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Review

The role of green coffee extract on weight loss, glucose and lipid metabolism

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Summary. The purpose of this paper was to perform a review about the role of green coffee extract on weight loss, glucose and lipid metabolism. It has been shown that overweight and obesity are important problems for health and the financial and psychological aspects have been imposed many damages to governments and health care providers. The management of overweight and obesity is related to lifestyle, physical activity, and diet. In the past decade, the studies have been published about the effects of green coffee extract on hypoglycemic, weight losing and hypotensive have been increasing. there are limited number of human studies in this area. However, the majority of interventional and epidemiological studies have been shown the beneficial effects of green coffee extract on weight and blood glucose management and metabolism of lipids. Green coffee extract reduces the fat reserves in adipocytes and regulate blood glucose by several mechanisms. Accordingly, green coffee extract supplementation may be effective in weight management, glucose and lipid metabolism.

Key words: green coffee extract, chlorogenic acid, weight management, obesity

Introduction

Quality health care, any action to prevents stroke, is an important issue that many people have been facing. One of these cases is the prevention of obesity. Obesity is the accumulation of excess fat in the body and it is known as a sort of slight inflammation condition(1-3). Obesity is an important public health concern that is affecting over half a billion people in worldwide(4). The increase of obesity has not limited only to developing countries but also in developed countries can be observed(5). This problem has been increasing rapidly in the world, not only has been associating with increase in chronic diseases including type 2 diabetes, hypertension, insulin resistance, cardiovascular disease respiratory problems and many other diseases, that threatens an individual's life, but also effect on confidence and body image(6-8). Therefore, it is important to found a safe and effective way for body weight control. Losing weight can be difficult. Thus, people have been consuming to several kinds of supplements in order to make things easier. One of these supplements is green coffee extract (GCE). Green coffee beans are basically just unroasted coffee beans. Coffee beans are naturally green, but usually they are roasted before be sold to the consumer. This process changes the color green to brown(9). The consumption of green Coffee extract has effect on blood pressure, weight, lipid profile and glucose metabolism and has potential antioxidant activity (10-13). It also reduces the risk of cardiovascular disease, Alzheimer's disease, type 2 diabetes and it has anti-inflammatory and an-

tibacterial activity (14, 15). The purpose of this paper was to perform a review about the role of green coffee extract on weight loss, glucose and lipid metabolism.

The general characteristics of green coffee extract

Coffee is a popular drink in the world. It is produced usually of two types of Coffea arabica and Coffea canephora. It has reported that regular consumption of coffee reduced the risk of type 2 diabetes(16), stimulated lipolysis, enhanced energy expenditure and consumed before exercise improves ventilation(17). Investigations in field of identification of compounds in green coffee indicated the existence of more than 200 compounds in the green coffee of many chemical classes such as alcohols, hydrocarbons, aldehydes, ketones, esters, nitrogen and sulfur compounds, phenols, furans and even halogenated compounds(18). The difference between green coffee and roasted coffee is in the production process. Because of the Maillard reaction in the roasting process, the coffee beans changed into a chemical composition(9). The major changes are trigonelline denaturation, loss of proteins and carbohydrates, formed melanoidin and destruction of Chlorogenic acid (CGA)(19). the content of CGA is decreased by approximately 90% in roasted coffee beans(20). CGA is the most important polyphenolic compound in green coffee that is account for up to 10% of the weight of green coffee(9). A typical cup of Arabica coffee contains 70-200 mg CGA and a cup of Robusta coffee contains 70-300 mg chlorogenic acid(11). CGA exist in coffee beans, apples, Western pears, Japanese apricot, tomatoes, potatoes and eggplant(21). CGA is compose of esterification of cinnamic acids (such as caffeic and ferulic) with quinic acid. The most CGA in green coffee are 5-caffeoylquinic acids(CQA) and dicaffeoylquinic acids (diCQA) and feruloylquinic acids (FQA)(22). Studies have shown that bioavailability CGA from green coffee is about 7.8 to 72.1%(23). after consumption of the GCE, CGA hydrolyze to quinic acid and caffeic acid in the small intestine, colon, mucosa and liver(24). In the plasma of subjects after consumption of the GCE was identified small amounts of caffeic, isoferulic, ferulic, and p-coumaric acids(23). Ferulic and isoferulic acid are methylate form of caffeic acid(25). CGA is excreted through the urine and major metabolites excretion are sinapic acid, gallic, p-hydroxybenzoic, and vanilic acid (22). In Figure1 proposed simplified scheme of Chlorogenic acid metabolism.

Effect of green coffee extract on weight loss

Several epidemiological studies have been conducted to investigate the effect of green coffee weight loss in animals. In a study on mice to determine the effect of GCE to prevent obesity. The mice were divided into 6 groups: chow diet, high fat diet, high fat diet-supplemented with 0.1%, 0.3%, and 0.9% decaffeinated green coffee bean extract, and 0.15% 5-caffeoylquinic acid. Results showed that consumption of GCE has the opposite effect on fat accumulation in the body (26). The results of studies conducted on animals, lead to undertaking research in this field on humans. Articles that have been found in this area are including articles Randomized Clinical Trial and Systematic Review and Meta-Analysis. In one study was conducted to evaluate the weight loss on 50 volunteers. The volunteers were divided into two groups of intervention and control. After 60 days of follow-up, results showed regular consumption of green coffee was Led to significant weight loss (27). A Systematic Review and Meta-Analysis study have shown consumption of green coffee leads to weight loss but due to low literature in this field suggested more research is needed to evaluation this subject

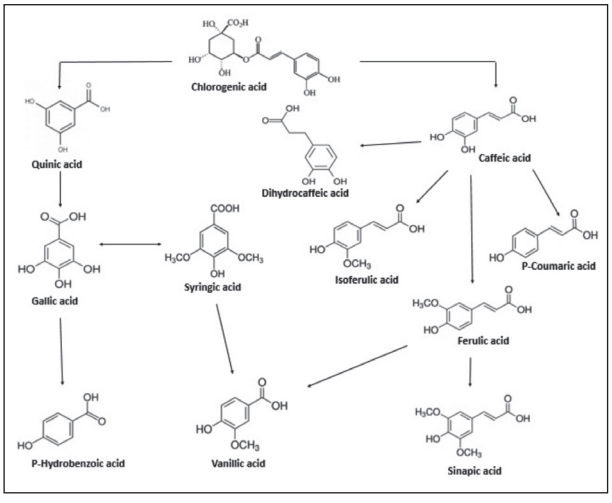

Figure 1. Proposed simplified scheme of Chlorogenic acid metabolism

(28). Other studies also confirmed that effect (29, 30) but studies have also been seen to reverse effect. In a study was conducted on mice with metabolic syndrome. The mice were divided into three groups: normal diet, high fat diet and the high fat diet supplemented with 0.5% w / w green coffee bean extract. The diets were continued for 12 weeks. Results showed consumption of green coffee has no effect on preventing obesity. These results could be due to different in dose and the concentration of chlorogenic acid (11). Other findings from these studies were hypotensive activity, reduce inflammation and improve insulin sensitivity (26, 31). Summary studies are presented in table1.

The dosage of Green coffee

Currently, there is no study determines an optimal dosage for GCE. In an animal study, the best dosage effect to decreases in body weight, plasma lipids and glucose profiles and visceral fat-pad weights was 0.3% green coffee bean extract that this amount was calculated in humans around 1,460mg / 60kg body weight (26, 32). In order to achieve 1.460mg of green coffee bean extract, 9.7 grams of green coffee beans is needed as computed from its extraction yield of 15% (26) but this amount may have side effect. In human studies have done, the range dosage of green

Table1. Summary of Clinical Trials Examining Effects of GCBE on Weight Loss

Topic	Author	year	result
Green Coffee Bean Extract as a Weight Loss Supplement	Mehnoosh Samadi and et.al.	2015	green coffee introduced as the sources of chlorogenic acid that be able to play a role in weight loss
Antioxidant activity and protective effects of green and dark coffee components against	Jose ´ A ´ ngel Go ´mez-Ruiz and et al.	2008	The coffee protected human low-density human low density lipoprotein oxidation lipoprotein (LDL) against oxidation, although green coffee extracts exhibited more protection
The blood pressure-lowering effect and safety of chlorogenic acid from green coffee bean extract in essential hypertension. Clinical and experimental hypertension	Takuya Watanabe and et al.	2006	Chlorogenic acid from green coffee extract is effective in decreasing blood pressure
Decaffeinated green coffee bean extract attenuates diet-induced obesity and insulin resistance in mice	Su Jin Song and et al.	2014	green coffee extract downregulating the genes involved in adipogenesis
Inhibitory effect of green coffee bean extract on fat accumulation and body weight	Hiroshi Shimoda and et al.	2006	Green coffee extract is possibly effective against weight gain and fat gain in mice accumulation
Dietary supplementation with decaffeinated green coffee improves diet-induced insulin resistance and brain energy metabolism in mice	Lap Ho	2012	green coffee extract may beneficially influence the brain, promoting brain energy metabolic processes
Svetol, green coffee extract, induces weight loss and increases the lean-to fat mass ratio in volunteers with overweight problem	Dellalibera O	2006	decrease weight, body mass index and fat mass
Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine.	Kelly L Johnston	2003	chlorogenic acid might have an antagonistic effect on glucose transport
The Effect of Chlorogenic Acid Enriched Coffee on Glucose Absorption in Healthy Volunteers and Its Effect on Body Mass When Used Long-term in Overweight and Obese People	Erling thom	2007	if the coffee is used for an extended time, may result in reduced body mass and body fat when compared with the use of normal instant coffee

coffee extract was 10-200mg/kg green coffee bean extract (10, 13, 33).

Side effect of green coffee extract

According to the evidence available, GCE appears to have a good safety profile. However, some participants abandon one study due to headache and urinary tract infection (33) but this study was too small to exhibit that the side effects were caused by the supplement itself, it may just have been a coincidence. It is important to understand that GCE contains caffeine, like regular coffee. Therefore, green coffee can cause caffeine-related side effects like coffee when consumed in large amounts. This side effects includes restlessness, jitteriness, insomnia, stomach upset, nervousness, nausea, increased heart, breathing rate and vomiting. Consuming large amounts of coffee could also cause headache, agitation, ringing in the ears, anxiety, and irregular heartbeats (34, 35). The CGA may also have a laxative activity and cause diarrhea (36, 37).

Mechanisms of green coffee extract to lose weight

Obesity is one of the major problems in the world that affect the quality of life and life expectancy. changing lifestyles is not easy so in order to achieve the desired goal, ideal body weight, the use of pharmaceutical products as a food supplement helps to disturb the balance between Calorie intake and energy expenditure and by doing fat burning gets weight loss(38). When an amount of carbohydrates in the diet is high, insulin increasing and stimulates the production of fat which first fat reserves is not used for energy production second leads to increased fat reserves in the adipocytes (39). GCE by various mechanisms lead to regulate blood glucose level and increase lipids metabolism.

Deactivation of the α-Glucosidase enzyme

Glycosidases, hydrolytic enzymes, play a key role in digestion of carbohydrates. Suppress of α-glucosidase may potentially decrease the progression of diabetes by reducing the digestion and absorption of carbohydrates(40). In studies, Bassoli et al. (2008) found administration of CGA reduces the peak plasma glucose in the oral glucose tolerance test which can be slow down the absorption of glucose from the intestines and this indicates that CGA is a reducing glycemic index agent and reduce a risk of type two diabetes(41). CGA has been shown via deactivation of the α-Glucosidase enzyme and α-glucosidase enzyme lead to reduce peak blood sugar after consuming the food. That it has a performance such as acarbose, miglitol and voglibose(42). CGA inhibits intestinal α-glucosidase in a non-competitive manner and leads to a reduction blood glucose levels after eating a meal(43).

Modulation of GIP Concentration

Glucose-dependent insulinotropic polypeptide (GIP) is an amino acid hormone that is manufactured by enteroendocrine K-cells and released into the blood stream in response to nutrient stimulation and stimulate insulin secretion in a glucose dependent method (44, 45). GIP inhibit hepatic glucose production and to increase glucose uptake in isolated mouse diaphragm muscle, promote glucose transport, increase fatty acid synthesis and intensify lipoprotein lipase activity(46). CGA consumption through stimulation of secretion of Plasma GIP effects on pancreatic beta cells to respond to glucose(47).

Activation of AMP- activated protein kinase (AMPK)

This system is key to regulating cell energy balance. Activation of this system leads to translocation Glucose transporter type 4)GLUT4(from intracellular membrane to plasma membrane and increase the movement of glucose into the cell(48). Experiments have been shown the CGA through increased expression of GLUT4 and PPAR-γ transcript stimulate glucose transport into the L6 myotubes that can be managed by controlling the dose and time(49). Activation of AMPK leads to metabolic effects such as suppression of hepatic glucose production and synthesis of fatty acid. Prevention of action and knockdown of AMPK leads to the obsolescence of these activities (50).

Increasing GLUT4 translocation

The role of GLUT4, the insulin-sensitive glucose transporter, is glucose uptake and induced by insulin and regular exercise in adipose tissue, the heart, skeletal muscle and tissues that express this protein (51, 52) and its rate of expression is a main determinant of the capacity for glucose uptake by muscle (53). Overexpression of GLUT4 in muscle stimulates glucose uptake and reduces insulin resistance (54). Inflammatory cytokines generated by the adipose tissue, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) have been associated to reduce GLUT4 expression(55, 56). When white adipose tissue(WAT) becomes inflamed, c-Jun N-terminal kinase (JNK) is phosphorylated and p-JNK deactivates insulin receptor substrate -1 by phosphorylating its serine residue (57). GLUT4 translocation is blocked by Serine phosphorylation and therefore impairs insulin sensitivity (58). GCE have reversed High Fat Diet- induced insulin resistance by decreasing JNK activation and rising GLUT4 translocation (26).

Inhibitors of Hepatic Glucose-6-phosphatase Activity

The enzyme glucose-6-phosphatase is known to play a key role in regulation of blood glucose(59). Starvation and diabetes cause a 2-3-fold increase in Glc-6-Pase activity in the liver that making this enzyme a potential target for nutritional compounds. By suppress hepatic glucose production to improve diabetic hyperglycemia(60). GCE the inhibit Glc-6- P hydrolysis in human liver microsomes. It is known that GCE to be a competitive inhibitor of Glc-6-Pase in a dose dependent manner(61). It has reported that CGA inhibits the activity of glucose-6-phosphate translocase up to 40% in the hepatocytes(41). CGA reduces the outflow of glucose from the liver and prevent insulinemia by inhibiting the activity of G-6-Pase(62, 63). This mechanism, however, depends on the bioavailability of CGA and its isomers. 5- caffeoylquinic acids, 4- caffeoylquinic acids, 3,4 dicaffeoylquinic acids and 4,5 dicaffeoylquinic acids are most kind of CGA that have inhibitor activity of Gl-6-Pase(61).

Inhibition of adipogenesis

Inhibition of adipogenesis is another green coffee mechanism to control weight. A procedure of mesenchymal precursor cells differentiating to adipocytes called adipogenesis(64). Peroxisome proliferator-activated receptor γ2 (PPARγ2) and CCAAT/ enhancer-binding protein α (C/EBPα) have an important role in transcriptional regulators in adipogenesis. Downstream targets for PPARγ2 consist of lipoprotein lipase (LPL), fatty acid synthase (FAS) and adipocyte lipid binding protein (aP2), which together control lipid accumulation and metabolism(26). Activation of PPARγ2 and C/EBPα cause beginning adipogenesis. Some upstream molecules such as galanin, wingless-type MMTV integration site family 10b (WNT10b) and fibroblast growth factor 1 induce PPARγ2 and C/EBPα(65, 66). Activated of PPARγ2 and C/EBPα induce adipogenesis. WNT10b signaling activation started chain reactions that lead to suppresses PPARγ2 and C/EBPα. The WNT10b signaling pathway is inhibited by extracellular antagonists, for example, secreted frizzled receptor protein 5(SFRP5) and dickkopf 2(DKK2) (65). Regularly consumption the GCE demonstrated decrease gene expression of SFRP5 and DKK2(26)(Fig2).

Galanin

Galanin is a neuropeptide that widely expressed in the brain, spinal cord, gut of human as well as other mammals and distributed in the central nervous system stomach, white adipose tissue and taste buds(67). Galanin by binding to receptors in the hypothalamic regions regulates memory, food consumption, neurogenesis and neuroendocrine functions(68). Consuming high-fat diet stimulate of Galanin receptor1 and Galanin receptor 2 in chain reactions leads to the activation of extracellular signal regulated kinases (ERK) which lead to raises the expression of PPARγ2 and C/EBPα and stimulates adipogenesis(69). GCE looks to suppress adipogenesis by decrease expression of galanin and its receptors(26).

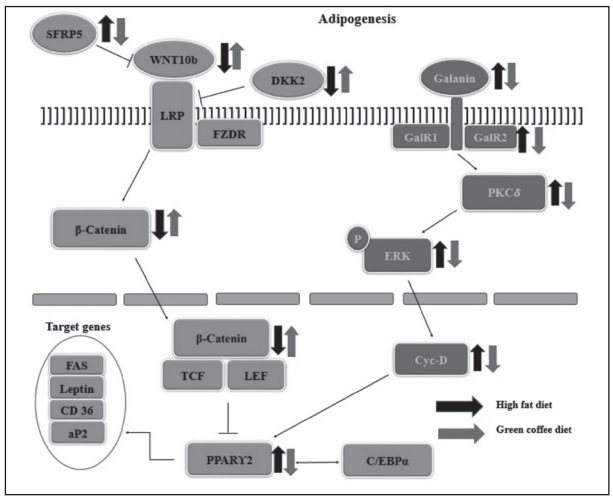

Figure 2. The possible molecular mechanisms of green coffee extract in attenuating adipogenesis induced by HFD. green coffee extract by changes in expression of genes included WNT10b and galanin-mediated adipogenesis cascades reverses HFD-induced in the adipose tissue. The downstream adipogenic transcription factors (C/EBPα and PPARγ2) and their target genes were also inhibited by green coffee extract in the adipose tissue.

Leptin regulation

The amount of secretion of leptin from adipocyte is positively correlated with triglyceride reserve in the adipocyte. Increases in serum leptin level usually happen together with adipocyte hypertrophy (70). GCE seems to reduce plasma leptin and the average adipocyte diameter(26).

It also identified that CGA can indirectly cause inhibition of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA Reductase), Strengthening the activity of Carnitine Palmitoyl Transferase, which in turn reduces the synthesis of cholesterol and increase lipid oxidation(71).

Conclusion

In conclusion, this paper, we show several mechanisms of the GCE that decreases visceral fat-pad accumulation, improves insulin resistance and regulate blood glucose. We suggest that polyphenols in green coffee extract may bring an additive effect in increasing insulin sensitivity, glucose and lipid metabolism and weight. These beneficial effects are due to the down-regulation of genes related with adipogenesis. Can be considered, GCE may be consumed as a therapeutic agent that inhibits obesity and metabolic syndrome.

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