 and the amount of lipid was reduced to 50% compared to the control at day 8, suggesting that catechins inhibit both early-stage and late-stage differentiation programs Furuyashiki et al. [33] demonstrated that catechin, CG, EGC, ECG, and EGCG at 5 lM suppressed lipid accumulation induced by the same mixture in another adipocyte model, 3T3-L1 cells. In a time-course experiment, CG and EGC attenuated lipid accumulation starting from day 3 and the amount of lipid was reduced to 50% compared to the control at day 8, suggesting that catechins inhibit both early-stage and late-stage differentiation programs.

+ In Sprague−Dawley rats fed a high-fat diet, consumption ofa water extract of green tea for 2 wk resulted in decreasedbody fat accumulation [49]. This effect appeared to bemediated by increased energy expenditure and a slight, butstatistically significant, reduction in food digestibilitywhereas food intake was not changed [50].

+ EGCGdecreased lipogenesis and increased fat oxidation. Totalfood intake and food digestibility were not changed byEGCG supplementation. However, the energy content of the feces was slightly, but significantly, increased at the highest dosage of EGCG. This finding is in line with arecent investigation, in which EGCG caused a small, butstatistically significant, reduction of fat absorption [36].

4. The effect of green tea on adipogenesis

Most fatty acids are synthesized and stored in white adipose tissue (WAT) known as the energy storage in the body. Therefore, modulation of adipogenesis in the WAT is one of the most important ways in the anti-obesity strategies. Many investigations have showed green tea suppressed lipogenesis as well as adipogenesis [51]. Green tea and its components had reduced miRNA levels of lipogenic, adipogenic and fatty acid uptake genes. EGCG, a bioactive component in green tea, reduced expression of acetyl coenzyme A carboxylase-1, FAS and glycerol-3-phosphatase acyltransferase, sterol-coenzyme A desaturase 1 (SCD1) mRNA [52,53]. EGCG supplementation decreased lipid incorporation and adipose differentiation in obese Sprague−Dawley rats. Additionally, green tea catechins suppressed both early and middle stages of adipocyte differentiation, resulting in the suppression of adipogenesis-related transcription factors as $PPAR_{\gamma}$ and SREBP-1 genes [42,54]. Moreover, EGCG caused statistically significant reduction of fatty acid absorption [52], it also induced apoptosis of mature adipocytes without effects on preadipocytes and mature adipocyte viability in a time- and dose dependent manner [55]. Green tea significantly suppressed glucose uptake in adipose tissue, which is an input for lipogenesis [54]. However a dose-dependent-study has shown that low concentration of green tea, catechins or caffeine did not have any influence on the expression of fatty acid gene [45].

Besides catechins, other bioactive components of green tea showed partly role in adipocyte differentiation. Quercetin and genistein, green tea flavonoids, inhibited tyrosine kinase activity of insulin receptor IRS-1, IRS-2 and epidermal growth factor receptor, resulting in suppression in white adipose tissue mass [52,56–58]. Fermented green tea product, which contained higher EGCG and EGC, also showed anti-adipogenic effects [59].

5. The effect of green tea on lipolysis

These data indicate that the anti-obesity effects of green tea catechins, such as EGCG, are not mediated via increased lipolysis.

Lipolysis is the breakdown of lipids and involves hydrolysis of triglycerides into glycerol and free fatty acids. It is known that anti-obesity effects of green tea catechins, such as EGCG, are not mediated via increased lipolysis. Daily consumption of green tea has been shown to result in the body mass and blood lipid reduction. EGGC increases lipolysis and stimulates FA β-oxidation. Treatment using dose-dependent EGCG (1−50 μM) to differentiate adipocytes reduces lipolysis through direct modulation of HSL and FA-oxidative gene expression CPT-1, UCPs, and PGC-1α [41,53,60,61]. Additionally, EGCG stimulates significantly glycerol release in 3T3-L1 cells after the incubation for 24 h at 10 μM EGCG [41]. Moreover, catechins enhance lipolysis by increasing HSL phosphorylation in protein kinase A-dependent pathway in adipocytes [62], which promotes the translocation of HSL protein to the surface of lipid droplets to hydrolyze triglycerides. Green tea can also reduce oxidative stress by inducing antioxidant effects in adipose tissues. Green tea polyphenols inhibit proinflammatory genes expression as resistin, IL-6, TNFα and cytokines [60,63], which directly develops obesity [64]. The effects of green tea are enhanced by combining with other anti-obesity strategies, such as physical exercises [65]. Physical exercises promote fat oxidation, norephedrine expression, thus making green tea plus exercises

increase fatty acid release from adipose tissues [66,67]. Green tea extract (25% catechins) reduces digestive lipase activity, such as gastric lipase and pancreatic lipase, 60 mg green tea extract alternates lipid emulsification in gastric or duodenal media which consequently reduces fat digestion [68]. A double-blind study in healthy Japanese men confirmed that frequently a consumption of 690 mg catechins decreased significantly the body weight and fat mass by inducing fat oxidation after 12 weeks diet [69]. In conclusion, green tea extract expands lipolysis by increasing lipolytic proteins, anti-inflammatory cytokine while reducing proinflammatory cytokine TNF-α and lipid digestion which are enhanced by exercise and norephedrine treatment.

6. The effect of green tea on thermogenesis

Thermogenesis is the bioenergetic process, which is associated with blood glucose concentration, insulin sensitivity and adiposity in obesity and its related disorders [16,17]. The classical and inducible brown adipocytes are the two thermogenic cells which highly express uncoupling protein 1 (UCP1). In terms of thermogenesis, UCP1 protein is activated and dissipates energy as heat instead of ATP synthesis [70,71].

Several publications have shown that green tea and its components can induce thermogenesis and fat oxidation [71–75]. The main bioactive chemicals of green tea are catechins and caffeine. It has been supposed that catechins in green tea increase energy expenditure (EE) by inhibiting catechol O-methyltransferase enzyme (COMT), which degrades catecholamines, such as norepinephrine [72]. The inhibition results in stimulation of catecholamines and the increase of EE. The activity of COMT enzyme varies in different groups, which contributes to explain the difference in outcome of green tea treatment [76]. In addition, Ucp1 mRNA level in brown adipocyte tissue is increased by supplement 0.5% green tea catechin to non-fat mice in 8 weeks [71]. EGCG-fed mice induce body temperature by increasing mRNA levels of thermogenesis genes as Ucp1, Ucp2, Cpt-1β and mitochondrial biogenesis content in brown adipose tissues [77].

Caffeine in green tea also has effects on thermogenesis. A randomized, double-blind cross-over study indicated that the consumption of caffeine induces resting energy expenditure, heart rate and blood pressure in terms of weight loss [78]. Caffeine has been known to inhibit phosphodiesterase, which degrades cAMP to AMP. Therefore, caffeine blocks the activation of cAMP and promotes lipolysis [79]. Moreover, caffeine stimulates Cori and FFA turnover caused by increasing fatty acid oxidation and FFA recycling [80]. They also found that caffeine mimics the effects of adrenaline to increase EE and promote lipolytic activity. Caffeine increases glycolysis and ATP turnover by antagonizing the ryanodine receptor, consequently increasing thermogenesis [79]. Therefore, bioactive compounds of green tea have strong impact on the stimulation of thermogenesis and lipid oxidation. These effects can be beneficial to control body fatty acid content as well as for the treatment of obesity.

7. The effect of food intake

Increasing food intake is the critical problem of overweight and obesity [81,82]. Controlling food intake is one of the priority methods to prevent weight gain, including the control of food intake, food selection and food absorption. Food intake-mediated obesity partly associates with insulin sensitivity, leptin activity and hypothalamic regulation [83,84]. Insulin regulates glucose homeostasis, lipogenesis, lipolysis and control food intake by hypothalamic action. Leptin directly enhances lipid oxidation, suppresses lipogenesis and upregulates hypothalamic action [83,85].

Green tea affects both food utilization and stomach enzyme system. Sayama L et al. indicated that food intake and serum leptin were significantly suppressed by feeding 4% green tea diet in 16 weeks [86], leading to reducing lipid components in mice serum. Kao et al. also reported a 50–60% reduction of food intake in both lean and obese rats by green tea catechin intraperitoneally injection [87]. Green tea produces certain effects on various endocrine parameters. For example, it reduces leptin circulating in EGCG-treated rats as a result of low food intake. Lower glucose and insulin serum levels stimulate leptin expression and activity, which may contribute to the effects of EGCG in reducing food intake [88,89]. Moreover, green tea catechins, especially EGCG, also modulates carbohydrate and lipid absorption [51]. EGCG inhibits emulsification, digestion, and micellar solubilization of lipids [90] and starch-mediated amylase activity [91,92], thus limits intestinal absorption of lipids and starch digestion.

However, recent studies have shown that the effect of green tea on fat mass reduction was independent from energy intake, which means they are not important effects of green tea on food intake [93,94]. The effects of green tea on satiety are still unclear, which might result from their dosing (lack of action at low concentrations [86]) and the route of administration [87]. Moreover, it is necessary to verify various factors (gender, age, dose, etc.) that can also affect green tea properties.

8. The potential application of green tea for preventing obesity and its related disorders

8.1. Potential application of green tea for obesity and overweight

Green tea catechins (GTCs) are polyphenolic flavonoids once called vitamin P (7). Since the discovery that they have unique chemical structures and are major ingredients of unfermented tea (8,9), they have been found to possess widespread biological functions and health benefits (10,11). GTCs, especially (≧)-epigallocatechin-3-gallate (EGCG), have been shown to lower the incidence of cancers (9–12), collagen-induced arthritis (13), oxidative stress-induced neurodegenerative diseases (14), and streptozotocin-induced diabetes (15). EGCG can also reduce body weight and body fat (16). In support of this anti-obese effect, other in vivo data have shown that EGCG or green tea extract containing EGCG reduces food uptake, lipid absorption, and blood TAG, cholesterol, and leptin levels and stimulates energy expenditure, fat oxidation, high-density lipoprotein levels, and fecal lipid excretion (8,16). These in vivo observations may be explained by the following in vitro findings: EGCG and caffeine act synergistically with norepinephrine to stimulate the thermogenesis of brown adipose tissue (17); EGCG regulates various enzymes related to lipid anabolism and catabolism, such as acetyl-CoA carboxylase (ACC), fatty acid synthase, pancreatic lipase, gastric lipase, and lipoxygenase (8,18); EGCG is a potent pro-oxidant and antioxidant (19,20); and EGCG reduces serum- or insulin (INS)-induced increases in cell number and TAG content during a 9-day period of differentiation (20,21). Together, these in vivo and in vitro observations suggest that green tea EGCG modulates the mitogenic, endocrine, and metabolic functions of fat cells.

Studies based on green tea and green tea extract supplementation have shown an important role of this factor in lipid metabolism, including the suppression of lipid accumulation, adipogenesis, food intake and induction of lipolysis, fat oxidation and thermogenesis, resulting in body and fat weight losing in overweight and obesity. Catechins and caffeine are the major bioactive components of green tea to prevent and treat obesity. There has been several investigations conducted to show the effects of green tea extract, catechins, caffeine and their mixtures with

different dose in mouse experiments and human trials. Since the health beneficial effects, green tea will be applied to lose weight and control weight re-gain in overweight and obese human.

Firstly, the effects of green tea are in time- and dose-dependent manner. It is apparent that the longer tea is consumed, the lower body weight and other body parameters can be found. A 1210-participant survey reported that habitual drinking of tea for more than 10 years reduced 19.6% fat mass and 2.1% waist-to-hip ratio comparing to the non-habitual group [95]. High habitual caffeine (270 mg EGCG and 150 mg caffeine/day) consumption was found to reduce the body and fat mass and waist circumference (WC) more significantly than in lower caffeine consumption, through thermogenesis and fat oxidation.

Secondly, the effect of green tea can be strengthen by other anti-obesity methods. The supplement of green tea with physical exercises and diet control promote fat oxidation [42] and induce thermogenesis, leading to body weight and body fat loss [51,66,67]. Shuya Yamashita et al. emphasized that the anti-obesity effects of green tea were attenuated by feeding mouse model with saturated fatty acids [96].

Thirdly, the effect of green tea is a combination of catechins and caffeine outcomes as well as the minimal effects of green tea flavonoids. Most investigations showed that high catechins and caffeine mixture proved to be better in regulating lipid accumulation, fatty acid oxidation, adipogenesis, thermogenesis and body weight loss than ingesting catechins or caffeine alone [45,46]. However, lower concentration of catechins more effectively suppresses body weight than their combination with caffeine. Additionally, high caffeine was associated with a higher ability to weight regain comparing to low caffeine consumption [97,98]. Therefore, the anti-obesity effects vary on populations with different physiological and dietary conditions.

Lastly, the consumption of green tea has been reported to produce several side effects on health caused by high amount of caffeine intake such as nervousness, sleep disorders, vomiting, headache, anxiety, restlessness, dizziness and high blood pressure [99,100]. Tannis M Jurgens et al. conducted a double-blind trial with green tea extract. The trial used a higher catechins and caffeine tea than typical green tea in 1945 participants during 12–13 weeks intervention [101]. The results showed the minimal side effects of using green tea such as nausea, constipation, increased blood pressure has been also observed in this trial.

8.2. Potential application of green tea for obesity –related metabolic diseases

Moreover, AMPK cascades have emerged as novel targets for the Diabetes, cardiovascular diseases and cancer are mostly related to obesity. Many publications were reported that consuming green tea or catechin and caffeine preparation improved glucose and lipid metabolism by decreasing glucose level, total cholesterol, triglycerides, blood pressure and improving insulin sensitivity.

Type 2 diabetes, followed by high glucose level and high insulin resistance, was improved by consuming green tea extract, catechins and mixture of catechins and caffeine. Ingestion of green tea catechins induced glucose uptake, inhibited glucose absorption and suppressed gluconeogenesis genes [102,103]. Additionally, catechins EGCG enhanced directly glucose metabolism by increasing insulin secretion and improve insulin sensitivity [104,105]. A cross-sectional trial in adults showed that drinking more than 4 cups of tea per day could lower 30% the risk of developing type 2 diabetes [106]. Other cohort study revealed similar results with 33% risk lower when consuming green tea more than 6 cups per day [107].

The consumption of green tea lowered serum cholesterol, serum triglyceride, blood pressure and risk for cardiovascular diseases (CDs) in human trials [29,51,105,108]. EGCG in green tea upregulated sirtuin 1 and AMPK as well as decreased the expression of lipogenesis genes after 12 weeks of feeding with various dosages of tea catechins in male c57BL/6 mice [108]. Tea catechins also prevented bile acid reabsorption from small intestine, thus suppressed liver cholesterol to restock bile acid [109]. Moreover, EGCG also inhibits cholesterols absorption, together with LDL receptor induction, leading to lower blood cholesterol level [105,110,111], resulting in the reduction of blood cholesterol. In a large retrospective study of 76.979 Japanese people, green tea was associated with CDs mortality [112] in which consuming 3–4 cups of tea reduced the risk of ischemic stroke [113,114].

Tea and its components have been investigated for their anticancer ability in digestive tract, lung and prostate (reviewed in Ref. [115]). Many recent studies are consistent with the protective effects of green tea. It is believed that the mixtures of catechins or catechins with caffeine in green tea are more effective cancer protective agent than pure EGCG or any catechin alone [115]. Catechins and caffeine treatment inhibits selectively cell proliferation and promotes apoptosis in lung cancer [116], and decreases metastatic genes expression in prostate cancer [117]. Moreover, green tea and its components have strong antioxidant effects, high affinity binding to protein membrane and promote the cellular signaling, and the inhibition of enzyme activities, receptors and Wint signaling [115], resulting in the prevention of multiple type of cancers development [115]. Treatment with EGCG reduced the expression of oxidative DNA markers, which contributes to the decreased risk of DNA mutation and for cancer development [116].

In conclusion, habitual green tea extract consumption or green tea component supplements has brought a great number of positive effects on health, including anti-obesity, anti-diabetes, anti-cancer, and anti-inflammation. Green tea is highly recommended to prevent and treat weight gain in overweight and obesity, type 2 diabetes and cancers. Since the effects of green tea is complex, it is necessary to evaluate them in individuals by dose- and time-treatment manner, together with the frequency of doing physical exercises and diet control in preventing and treating diseases.

Conflicts of interest

No conflict of interest was reported by the authors.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.03.021.

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