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Original Article

Systematic Review For The Association Between CGA Consumption And Obesity Raised Health Disorders (CVD Risk)

Wasihun Alemayehu*

Department of Mechanical Engineering, Adama Science and Technology University, School of Material, Chemical and Mechanical Engineering.

ABSTRACT

chlorogenic acid (CGA) which can be extracted from Morus nigra leaf, Morus laevigata fruit, Morus alba leaf was the dominant phenolic constituent in mulberry and possessed excellent antioxidant activity more reports on CGA and its derivatives (extracted from Morus alba leaf) attenuated alcoholic steatohepatitis by inhibition of oxidative stress. CGA (extracted from Morus alba, Morus nigra leaf) has also been reported to exert anti-diabetic and anti-hyperlipidemia activity by decreasing non-fasting blood glucose levels, serum cholesterol, triglycerides and normalization lipoproteins in a dose-dependent manner. The effect of an intensive weight loss intervention (based on an energy-restricted Mediterranean diet, physical activity promotion and behavioral support) on CVD events. The World Cancer Research Fund (WCRF) recommends a dietary and lifestyle pattern (DLP) for reducing the risk of colorectal cancer that includes "consuming coffee (it contains Chlorogenic acid) and food and beverages that contain calcium…" In 2022, WCRF said "…there is strong evidence that coffee decreases the risk of liver and womb cancers. There's also some evidence that coffee decreases the risk of mouth, pharynx and larynx, and skin cancers because. Adipose tissue is a connective tissue, but it's also an interactive organ in your endocrine system. It communicates through hormone signals with other organs throughout your body, as well as with your central nervous system, to regulate body metabolism.Obesity is excess body fat. Obesity is linked to higher "bad" cholesterol and triglyceride levels and to lower "good" cholesterol levels. Obesity raises the risk of developing diabetes and high blood pressure, which are the most common causes of chronic kidney disease (CKD).raise the risk of developing health problems during pregnancy that can affect the pregnancy and the baby's health. Studies also looked at specific causes of death, and found that for each 5-unit increase in BMI above 25, the corresponding increases in risk were 49% for cardiovascular mortality, 38% for respiratory disease mortality, and 19% for cancer mortality.

Keywords: Chlorogenic acid (CGA), causes of chronic kidney disease (CKD). Hepatic steatosis, Inflammation, Insulin resistance, Obesity, mortality.

INTRODUCTION

1.1 Background

Researchers found that chlorogenic acid (extracted from Morus nigra leaf, Morus laevigata fruit, Morus alba leaf) was the dominant phenolic constituent in mulberry and possessed excellent antioxidant activity (Radojkovic et al., 2018; Saracoglu, 2018; Zhang et al., 2018). For example, Lee, Hsu, Lin, Kao, and Wang (2017) reported CGA and its derivatives (extracted from Morus alba leaf) attenuated alcoholic steatohepatitis by inhibition of oxidative stress. CGA (extracted from Morus alba, Morus nigra leaf) has also been reported to exert anti-diabetic and anti-hyperlipidemia activity by decreasing non-fasting blood glucose levels, serum cholesterol, triglycerides and normalization lipoproteins in a dose-dependent manner (Hunyadi et al., 2012; Zeni et al., 2017). Furthermore, CGA (extracted from Morus alba leaf) could prevent dyslipidemia-induced metabolic syndromes, such as non-alcoholic fatty liver disease, by regulating adipocytokines (leptin and adiponectin), inflammation (IL-6 and TNF-α) and oxidative stress (Peng, Lin, Chung, Huang, & Wang, 2018). Another study indicated CGA and its derivatives (extracted from Morus alba leaf) inhibit hepatocellular carcinoma cell proliferation by depressing IL-6 and

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TNF-α, inducing the inflammatory response of adipocytes to activate the proliferation signaling pathway (Chang, Chang, Tseng, & Wang, 2018). CGA is a natural plant extract with a vast array of sources[1], present in honeysuckle, potato, cork, encomia leaves, chrysanthemum , strawberry , mango, blueberries , mulberry leaves , and green coffee . Recently, some researchers have used high voltage discharge to assist in extracting a certain amount of CGA from the three components of tobacco waste (waste, dust, and midrib) .Adipose tissue is a connective tissue, but it's also an interactive organ in your endocrine system. It communicates through hormone signals with other organs throughout your body, as well as with your central nervous system, to regulate body metabolism. Within the matrix of body fat, also called adipose tissue, there is not only fat cells but nerve and immune cells and connective tissue. [2] Fat tissue releases hormones that control metabolism and appetite (i.e., leptin, adiponectin) and that affect insulin sensitivity (i.e., tumor necrosis factor-alpha, interleukin-6). Macrophages, neutrophils, and eosinophils are some of the immune cells found in fat tissue that play a role in inflammation—both anti-inflammatory and pro-inflammatory. Fat cells also secrete proteins and build enzymes involved with immune function and the creation of steroid hormones. Fat cells can grow in size and number. The amount of fat cells in our bodies is determined soon after birth and during adolescence, and tends to be stable throughout adulthood if weight remains fairly stable. [3] But eating too many calories in the long-term can cause fat cells to increase in size and be stored in various areas throughout the body, which leads to a risk of chronic inflammation and glitches in healthy metabolism, with the potential for new fat cells to grow. These larger fat cells become resistant to insulin, which increases the risk of type 2 diabetes and cardiovascular disease. Weight loss can reduce the size of fat cells but not the number.The World Health Organization defines a "normal" [4]weight as a BMI of 18.5 to 24.9, "overweight or pre-obesity" as a BMI of 25.0 to 29.9, and "obesity" as a BMI of 30 or higher. It further classifies levels of obesity as Class I (BMI 30.0 to 34.9), Class II (BMI 35.0 to 39.9), and Class III (BMI 40 or higher). A meta-analysis published in the New England Journal of Medicine showed a clear relationship between BMI and mortality, where both people with underweight (BMI <18.5) and with overweight and obesity (BMI >25) had greater mortality.[3]The lowest death rate from any cause was associated with the BMI range between 22.5 and 24.9.To address some methodological flaws in previous studies, this study excluded smokers who tend to have lower weight due to smoking, individuals with cancer and heart disease who might have lost weight due to these conditions, and individuals over the age of 85 who could have a normal BMI but suffer from frailty or other age-related unhealthy weight loss.

Another large meta-analysis in The Lancet that looked at data across four continents found that for every five units higher of a BMI above 25, risk of premature death increased by about 31%. [5] The study also looked at specific causes of death, and found that for each 5-unit increase in BMI above 25, the corresponding increases in risk were 49% for cardiovascular mortality, 38% for respiratory disease mortality, and 19% for cancer mortality. Obesity is excess body fat. Obesity is linked to higher "bad" cholesterol and triglyceride levels and to lower "good" cholesterol levels. Obesity can lead to high blood pressure and diabetes as well as heart disease. Eating a diet high in saturated fats, trans fat, and cholesterol has been linked to heart disease and related conditions, such as atherosclerosis. Also, too much salt (sodium) in the diet can raise blood pressure. Obesity raises the risk of developing diabetes and high blood pressure, which are the most common causes of chronic kidney disease (CKD).raise the risk of developing health problems during pregnancy that can affect the pregnancy and the baby's health. [6]Obesity can lead to high blood pressure and diabetes as well as heart disease. ***Unhealthy blood cholesterol levels*** [7-9]. Cholesterol is a waxy, fat-like substance made by the liver or found in certain foods. Your liver makes enough for your body's needs, but we often get more cholesterol from the foods we eat. If we take in more cholesterol than the body can use, the extra cholesterol can build up in the walls of the arteries, including those of the heart. This leads to narrowing of the arteries and can decrease the blood flow to the heart, brain, kidneys, and other parts of the body. There are two main types of blood cholesterol :-

LDL (low-density lipoprotein) cholesterol, which is considered to be "bad" cholesterol because it can cause plaque buildup in your arteries.

HDL (high-density lipoprotein) cholesterol, which is considered to be "good" cholesterol because higher levels provide some protection against heart disease.

High blood cholesterol usually has no signs or symptoms. The only way to know whether you have high cholesterol is to get your cholesterol checked. Your health care team can do a simple blood test, called a "lipid profile," to measure your cholesterol levels. Learn more about getting your cholesterol checked.

Diabetes mellitus. body needs glucose (sugar) for energy. Insulin is a hormone made in the pancreas that helps move glucose from the food you eat to your body's cells for energy. If you have diabetes, your body doesn't make enough insulin, can't use its own insulin as well as it should, or both. Diabetes causes sugar to build up in the blood. The risk of death from heart disease for adults with diabetes is higher than for adults who do not have diabetes 2.

Anatomy

Where is adipose tissue located? [10-12]It is found throughout your body. The primary depots are: -Subcutaneous adipose tissue (SAT) - is the fat that lives between your skin and muscles.-Visceral adipose tissue (VAT) -is the fat that surrounds the organs in your abdominal cavity. Other locations include:-In bone marrow, in breast tissue, between muscles, around your heart, in your eye sockets, in the palms of your hands and soles of your feet.

Conditions and Disorders

Is it healthy to have adipose tissue?

Adipose tissue is crucial for health. However, having too much — or too little — can cause its regulatory systems to malfunction. Healthy levels vary by age and sex, ranging between 10% and 35%. In the case of obesity, the body runs out of tissue to store lipids in, so the existing fat cells have to grow. Enlarged fat cells are associated with chronic inflammation and with a variety of metabolic disorders that follow. Ironically, a lack of overall fat tissue can cause the same effects because, again, the body doesn't have enough existing tissue to store lipids in. Besides genetic factors, most disorders of the adipose tissue result from malnutrition, which can mean either under-nutrition or over-nutrition.

Obesity is excess body fat. Obesity is linked to higher "bad" cholesterol and triglyceride levels and to lower "good" cholesterol levels. Obesity can lead to high blood pressure and diabetes as well as heart disease. ***Un-healthy blood cholesterol levels***. Cholesterol is a waxy, fat-like substance made by the liver or found in certain foods. Your liver makes enough for your body's needs, but we often get more cholesterol from the foods we eat. If we take in more cholesterol than the body can use, the extra cholesterol can build up in the walls of the arteries, including those of the heart. This leads to narrowing of the arteries and can decrease the blood flow to the heart, brain, kidneys, and other parts of the body. The World Health Organization defines a "normal" [4] weight as a BMI of 18.5 to 24.9, "overweight or pre-obesity" as a BMI of 25.0 to 29.9, and "obesity" as a BMI of 30 or higher.

1.2 Statements of the problem

Men with overweight or obesity are at a higher risk for developing cancers of the colon NIH external link, rectum NIH external link, and prostate NIH external link. Our liver makes enough for your body's needs, but we often get more cholesterol from the foods we eat. If we take in more cholesterol than the body can use, the extra cholesterol can build up in the walls of the arteries, including those of the heart. This leads to narrowing of the arteries and can decrease the blood flow to the heart, brain, kidneys, and other parts of the body which the reason for hypertension. Persistently high pressure causes arteries to become stiff and thickened (arteriosclerosis). It can also contribute to plaque buildup (atherosclerosis) or weaken vessel walls, leading to dangerous bulges (aneurysms). [13] Another analysis of the Cancer Prevention Study cohort found that increased weight was tied to increased mortality from all cancers and specific cancers;[14]in fact, study investigators estimated that overweight and obesity is responsible for 14% of all cancer deaths in women and 20% of all cancer deaths in men.

1.3 Objective: systematic review for the association between coffee consumption and obesity raised health disorders (CVD risk)

The current study aims to explore the underlying CGA in reducing cholesterol based health risk.

2. METHODS AND DATA SOURCE

2.1 Methods

Review chlorogenic acid (CGA) source and health benefit

Analysis obesity health risk and major reason

Review related experimental based literatures.

(Provides analytical discussion evidence)

Arrange in correlation form - draw conclusion

Document.

2.2 Study design and data source

Data sources: PubMed, Google scholar and Web of Science were searched for relevant studies.

3. REVIEW RELEVANT EXPERIMENTAL BASED LITERATURES

In a cross-sectional analysis using baseline data from the PREDIMED-Plus study was conducted in 23 Spanish centers, through randomized and controlled clinical trial which aims to evaluate the effect of an intensive weight loss intervention (based on an energy-restricted Mediterranean diet, physical activity promotion and behavioral support) on CVD events compared to a control group that is given usual care advice that good result intensive weight loss is obtained.[12

3.1 Health protective based review

Coffee consumption has been associated with higher insulin sensitivity, a lower risk of type 2 diabetes, and lower concentrations of inflammatory markers such as C-reactive protein and E-selectin[13]. And some a reverse causation problem in that individual with hypertension or other CVD-related conditions might switch from regular coffee to decaffeinated coffee. This reverse causation may mitigate an inverse association between decaffeinated coffee consumption and CVD risk. CGA significantly blocked the development of diet-induced obesity but did not affect body weight in obese mice. CGA treatment curbed HFD-induced hepatic steatosis and insulin resistance. CGA has been proven to have a good protective effect on the liver and kidney, and its protective mechanism can be summarized as the following: (15) It acts on the expression of enzymes and proteins related to the oxidative system and inhibit liver and kidney damage caused by oxidative stress; (16) The regulation is related to apoptosis. The expression level of the gene promotes apoptosis of necrotic cells; (17) directly or indirectly inhibits the expression of pro-inflammatory factors and related signal pathways.

3.2 Anti-bacterial

CGA has a better inhibitory effect on both Gram-positive and negative bacteria [15-17]. The main mechanisms can be summarized as follows:-Destroy the structure of cell membranes, causing leakage of intracellular metabolites and trigger cell inactivation; Interfering with normal cell cycle progression, thereby inhibiting the growth of microorganisms; Disturb the normal metabolic activities of bacterial cells, leading to metabolic disorders within the cells.

3.2 Anti-tumor

CGA plays a major role in the prevention and inhibition of tumor growth, and the anti-tumor mechanism can be summarized as follows: [15] Regulate the expression of apoptosis-related factors and promote apoptosis of cancer cells; [16] It acts on the cell division cycle and hinders the reproduction, metastasis, and invasion of cancer cells; [17] Affect the metabolism level of cancer cells and the normal growth of cancer cells. .CGA can also protect kidney damage induced by the imbalance of the oxidative system. Additionally, CGA can also achieve liver and kidney protection by controlling cell apoptosis. Accumulation of saturated fatty acids can readily[18] cause liver cell apoptosis and endoplasmic reticulum stress, which can be the fuse of hepatitis, liver fibrosis, cirrhosis, and even liver cancer. GA controls the metabolic response of cancer cells and disrupts normal cell growth. Melanoma is most commonly found in skin cancer and often causes death associated with skin cancer. Static magnetic fields (SMF) and

bioactive compounds found in food are potential for cancer treatment.

3.3 Protect the Nervous System

The purpose of apoptosis is to eliminate dead cells during cell proliferation or differentiation. More studies have shown that autophagy and apoptosis are involved in nervous system damage [19]

4. DOSE-DEPENDENT REVISION AND DISCUSSION

4.1 Dose-dependent revision

Green coffee accounting for 50% of the total CGA (based on dry weight) and [18] Unroasted coffee beans are as high as 543.23 (mg/L), but with the increase of roasting degree, the content gradually decreases. Chlorogenic acid could dose-dependently suppress the increased plasma total cholesterol and increased LDL induced by the HCD[18]. Chlorogenic acid (10 mg/kg/day) significantly reduced the plasma total cholesterol (4.83 ± 0.32 mmol/L, $p < 0.01$) and LDL (6.93 ± 0.80 mmol/L, $p < 0.05$), as compared with those in the HCD group (total cholesterol, 5.70 ± 0.33 mmol/L; LDL, 9.91 ± 1.62 mmol/L).

4.2 Discussion

Unroasted coffee beans are as high as 543.23 (mg/L), 543.23 (mg/L)/ implies its quarter will have 135.8075 (mg) CGA by weights in other words green coffee accounting for 50% of the total CGA implies quarter has almost 1/8 of the content will be CGA depending on the concentration a cup alone may not define instead milligram is best. To reduce the plasma total cholesterol (4.83 ± 0.32 mmol/L, $p < 0.01$) and LDL (6.93 ± 0.80 mmol/L, $p < 0.05$),one has to take Chromogenic acid (10 mg/kg/day) it's to mean a litter of Unroasted coffee is used for 54days this all shows even small amount of coffee has value on health but if too much has the reverse effect. And finally all above data and summery gives clear evidence that coffee consumption has medical value for obesity health disorder.

CONCLUSION

The supplementation of chlorogenic acid could demonstrate good hepatoprotective function, in terms of reducing fat depositions in liver. GA treatment also attenuated inflammation in the liver and white adipose tissue accompanied by a decrease in mRNA levels of macrophage marker genes and CGA significantly blocked the development of diet-induced obesity but did not affect body weight in obese mice. CGA treatment curbed HFD-induced hepatic steatosis and insulin resistance. Finally this study (review) provides direct evidence in support of CGA as a potent compound in preventing diet-induced obesity and obesity-related metabolic syndrome. Thus drinking coffee is beneficial in maintaining metabolic homeostasis when on a high fat diet. The precise molecular mechanism by which chlorogenic acid stimulates lipid metabolism and the dosage per risk level needs detail experiment and analysis but all the above data and review provides more evidence of chlorogenic acid's consumption has health protective effects.

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