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Green Tea Facts and Evidences

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Green tea has been consumed in China and other Asian countries since ancient times. Nowadays, green tea is considered to be one of the most promising dietary agents for the prevention and treatment of many diseases and is consequently being studied extensively worldwide. The main objective of this research paper is to clarify the benefits and the impacts of green tea on human health. Numerous studies in humans and a variety of experimental animal models have demonstrated that green tea possess antioxidant, antidiabetic, anti-inflammatory, antibacterial, and anticarcinogenic effects. Furthermore, green tea consumption has been reported to act positively against cardiovascular diseases, obesity, insulin sensitivity, oral infections, and arthritis. On the other hand, the excess consumption of green tea can cause several health complications such as hepatotoxicity in liver and pancreatic cells, goiters, sleep disorders and epigastric pain. The green tea beneficial health impacts have resulted in recent recommendations by many nutritionists to support the regular consumption of 2-3 cups of green tea per day. However, since human clinical evidence is still limited, future research is still needed to implement a system that defines the actual size of health benefits, the safe and right amounts of tea consumption, and the mechanisms of actions.

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TABLE OF CONTENTS

LIST OF TABLES

CHAPTER ONE

INTRODUCTION

Many decades ago, water was the only option for people to drink, but now there are thousands of drinks with various flavors to choose from. One of these drinks is tea, which comes in many colors and flavors. In many traditions all over the world, especially in my country of Saudi Arabia, coffee and black tea are generally served when entertaining guests. However, in this paper, the focus will mainly be on green tea. So, what is green tea? Why green tea is considered a healthier drink? There are a lot of questions about green tea and the importance of its use. Some people are confused about the benefits or impacts on the human health from drinking green tea. Therefore, the objectives of this research are to clarify the benefits and the impacts of green tea on the human health, and to answer some of the questions about green tea that occupy individuals' minds and make them concerned about drinking it.

Research paper questions:

1. What are the active compounds in green tea?
2. What are the benefits and impacts of drinking green tea on the human health?
3. What are the health consequences of overconsumption of green tea?

Background

Tea is one of the most popular beverages consumed worldwide. In fact, it is considered as the most widely consumed beverage in the world after water. About 20 decades ago, the harvesting of green tea leaves began in India and China. It is assessed that around 2.5 million tons of tea leaves are produced every year throughout the world, with 20% of those being green tea (Webb, 2000). Green tea is mostly consumed in Asia, a few countries in North Africa, United States, and Europe. Webb (2000) reported that tea is grown in about 30 countries, and green, black, and oolong tea are cultivated mostly in East Asia. Hence, Asians consume green and oolong tea the most, while Americans consume mostly black tea. Nordqvist (2014) indicated that about 78% of the tea consumed in the worldwide is black, and only about 20% is green.

There are three main types of tea, which are known as green tea, black tea, and oolong tea. The alternative name of green tea is *Camellia sinensis* and because of its very high concentration of polyphenols, green tea taste extremely bitter. The active compound of green tea is catechins which contain six primary compounds known as catechin, gallaogatechin, epicatechin, epigallocatechin, epicatechin gallate, and apigallocatechin gallate, or abbreviated as EGCG (Steven, 2011). EGCG is the most studied polyphenol component in green tea, and it is also the most active one (Steven, 2011). Additionally, green tea contains alkaloids including caffeine, theobromine, and theophylline. For example, a cup of green tea contains 20-45 milligrams of caffeine compared to 50 milligrams in black tea, and 95 milligrams in coffee. Nordqvist (2014) reported that green tea leaves contains approximately 20-45% of polyphenols, and 60-80% of catechins of green tea leaf's weight. According to Cabrera et al. (2006), the main flavonoids present in green tea are catechins compounds, and the amount of catechins is always

greater in green tea than other teas. Adnan et al. (2013) reported that oxidation of catechins compounds in black tea makes theaflavins and thearubigins, which are responsible for its red-orange appearance, and black tea's color and flavour. Moreover, theaflavins and thearubigins concentrations in black tea are 20% greater than in others teas (Table 1; Adnan et al., 2013)

Table 1: The differences between black and green tea compositions as reported by Adnan et al. (2013)

	% of Black Tea Dry Weight	**% of Green Tea Dry Wight**
Catechins	8	70
Thearubigins	71	0
Theaflavins	12	0
Flavonols	10	10

Chemical Composition

Drinking tea is an ideal method for battling thirst because of its invigorating properties, distinct taste, and its fruity and acceptable smell. Nevertheless, the chemical composition of green tea is rather complex to say the least (Table 2; Cabrera et al., 2006).

Table 2: Green tea's chemical composition and nutritional value as reported by Cabrera et al. (2006).

Chemical Composition of Green Tea	**% of Dry Weight**	**Examples**
Proteins	15–20%	Enzymes
Amino acids	14%	Teanine, 5-Nethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, lysine
Carbohydrates	5–7%	Cellulose, pectins, glucose, fructose, sucrose
Lipids	-	Linoleic acid, linolenic acid
Sterols	-	Stigmasterol
Vitamins	-	(B, C, E)
Xanthic bases	-	Caffeine and theophylline
Pigments	-	Chlorophyll and carotenoids
Volatile	-	Aldehydes, alcohols, esters, lactones, hydrocarbons
Minerals and trace elements	5%	Ca, Mg, Cr, Mn, Fe, Cu, Zn, Mo, Se, Na, P, Co, Sr, Ni, K, F and Al.

Adnan et al. (2013) evaluated the quality of black and green tea samples that commercialized in Pakistan. They used physicochemical analysis, mineral analysis, and sensory evaluation to access fifteen samples (10 black tea and 5 green tea). In their results, they found significant variations in physicochemical and organoleptic parameters. For example, they observed different ranges of moisture with (2.46-7.47%), protein (0.87-1.141%), fat (0.94-2.15%), crude fiber (11.23-17.21%), water extracts (32.34-53.61%), ash (3.29-5.86%), caffeine

(2.34-4.33%) and catechins (0-7.44%). In addition, they reported that green tea samples had the highest percentages of moisture, fat, protein, and crude fiber, while black tea samples had the highest percentage of ash and water extracts. Moreover, green tea samples had greater amounts of calcium (1.47-3.84 mg/l), magnesium (2.97-5.66 mg/l), sodium (0.39-1.83 mg/l), potassium (3.01-4.00 mg/l), and manganese (1.09-2.43 mg/l) compared to black tea. Cabrera et al. (2006) observed that in green tea there are large differences in mineral content values such as aluminum, calcium, magnesium, and manganese, which came from different origins. However, they did not find any clear differences between mineral contents of both green and black tea. In addition, they indicated that black tea had higher aluminum and fluoride concentrations than green tea, but polyphenols are found at greater concentrations in the leaves of green tea. Additionally, although black and green tea both contain similar amounts of flavonoids, they differ in their chemical structure.

According to Cooper et al. (2005), although green tea contains more vitamin C (436 mg) than black tea (239 mg), the aggregate substance of vitamin C in green tea leaves is reduced during the manufacturing process of fermenting the tea. For example, Pulido et al. (2003) evaluated and compared the contribution of the most consumed beverages to the antioxidant intake of lipophilic and hydrophilic in the Spanish diet by doing an annual survey for 5400 households, 700 hotels and restaurants, and 200 institutions, for their daily beverage consumptions They estimated the dietary antioxidants intake in beverages by comparing with antioxidants vitamins C and E daily requirements. Based on their findings, the antioxidants intake in Spanish diet is estimated at 1623 mg of vitamin E and 598 mg of vitamin C. However, tea contributed only 3–5% of the total antioxidants while coffee and red wine were the main contributors with 16-22%.

Green Tea Processing

Green tea leaves are produced from *Camellia sinensis*, which contain high amounts of polyphenols. Green tea production is characterized by an initial and partial withering (heating) process, which kills polyphenol oxidase enzyme that are responsible for the conversion of the flavanols in the leaf into the dark polyphenolic compounds, which color black tea. The next processing step is the steaming stage, and according to Cabrera et al. (2006), the advantages of this step are more attractive, dried leaves, brewed liquor, and brewed leaves. However, the disadvantages are that the smell is grassy and the taste is bitter. The other important process is rolling and drying where leaves are cut and twisted. The final firing process (roasting; Figures 1 and 2) in order to form and produce green tea depends on the particular variant being produced.

Cabrera et al. (2006) stressed that green tea processes (non-fermentation process) preserve natural polyphenols with respect to the health-promoting properties. As green tea is fermented into oolong tea, and then to black tea (fermentation process), non-oxidized phenolic compounds (catechins) in green tea are converted to oxidized phenolic compounds to form a variety of theaflavins (black tea) which may have different biological activities.

According to Leaves of Tea (2009), all types of tea come from the same plant which is *Camellia Sinensis*, but the differences between the teas is related to the differing oxidation levels that the tea leaves undergo during processing steps after green tea is picked. Pure water is very important for preparing the tea. Water free of lime, impurities, and other undesirable elements can make better tea. For example, teas prepared by filtered or bottled water had a better taste than teas prepared by tap water Leaves of Tea (2009). Additionally, Leaves of Tea (2009) suggested that using cold water to make tea is better than using hot water because hot water can add contaminants and reduce the oxygen amount in water, which is important for flavor

extraction. Different types of tea have different water temperatures and different length of time for preparing (Table 3). Moreover, using boiling water in green or white teas can burn their leaves creating a bitter flavor. In most high quality tea leaves, consumers can use the same tea leaves several times after the tea leaves have been brewed in the cup. For example, white and oolong teas are specially produced to be used several times without causing taste changes and they are better in this regard than other types of teas (Leaves of tea, 2009).

Table 3. The differences between teas steeps (Leaves of Tea, 2009).

Tea Type	**Temperature**	**Amount/ 6-8 oz. Serving**	**Steep Time**
White	175-185	1 tablespoon	1-3 minutes
Green	185	1 teaspoon	2-3 minutes
Black	206	1 teaspoon	3-5 minutes
Darjeeling	185	1 teaspoon	3 minutes
Oolong Long Leaf	185-206	1 tablespoon	3-5 minutes
Botanical Infusions/ Tisane	206	1 tablespoon	5-7 minutes
Raw Pu-erh	195	1 tablespoon	First soak for 30 seconds then flush. 3-5 minutes

Caffeine content in tea varies depending on source and processing (Table 4). Lin et al. (2003) have compared the caffeine content in tea that was manufactured using a different

fermentation processes by using an isocratic HPLC process. Several tea samples were extracted by boiling water and other by 75% of ethanol. The levels of EGCG and total catechins in tea were highest in green tea (old leaves), followed by green tea (young leaves), oolong tea, black tea, and pu-erh tea, respectively. The group of tea samples that were extracted by 75% ethanol had higher levels of EGCG and total catechins than tea samples extracted by boiling water. Additionally, they reported that young tea leaves contain more caffeine than old leaves. Lin et al. (2003) concluded that the amount of caffeine and catechins in teas each changes depending on manufactured and fermentation processes. The caffeine level presented in the following order: black tea, oolong tea, green tea, and fresh tea leaf, but EGCG and total catechins levels presented in order: green tea, oolong tea, fresh tea leaf, and black tea. Cabrera et al. (2006) determined the caffeine content in 45 samples of tea, which included fermented red tea, black tea, oolong tea, and green tea. The results showed that the caffeine content was higher in black tea than in green and oolong tea. In addition, they reported that caffeine content is higher in fermented tea than in non-fermented tea. Furthermore, the caffeine content in green tea may differ as per the type of tea and the form of preparations such as its fermenting time. Additionally, they reported that the relative catechins content of green tea depends on other factors such as the processing of the leaves before drying, the location and the requirements of growing, the type of green tea products, and the preparation conditions such as the amount of the product used, the brew time, and the temperature.

Table 4. Caffeine content of tea (Food and Chemical Toxicology, 2014).

Type of tea	Size	Caffeine
Brewed tea		
Black tea	8 oz. (237 mL)	14-70 mg
Black tea, decaffeinated	8 oz. (237 mL)	0-12 mg
Green tea	8 oz. (237 mL)	24-45 mg
Iced tea		
Instant, prepared with water	8 oz. (237 mL)	11-47 mg
Ready-to-drink, bottled	8 oz. (237 mL)	5-40 mg

During food processing, green tea catechins can undergo degradation, oxidation, epimerization, and polymerization. Factors that can make some changes in the chemical structures of green tea catechins during processing includes temperature, pH of the system value, oxygen availability, presence of metal ions, and ingredients added. Victoria et al. (2013) evaluated the stability of green tea catechins during food processing and storage. Their results showed that green tea catechins decreased if the temperature was increased, and catechins degradation declined if the temperature was decreased. Green tea catechins were very stable when pH was below 4, however, when the pH was higher than 4, catechins were unstable. Additionally, higher oxygen levels increased catechin oxidation, but low oxygen levels made catechin degradation stable with only 5%. Moreover, green tea catechins stability can also affect by food storage (i.e., temperature, and humidity). For example, the highest degree (85 ˚C) of temperature and humidity lost the most green tea catechins. Additionally, when the temperature and humidity increased to a higher degree (90 ˚C), the speed of catechin degradation increased.

According to Kim et al. (2007), controlling the temperature during the heat processing is very important to maintain the stability of tea catechins in ready-to-drink tea product. They investigated the effects of heating on chemical compositions of green tea liquor by using high performance liquid chromatography and gas chromatography-mass spectrometry. They found that green tea liquor became darker and less green when heating temperature was increased from 85 ˚C to 120 ˚C. In addition, heating had an effect on tea catechins epimerization (EGCG, EGC, EC, and ECG) and total catechins were reduced after processing. Because the heating at 85 ˚C can cause fewer changes in green tea liquor color and concentrations of catechins, authors suggested heating at 85 ˚C for extraction and pasteurization for canned ready-to-drink green tea. Pasteurization at 85 ˚C decreased EGCG by 2% and EGC by 0.85% compared to 40.22% and 16.67% when pasteurized at 120 ˚C, respectively. Authors concluded that with increasing the temperature, the total amounts of green tea catechins can decrease, and the oxidation can occur during heating process besides the epimerization.

Chen et al. (2001) examined the stability of GTC under different processing conditions. When they used GTC in water at room temperature, GTC was stable, however, when they brewed GTC at 98 ˚C for 7 hours, they found that GTC decreased by 20%. Additionally, when they autoclaved GTC and pure EGCG at 120 ˚C for 20 minutes, the epimerization of EGCG to GCG was apparent. Moreover, they observed that with lower the pH values, the more stability of GTC during tea storage. When authors added sucrose solutions that contained citric acid and ascorbic acid to tea drinks, GTC exhibited the stability irrespective of low pH value. The authors concluded that the addition of ascorbic acid could maintain the stability of GTC only for one month, but at long storage period, ascorbic acid can enhance GTC degradation due to its impact

as a prooxidant. Authors suggested that the degradation of GTC must be considered when canned and bottled tea drinks were produced, stored, and transported.

Bioavailability of Green Tea Catechins

Based on Manach et al. (2004), the potential health effects of catechins do not only depend on the amount of consumption but also on their bioavailability, which appears to be very variable. Therefore, it is important to know the catechins bioavailability and metabolism and to evaluate their biological activity within target tissues. Moreover, the effect of drinking green tea may also differ by genotype because the differences between the species in the bioavailability of EGCG compared to other tea catechins. According to Manach et al. (2004), catechins compounds cannot be totally extracted from the fresh green tea's leaves through its preparation and therefore, the concentration of catechins differs from the absolute values. Moreover, catechins are comparatively unsteady and could be quantitatively and subjectively changed during the time period of any given experiment. Thus, the comparison of ingested doses in animal studies is not possible due to the catechins quantification before administration is frequently not known. For example, Kim et al. (2000) measured the levels of tea catechins in plasma and tissue of mice after chronic consumption of green tea polyphenols. For a period of 28 days experiment, both sexes of mice were given different concentrations (0.2%, 0.4%, and 0.6%) of green tea polyphenols (GTP) in their drinking water. They reported that large amounts of epicatechin gallate (EGC) and epicatechin (EC) were seen in the mice’s esophagus, large intestine, kidney, bladder, lung, and prostate. However, low concentrations of EGC and EC were found in mice’s liver, spleen, heart, and thyroid. Because of the poor absorption, EGCG levels were lower in some organs but were higher in esophagus and large intestine. Furthermore,

according to Lu et al. (2003), the considerable differences in the bioavailability of GTP in individuals may be due to the differences in colonic microflora and genetic polymorphism among the enzymes involved in polyphenol metabolism.

According to Xu et al. (2004), green tea canned and bottled not only contain epicatechins (GTE) which are epigallocatechin gallate (EGCG), epicatechin gallate (ECG), epigallocatechin (EGC), and epicatechin (EC), but also contain four GTE epimers, which are gallocatechin gallate (GCG), catechin gallate (CG), gallocatechin (GC), and catechin (C). So, in their study, they examined the antioxidant activity and bioavailability of tea epicatechins with their corresponding precursors. Their results showed that CG and ECG had the same antioxidants activity, but they were different in antioxidant potency in all assays. In addition, EGCG and GCG had the same antioxidant activity in LDL oxidation and DPPH free radical. Generally, GTE and epimers have small differences and low bioavailability in both. The authors concluded that the epimerization reaction that happens in manufacturing canned and bottled tea beverages would not impact the activity and bioavailability of antioxidant of total tea polyphenols.

Egert et al. (2013) investigated the effects of dietary proteins (casein and soy) and skimmed milk on the plasma kinetics of green tea catechins (GTC). They used a randomized crossover design in their methods, in which 24 healthy normal-weight females consumed a test drink that contained 1.75 g of GTC extracts with or without protein additions for one week. The treatments were: GTC (control group), GTC plus skimmed milk (GTC+M), GTC plus caseinate (GTC+ CS), and GTC plus soy protein (GTC+ S). The blood samples were taken before the experiment and every 4.5 hours after they took the treatments. In their results, they found that the consumption of GTC with the three protein treatments (milk, caseinate, and soy) significantly decreased the bioavailability of total catechins with means (GTC+M, 87 +/- 5%), (GTC+CS, 79

+/- 5%), and (GTC+S, 88 +/- 4%), epigallocatechin gallate with means (GTC+M, 68 +/- 4%), (GTC+ CS, 63 +/- 5%), and (GTC+S, 76 +/- 5%), and epicatechin gallate with means (GTC+ M, 68 +/- 5%), (GTC+ CS, 66 +/- 6%), and (GTC+S, 77 +/- 6%) compared with control group. However, the bioavailability of non-galloylated catechins were significantly increased for epigallocatechin with means (GTC+ M, 134+/- 9%), (GTC+ CS, 118 +/- 9%), and (GTC+ S, 123 +/- 8%), and epicatechin with means (GTC+ M, 125 +/- 10%), (GTC+ CS, 114+/- 11%), and (GTC+ S, 110 +/- 8%). In addition, they observed that no significant differences were found in the bioavailability of GTC between the three proteins treatments and GTC. They concluded that the bioavailability of galloylated catechins from GTC is reduced by the simultaneous ingestion of dietary proteins in human body.

CHAPTER TWO

LITERATURE REVIEW

Researchers differ in opinion concerning the use of green tea, where some of them support its consumption while others oppose the idea. Nevertheless, regardless of their varying opinions, extensive evidence exists to support their views. Therefore, this paper discusses their different opinions and the relationship between green tea consumption and some of the human health-related diseases.

According to Jigisha at el. (2012), green tea is the purest and the most unadulterated form of tea, which has always impacted human health since the beginning of time. Throughout the world, people have made aware of the numerous health benefits associated with this herbal drink. For example, Chinese and Indian practitioners used green tea as a stimulant, a diuretic to assist the body in ridding itself of excess fluid, an astringent to control bleeding and assist in healing injuries, and to improve heart health (Nordqvist, 2014). Other people have also used green tea to treat heartburn, to regulate body temperatures and blood sugar, to facilitate digestion, and to improve mental processes (Nordqvist, 2014).

According to Cooper et al. (2005), despite the fact that green tea is not authoritatively perceived as a medicinal agent, it certainly stands out amongst the most examined plant-based cures whose conceivable profits incorporate the advancement of some health situations such as cardiovascular health, cancer prevention, skin protection, cholesterol levels, infection, impaired immune function, diarrhea, fatigue, and many others. Although the exact mechanisms by which green tea improves health are still debatable at large; the strong antioxidant properties of green tea, effects on body energy expenditure and lipid and sugars metabolism, and their abilities to

defeat free radicals in cells have been suggested as possible mechanisms (Dulloo et al., 1999; Juhel et al., 2000; Cooper et al., 2005; Shoji et al., 2006). In this research report, I will focus on some off health promoting effects of green tea such as cancer, cardiovascular, obesity (body weight control), insulin sensitivity, oral health, and arthritis.

Obesity

Obesity in America has increased at an extremely high rate and is now considered a global health problem. Current enthusiasm for the consumption of healthy foods for weight control is concentrated on plant components that are capable of interfering with the sympathoadrenal systems in the body (Cooper et al., 2005).

Cooper et al. (2005) studied the anti-obesity impact of green tea on female mice fed green tea at 1 to 4% of their diets for four months. Their results showed that mice fed the green tea had a significant suppression of food intake, body weight gain, and fat tissue accumulation. Moreover, the levels of cholesterol and triglycerides were also lower in their blood. The inhibitory activity of green tea extract (AR25 standardized at 25% of catechins) on gastric and pancreatic lipase activities were examined *in vitro* by Juhel et al. (2000a). Tributyrin was used in this experiment as a substrate to evaluate the capability of AR25 catechins to induce digestive lipase inhibition. Gastric lipase was completely inhibited by 40 mg of AR25/g tributyrin. However, pancreatic lipase was inhibited maximum (78.8+/-0.7%) with 80 mg of AR25/g tributyrin. Using triolein (a long-chain triglyceride) treatment but under *in vivo* conditions, Juhel et al. (2002b) reported a great decrease in gastric lipolysis (96.8+/- 0.4%) by AR25 of 60 mg/g triolein however, the inhibitory effect was less significant on pancreatic lipase (66.50+/- 0.92%). Moreover, they measured lipid emulsification and emulsion droplet size in gastric and duodenal

area in existence of AR25 catechins. They found that AR25 catechins inhibited lipids emulsification-process, suggesting that the inhibition of gastric and pancreatic lipase could be related to changes in lipid emulsification in gastric or duodenal areas.

The relationship between green tea extract and energy expenditure was studied by Dulloo et al (1999). The authors investigated whether a green tea extract high in caffeine and catechin polyphenols affects energy expenditure (EE) and fat oxidation in humans. The study was done on 10 healthy men and EE and the respiratory quotient (RQ) were measured in a respiratory chamber during a 24 hr. The subjects were randomly assigned into three treatments and received either green tea extract with 50 mg caffeine, 90 mg epigallocatechin gallate, and 50 mg caffeine or placebo. The three treatments were ingested at all three meals: breakfast, lunch, and dinner. Compared with placebo, there was a significant 4% increase in EE and a significant decrease in RQ for the treatment with green tea extract. Additionally, authors reported no effects on EE and RQ during the treatment with caffeine in amounts equivalent to those found in green tea extract. Authors concluded that green tea has thermogenic properties and encourages fat oxidation beyond that clarified by its caffeine content. In addition, authors suggested that green tea could play an important role in body composition control by sympathetic activation of thermogenesis, fat oxidation, or both. Their findings are further supported by Cabrera et al. (2006) whom also reported that green tea extracts stimulated brown adipose tissue thermogenesis to an extent, which is much greater than can be attributed to its caffeine content, with thermogenic properties residing primarily in an interaction between its catechin polyphenol and caffeine content.

A study by Murase et al. (2002) investigated the long-term effects of consuming green tea catechins on the development of obesity in mice. Mice were fed diets containing low fat (5%

triglyceride), high-fat (30% triglyceride), or high fat supplemented with 0.1-0.5% green tea catechins. Diets were fed for 11 months, and body weight, adipose tissue mass, and liver fat content were measured. Additionally, after one month of feeding, beta-oxidation activities and mRNA levels were also measured. Their results showed that diets with tea catechins had significantly reduced the high-fat diet-induced body weight gain, visceral and liver fat accumulation, and the development of hyperinsulinemia, and hyperleptinemia. Moreover, they found that feeding mice green tea catechins for one-month significantly increased acyl-CoA oxidase and medium chain acyl-CoA dehydrogenase mRNA expression as well as beta-oxidation activity in the liver. Authors concluded that the responsible factor for the anti-obesity effects of green tea catechins is the stimulation of hepatic lipid metabolism suggesting that the consumption of green tea catechins for a long period is beneficial for the repression of diet-caused obesity.

Chacko et al. (2010) investigated the effect of green tea cateshins on body weight of obese mice. In their study, three groups of obese mice were fed the leaves of oolong, black, and green tea for one week. Results from their study showed that the body weights of mice, plasma triglyceride, cholesterol, and low-density lipoprotein cholesterol were essentially lessened by all treatments (black, oolong, and green tea) and the decrease was greatest with the green tea treatment. Their results also showed that the decreases in body weight and plasma cholesterol were via decreasing energy absorption, increasing fat oxidation, and increasing postprandial thermogenesis and fat oxidation.

Boschmann and Thielecke (2007) investigated the effect of green tea (EGCG), but on human body weight. A randomized, double blind, placebo-controlled, cross-over pilot study was used where six obese men were given 300 mg EGCG just for two days. They reported that the

resting energy expenditure did not vary fundamentally between EGCG and placebo treatments, however, respiratory quotient values were significantly lower with EGCG treatment compared with the placebo. Authors suggested that EGCG alone can possibly increase fat oxidation in men and may accordingly add to the anti-obesity effects of green tea. However, they conclude that more studies with a more prominent sample size and a broader range of age and body mass index are needed to characterize the ideal dose.

In a recent study by Chuanwen et al. (2012), three groups of Sprague Dawley female mice (12 per group) were fed either low fat diet (control), high fat diet (HF), or high fat diet plus green tea polyphenols (HF+GTP +in drinking water). Compared with the control group, the body weight of HF mice was increased. However, the body weight of HF + GTP mice was lower than that of the HF mice. Additionally, after analyzing eighty-four genes related to obesity in liver samples from mice, the authors noticed that the HF group had significant changes in 12 genes related to obesity and energy expenditure compared with the control group. These 12 genes, however, were interestingly restored by the HF + GTP group. Authors concluded that green tea beneficial impact on obesity is via regulating obesity-related genes in the liver.

A study by Cunha et al. (2013) assessed green tea extract effects on lipolytic protein levels in adipose tissue of obese mice. In their experiment, four groups of 8 weeks old obese mice were fed treatment diets for two months. Treatments were: chow diet + water (CW), chow + water + green tea extract (CG), high fat diet + water (HW), and high fat diet + water + green tea extract (HG). Their results showed that green tea fed with high-fat diet increased hormone sensitive lipase (HSL), ABHD5, comparative gene identification-58 (CGI-58), and perilipin in mesenteric adipose tissue. Additionally, green tea supplementation also decreased inflammatory cytokine TNFα levels, toll-like receptor-associated factor 4 (TLR4), myeloid differentiation

primary response gene 88 (MYD88), tumour necrosis factor receptor-associated factor 6 (TRAF6), and proinflammatory signaling. Authors concluded that green tea could reduce adipose tissues by increasing the lipolytic pathway, and reducing inflammation in adipose tissues of obese mice.

A study on male mice by Klaus et al. (2005) investigated the effects of the green tea EGCG on high fat Western diet that influenced obesity and symptoms of metabolic syndrome. There were two groups of male mice; the first group was fed a high fat Western diet (60% of energy from fat) while the other group was fed a high fat Western diet with 0.32% EGCG for 17 weeks. Additionally, there were two other groups of mice fed either a low fat diet (10% of energy as fat) or a high fat diet (60% of energy as fat). Results from their study showed that the group of mice fed the high fat Western diet gained more weight in their bodies and had more severe symptoms of metabolic syndrome than the high fat diet group. However, comparing with the high fat Western diet group, the high fat Western diet with EGCG treatment significantly reduced body weight gain, increased fecal lipids, and decreased blood glucose and alanine aminotransferase levels. Moreover, EGCG treatment also reduced fatty liver incidence, liver damage, liver triglyceride levels, insulin resistance, and levels of plasma cholesterol. Authors concluded that high fat Western diet creates more severe symptoms of metabolic syndrome than high fat diet however, EGCG supplementation can lessen these symptoms and body fat accumulation.

In summary, green tea and green tea extract have beneficial impacts on obesity by altering some metabolites, enzymes, genes,etc. associated with lipid metabolism. For example, green tea and green tea extract reduced cholesterol, low-density cholesterol, respiratory quotient, and triglycerides levels, and inhibited gastric and pancreatic lipases and lipid-emulsification.

Moreover, green tea increased acyl-CoA oxidase, medium chain acyl-CoA dehydrogenase mRNA expression, beta-oxidation activity in the liver, and lipolytic pathway. Additionally, consuming green tea for a long period reduced the high fat diet-induced body weight gain, visceral and liver fat accumulation, and the development of hyperinsulinemia, and hyperleptinemia.

Diabetes

Cabrera et al. (2006) reported that African black tea extracts have been indicated to stifle the rise of blood glucose amid diabetic's food allowances and reduce body weight in mice with diabetes. Shoji et al. (2006) studied the repression effect of powder formulation of African black tea extract, prepared from green tea leaves, on 8 weeks old diabetic mice that have had type 2 diabetes (non-insulin dependent). These mice were starved for one day before doing OGTT test (oral glucose tolerance test). The mice were fed with 5, 10, or 50 mg/kg of the powder formulation of black tea extract and control mice were administered water for the 4 weeks of the experiment. After 4 hours, the mice were orally administered 2 mg/kg of glucose and blood samples were then collected at 0, 30, 60, 120 minutes after administered to measure blood glucose level. After 3 months for long-term treatment, the same OGTT was tested again. Their results showed a 33% suppression in blood glucose level in mice fed the African black tea relative to control. Moreover, mice's intestine weight and body weight also decreased by 15% and 47%, respectively, in mice fed the African black tea.

Benaraba et al. (2009) used air model of insulin resistance in their study to determine green tea extract's effects on oxidative stress parameters and insulin sensitivity. Ten individuals per group were fed either 10 g/kg diet of high fructose (control) or the control diet plus 2 g of

green tea solids/kg diet for 6 weeks. Their results showed that the group fed a high fructose diet plus the green tea developed the signs of insulin resistance such as, hyperglycemia, hypertriglyceridemia, and hyperinsulinemia, but not in those of the control group who just fed the high fructose diet. However, when authors repeated the same experiment on mice, their results showed that mice fed the high fructose diet plus the green tea diet had decreases in glycemia, insulinemia, and triglyceridemia consistent with an insulin-potentiating effect of tea. Moreover, they found that tea consumption reduced the oxidative stress, plasma lipid peroxidation, sultbydry l group oxidation, and DNA oxidative damages, suggesting that green tea has protective effects against oxidative stress and insulin resistance.

Anderson and Polansky (2002) investigated the insulin-enhancing properties of tea and its components on mice. Ten mice per group were fed 5g/kg diet of green, black, or oolong tea for one week. Their results showed that the consumption of all three teas increased insulin activity in epididymal fat cell mice. However, green tea was more effective for increasing the insulin activity by 63% than oolong tea (54%) and black tea (42%). Additionally, authors indicated that the insulin activity for green and oolong tea was due to EGCG and compounds in green tea such as, epigallocatechin gallate, epicatechin gallate, tannins, and theaflavins enhanced insulin activity. When a piece of lemon was added to the mice's diets, authors reported no changes in the insulin-potentiating activity. However, when they added 5g of 2% milk per cup/diet, the insulin-potentiating activity decreased by one-third, and by 90% when 50g of milk per cup/diet was added. The authors concluded that green tea contains compounds that affected the insulin activity and this activity is further altered by milk addition to green tea.

Wu et al. (2004) analyzed the effect of green tea supplementation on glucose resilience and insulin sensitivity in rats. Rats were separated into two groups, where the control group fed

standard chow and deionized refined water, while the experimental group fed the same chow diet but with green tea instead of water (0.5 g of lyophilized green tea powder dissolved in 100 mL of deionized refined water). Following 12 weeks of green tea supplementation, the results showed that rats received the green tea had lower fasting plasma levels of glucose, insulin, triglycerides, and free fatty acids than the control rats. Likewise, green tea polyphenols (GTP) significantly raised basal and insulin-stimulated glucose uptake of adipocytes. Authors concluded that EGCG does not only control the glucose level in blood, but may also rehabilitate harmed beta-cells, which are responsible for insulin production.

Venables et al. (2008) investigated the effects of green tea extract (GTE) ingestion on glucose resilience and fat oxidation amid moderate-intensity exercise in people. In the first study, 12 healthy men performed a 30-min cycling exercise at 60% of maximal oxygen consumption ($\dot{V}O_{2max}$) before and after supplementation. In study two, 11 healthy men took an oral-glucose-tolerance test before and after supplementation. In the 24-h period before the experimental trials, participants ingested 3 capsules containing either GTE (total: 890.13mg polyphenols and 366.5 mg EGCG) or a corn-flour placebo (total: 1729.22 mg). Results showed the average fat oxidation rates were 17% higher after ingestion of GTE than after placebo ingestion. Additionally, the contribution of fat oxidation to total energy expenditure was also significantly higher by a similar percentage after GTE supplementation. Authors concluded that GTE ingestion can increase fat oxidation during moderate-intensity exercise and can improve insulin sensitivity and glucose tolerance in healthy young people.

Spadiene et al. (2014) investigated the antioxidant effects of green tea extract in patients with type-2 diabetes in a double blind placebo controlled study. Patients (aged 35 to 80 years) received either green tea extract liquid (contained 200 mg standardized extract of green tea

leaves and adjusted to 70% polyphenols) or placebo capsules. Authors emphasized that the status of type-2 diabetes and its complications, oxidative stress parameters, and biochemical measurements were evaluated at the baseline measurements that repeated after 9 and 18 months of receiving results. In the first 9 months, all patients took capsules twice/day, and in the second 9 months, they took capsules three times/day. In their results, they found that EGCG was the most active antioxidant by 50% of green tea extract capacity. After 9 and 18 months, they also found a noticeable decreased of lipid peroxidation in patients and increased antioxidant enzymes activity. Authors concluded that all findings were very helpful and attractive for type-2 diabetic patients.

Using a double-blinded, randomized and placebo-controlled clinical trial, Liu et al. (2014) investigated the effects of green tea extract on patients with type-2 diabetes mellitus and lipid abnormalities on glycemic and lipid profiles and hormone peptides. Patients in therapeutic group (39 individuals) took 500 mg of green tea extract three times a day. Control group (38 individuals) took the same dose but with cellulose for 16-weeks. After 16 weeks on supplements, glycemic and lipid profiles, safety parameters, and obesity-related hormone peptides were measured in all individuals. Individuals received green tea extract showed significant decreases in triglyceride and homeostasis of insulin resistance index compared to control group. Moreover, adiponectin, apolipoprotein A1, and apolipoprotein B100 increased in both groups, but in therapeutic group only glucagon-peptide 1 was increased. Authors concluded that green tea extract has some significant improvements in type-2 diabetic patients such as insulin resistance and glucagon-peptide.

In summary, consuming green tea or green tea extracts seems to have beneficial effects on individuals with diabetes. For example, green tea or its extracts has been shown to rehabilitate

harmed beta-cells, which is responsible for insulin producing, lessens the signs of insulin resistance, and lower fasting plasma levels of glucose, insulin, triglycerides, and free fatty acids.

Green Tea and Cancer

The role of green tea and its fight against cancer has been recognized by numerous studies in cell culture and animal models. According to Chacko et al. (2010), green tea consumption has been connected with the prevention of many types of cancer including lung, colon, esophagus, mouth, stomach, small intestine, kidney, pancreas, and mammary glands. The preventative effects of green tea were attributed to its antioxidant action; the particular induction of detoxifying enzymes; its molecular regulatory capacities on cellular development, growth and apoptosis; and/or a selective development in the function of the intestinal bacteria flora (Chacko et al., 2010).

Yang et al. (2012) investigated whether EGCG can enhance 5-Fluorouracil (5-FU)-induced cell growth inhibition or not. They took 96-plates of humans' cells that were separated into two groups. The first group was treated with 5, 10, 25, and 50 mmol/L of EGCG drugs and incubated for 48 hours while the second group was not treated with any things. In the authors' results, the anti-tumor effect of 5-FU was increased by EGCG, which inhibited hepatocellular carcinoma (HCC) cell growth. Cells viabilities were (92.94/ 2.26) % for 5 mmol/L of EGCG, (83.95/2.78)% for 10 mmol/L of EGCG, (47.32/3.18)% for 25 mmol/L of EGCG, and (25.40/3.06)% for 50 mmol/L of EGCG. The 5-FU with EGCG reduced to (63.21/5, 98) % for 5 mmol/L of EGCG, (49.12/3.15)% for 10 mmol/L of EGCG, (14.21/2.66)% for 25 mmol/L of EGCG, and (5.21/1.34)% for 50 mmol/L of EGCG. Additionally, treating with EGCG reduced overexpression of COX-2 and PGE2 secretions. Such changes in COX-2 expression can decrease

the phosphorylation of Akt expression, which seemed to be followed by the activated protein kinase (AMPK) hyperactivation (Yang et al., 2012).

Gu et al. (2013) tested the inhibition of EGCG on both HIF-1α activation and VEGF expression, and the subduing of tumor angiogenesis and breast cancer development. Sixteen eight weeks old-breast cancer female mice were vaccinated with cells of breast cancer mouse in the left fourth mammary gland fat pad. For four weeks, eight mice were fed 50-100 mg/kg/d EGCG in drinking water while the other eight (control mice) were only given a drinking water. A dial caliper was used to evaluate tumor size and VEGF expression and capillary density (CD) were measured by collecting blood samples, tumors, heart, and limb muscles samples. Results from the study showed that compared with mice on the control group treatment, tumor weight was significantly reduced by EGCG treatment over the control (0.37/0.15 vs. 1.16/0.30g). Additionally, tumor CD and tumor VEGF expression were also lower in mice fed the EGCG by (109/20 vs. 156/12 pg/mg) and (45.72/1.4 vs. 59.03/3.8 pg/mg), respectively. Compared with the control group, the activation of HIF-1α and NFκB, and VEGF expression were inhibited by 50 μg/ml of EGCG in cultured cells. Authors concluded that green tea EGCG directly inhibited both tumor cells and tumor vasculature.

Kim et al. (2010a) investigated the modifying effects of green tea polyphenols (GTP) on dextran sulfate sodium (DSS)-induced acute colitis and on 1, 2-dimethylhydrazine (DMH) and DSS-induced colon carcinogenesis in male mice. Eighty-five 4 weeks male mice, which had specific pathogen-free ICR, were isolated for 1 week before the start of the experiments. The mice were given fresh water and commercial rodent-pelleted diet ad libitum. After 1 week of isolation, the mice were divided into seven groups, which were one untreated control group, and six experimental groups with 13 mice per group. Group one (control group) were given water

with ad libitum diet. Group two (GTP alone) fed a diet containing only 1% of GTP. Group 3 (DSS) were given a water with 2% of DSS, and fed a basal diet for 6 days. Groups 4, 5, 6, and 7 (GTP) fed diets with different concentrations of GTP (0.1%, 0.25%, 0.5%, and 1%) respectively. At day 6, all mice were killed by deep anesthesia with diethyl ether for determining the effects of dietary GTP on DSS-induced acute colitis. After the mice killed, authors reported that the colon shortening in groups three, four, and five was not changed when the mice were given 0.1% and 0.25% of GTP. However, in groups six and seven, it was increased when the mice were given 0.5% and 1% of GTP. Compared with the control group (group 1), the expression inhibitory factor was lower in group four (DSS plus 0.1% 0f GTP), but increased in group six (DSS plus 0.5% of GTP), and group seven (DSS plus 1% of GTP). In a follow up experiment using same materials and methods, Kim et al. (2010b) determined the effects of 0.01–1% GTP on inflammation-associated colon carcinogenesis induced by DMH/DSS. They found that 0.5-1% doses of GTP tended to increase the development of multiple colon tumors rather prevent it. Authors concluded the modifying effects of GTP on DSS-induced acute colitis and DMH/DSS-induced colon carcinogenesis depends upon its dosage and the expression of proinflammatory cytokines.

Tea has also shown anti-carcinogenic effects against breast cancer in experimental studies. Notwithstanding, existing epidemiologic proof that tea protects against breast cancer has been conflicting. Chacko et al. (2010) introduce a case-control study conducted in southeastern China during 2004 and 2005. The study objective was to proof that tea protects against breast cancer. The occurrence cases included 1009 female patients, 20 to 87 years old, and who were histologically confirmed breast cancer. The other group of 1009 healthy female, 20 to 87 years old and who were randomly engaged from the clinics of breast disease. The data used in their

study was based on duration, frequency, quantity, preparation, and type of tea consumption as well as diet and lifestyle were collected through face-to-face interviews using a validated and reliable questionnaire. After adjusting established and potential confounding factors, they concluded that green tea consumption was connected with a decreased risk of breast cancer by 58%.

A study by Wu et al. (2004) showed that women, who drank green tea, had a significantly reduced risk of breast cancer compared to women, who did not drink green tea regularly for at least less than once a month. Moreover, there were significant trends seen to reduce the risk of cancer by increasing the amount of green tea intake. Moreover, Cabrera et al. (2006) done two studies on Japanese women, who were diagnosed with breast cancer, to confirm the beneficial effect of green tea against breast cancer. The results showed that green tea consumption is inversely correlated with the rate of recurrence especially in women, who were in the early stages of breast cancer. Cabrera et al. (2006) also reported that breast cancer is significantly less common among Asian women, whose diets contain a high intake of soy products and green tea.

In summary, different studies have reported a strong correlation between green tea and anticancer. Green tea can reduce risks for many types of cancer including lung, colon, esophagus, mouth, stomach, small intestine, kidney, pancreas, and mammary glands. Studies have also shown that green tea inhibited tumor cells, tumor vasculature, tumor growth, proliferation, migration, and angiogenesis of cancer. Green tea anticarcinogenic effects however, it depends on EGCG content, duration of drinking green tea, and the number of cups consumed per day.

Cardiovascular Disease and Stroke

Green tea consumption has been associated with less development and progression of atherosclerosis. Geleijnse et al. (1999) in their study with 3454 adults, ages 55 years or older, examined the aortic atherosclerosis via X-ray measurement of calcified deposits in the abdominal aorta, and that with a follow-up duration ranging from two to three years. They concluded that drinking 1-2 cups of green tea daily increased the protection against atherosclerosis disease by 54%. However, the protection against atherosclerosis disease decreased by 31% when consumed more than four cups of green tea per day. They confirmed that high intake of green tea (more than 3 cups per day) is not recommended due to the rise caffeine level in blood. Moreover, the benefit of green tea in coronary atherosclerosis was also reported by Sasazuki et al. (2000) in their study with 512 patients, who had coronary atherosclerosis (302 men and 210 women ages 30 years or older). In their study, they divided the patients into two groups where the first group (men group) was given different concentrations and amounts of green tea (1, 2, 3, 4, 5, or 6 cups per day for one year), and the second group (women group) was given different concentrations and amounts of green tea (1, 2, 3, 4, 5, or 6 cups per day for one year). Their results showed that 117 men and 50 women had significant stenosis of one or more coronary arteries by 38.7% and 23.8%, respectively. Moreover, they recognized that green tea could be a protective factor against coronary atherosclerosis disease, but only in men, by giving high rates of protection with the consumption of 2–3 cups of green tea per day. However, such beneficial effects could decrease with more consumption of green tea (4 cups or more of green tea per day). Nonetheless, authors added that consumed one cup or less of green tea per day does not have the same effect in women. On the other hand, a potential cohort study by Nakachi et al. (2000) on 8522 men and women to confirm the beneficial effect of green tea on cardiovascular disease. Authors

concluded that consuming 10 cups of green tea per day is associated with decreased the risk of death from cardiovascular disease and that could occur in women more than men. Moreover, epidemiological studies suggested that green tea intake is connected with a decreased cardiovascular disease hazard. However, the mechanisms for these notices have stayed dubious. Some studies, including the study done by Cabrera et al. (2006) have exhibited that green tea may influence the cardiovascular function through mechanisms of action that correlate with LDL-cholesterol oxidation. The oxidation of LDL cholesterol, which is associated with a hazard for atherosclerosis and heart disease is inhibited by green tea because of EC and EGCG antioxidant activity.

Miura et al. (2001) studied the antiatherogenic effects of tea catechins in atherosclerosis-susceptible on 10-weeks old male apo protein (apo) E-deficient mice. These apo E mice were fed an atherogenic diet for 14 weeks. During that time, one of these two groups was drinking water supplemented with green tea extract, and the other control group was supplied with water only. The tea extract consisted of the following (g/100 g): EGCg, 58.4; (-)-epigallocatechin (EGC), 11.7; (-)-epicatechin (EC), 6.6; (-)-gallocatechingallate (GCg), 1.6; (-)-epicatechin gallate (ECg), 0.5; and caffeine, 0.4. The estimated actual intake of tea catechins was at 1.7 mg/d per mouse). Their results showed that the ingestion of green tea did not impact plasma cholesterol or triglyceride concentrations. At the week 8 of the experiment, plasma lipid peroxides were reduced in-group 1 that was receiving green tea extract in their drinking water. Moreover, atheromatous areas in the aorta from the arch to the femoral bifurcation and aortic weights were both significantly reduced by 23% in group 1 compared with the control group. They also reported that Aortic cholesterol and triglyceride were lower by 27% and 50%, respectively, in-group 1 than in the control group. Finally, Miura et al. (2001) suggested that chronic ingestion of

green tea extract can prevent the development of atherosclerosis without changing the plasma lipid level and that perhaps through the powerful antioxidative activity of the green tea.

Cooper et al. (2005) suggested that the strong antioxidant prevention agent properties of polyphenols lessens the free radical impacts to cells and prevents the oxidation of LDL cholesterol, both of which would inhibit the formation of atherosclerotic plaques. Maron et al. (2003) studied the effect of a theaflavin-enriched green tea extract on the lipids and lipoproteins of subjects with mild to moderate hypercholesterolemia. Their study was done on 240 males and females, who were 18 years or older, fed a low-fat diet with mild to moderate hypercholesterolemia. Subjects were then randomly allocated to get a day-by-day capsule containing theaflavin-enriched green tea extract (375 mg), or placebo for 12 weeks. Each active capsule contained 75 mg of theaflavins, 150 mg of green tea catechins, and 150 mg of other tea polyphenols, and measurements included the mean % changes in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels compared with baseline. Their results showed that after 12 wks, the mean changes from baseline in total cholesterol, LDL-C, HDL-C, and triglyceride levels were -11.3%, 16.4%, 2.3%, and 2.6%, respectively, in the tea extract group. However, the mean levels of all measurements did not change significantly in the placebo group. In addition, green tea extracts reduced total cholesterol and LDL serums by 11.3% and 16.4%, respectively. Authors concluded that the theaflavin-enriched green tea extract is an effective factor for low-saturated-fat diet to decrease LDL-C in adults diagnosed with hypercholesterolemic. Additionally, from their observations, each 1% decrease in LDL can result in 1.0 to 1.5% decrease in major CVD risks. Long-term consumption green tea extract decreased LDL by 16% and that can decrease the hazards of major CVD by 16 to 24%.

Furthermore, a 12 years study by Imai et al. (1997) on 8522 Japanese males and females showed that men, who consumed 10 cups of green tea per day, could have a 58% decreased hazards of death from heart disease compared with the individuals, who consumed 3 cups or less of green tea per day. Additionally, a 6 years Dutch study on 4807 men and women found that the individuals, who drank more than 3 cups of black tea per day, could have a 68% decreased hazards of myocardial infarction compared with non-tea consumers. Another study done by Geleijnse et al. (2002) over a period of more than 15 years on 552 elderly Dutch men, found that the risk of a stroke for the individuals, who consumed more than 4.7 cups/day of black tea was 31% less risk of a stroke than men, who consumed less than 2.6 cups/day.

Raederstorff et al. (2003) examined the dose-response and the mechanism of activity of EGCG on the parameters of plasma cholesterol levels and the rate of cholesterol absorption in rats. They fed diets contain high cholesterol and fat or none with different concentrations of EGCG (0.25% (0.2 g/day/kg BW), 0.5% (0.4 g/day/kg/BW) or 1.0% (0.7 g/day/kg BW)). Following 4 weeks of treatment, when compared with the non-treatment group, aggregate cholesterol and LDL cholesterol plasma levels were significantly decreased in the group fed 1% of EGCG. In addition, plasma triglycerides and HDL-cholesterol did not significantly change. When the control group was given a liquid test-meal, the absorption of intestinal cholesterol was 79.3%. However, in-group treated with 0.1 and 0.5 g of EGCG/kg, the absorption of intestinal cholesterol decreased to 73.7% and 62.7%, respectively. In control group, the absorption of the total fat was very effective, but it was moderately decreased in the treated group with the highest doses of EGCG (0.75 and 1 g/kg BW). Authors concluded that the lowering effects of green tea on cholesterol level are mainly produced by EGCG. Moreover, Raederstorff et al. (2003) advised that one of the basic mechanisms, by which EGCG influences lipid metabolism, is by meddling

with the micellar solubilization of cholesterol in the digestive tract, which then in turn reduce cholesterol absorption.

Kokubo et al. (2013) investigated the association of green tea and coffee consumption on stroke occurrence in the Japanese overall population. The study was done on 82,369 Japanese of both sexes, aged 45 to 74 years, and who were healthy and without cardiovascular disease or cancer, for three years and 13 years of follow up. They used self-administered food frequency questionnaires at baseline to assess the consumption of green tea and coffee (the frequencies and the amount, times/week or cups/day). Their results showed that compared with occasional drinking of green tea, 2 to 3 cups/day of green tea consumption significantly decreased the danger degrees of all strokes. However, they found that higher green tea consumption was linked with reverse dangers of CVD and strokes subtypes. Compared with moderate coffee consumption, the danger ratios of all strokes were significantly decreased by consumed coffee (3 to 6 times per week) and (1-2 times per day) but no more than 3 cups/day. Authors concluded that drinking coffee was connected with an inverse risk of CVD and cerebral infarction. Higher green tea or coffee consumption decreased the dangers of CVD and stroke subtypes. Moreover, they found that none of the significant connections were noticed in coronary heart disease, and higher green tea and coffee consumptions were conversely connected with the risk of CVD and strokes in the general population.

In clinical trial, Karah et al. (2011) evaluated the impacts of green tea on features of metabolic syndrome and inflammation in obese people. They used 35 obese individuals, 42 years old with BMI 36 kg/m, and with metabolic syndrome. Participants were divided into three groups and received treatments for 8 weeks. Group one received green tea (4 cups/day), group two received green tea extract (2 capsules and 4 cups water/day), and group three received no

treatment (4 cups water/day). Both green tea and green tea extract had the same dose of EGCG. They also collected blood samples in week four and eight of the study. The results of the study showed that there were no significant changes in metabolic syndrome or biomarkers of inflammation when used green tea or green tea extract supplementation. However compared with no treatment group, there was significant reduction in plasma serum amyloid alpha (SAA) when green tea and green tea extracts supplementations were used. Finally, the authors concluded that the daily consumption of green tea or green tea extracts can reduce plasma SAA and independent CVD risk factor between obese people with metabolic syndrome, but without impact the features of metabolic syndrome.

Miyazaki et al. (2013) investigated the impact of green tea catechins consumption (GTC) on CVD in active older people. Fifty-two adults, 20 males and 32 females, aged 69 years old were used in this study. All subjects participated in a walking program, but GTC group had an intake of 630.9 mg/daily for 14 weeks. They measured the cardiovascular risk indicators before and after the study. Their results showed that GTC group had significantly reduced the values of some indicators from the beginning of the study until the end. For example, waist circumference, hip circumference, total cholesterol, low-density lipoprotein cholesterol, and low-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio were lower with GTC group. The authors concluded that despite green tea catechins supplementation cannot impact the cardiovascular risk indicators in active older people, green tea catechins can reduce cholesterol levels.

In summary, a positive correlation between green tea and CVD, stroke, and other heart diseases have been reported by many studies. Green tea protective effect against heart diseases results in part from its effects of blood cholesterol, LDL-C, and triglyceride. Although the

optimum consumption rate for green tea still debatable, 2-3 cups a day seems to be what most studies recommended.

Oral Health

Oral illnesses including dental caries, periodontal disease, and tooth loss might significantly affect a person's overall health (Wu and Wei, 2002). Among these illnesses, dental caries is a multifactorial infectious illness in which nutrition, microbiological infection, and host reaction play key roles. Prior reports in experimental animals and people suggested that green tea consumption, without adding sugar, decrease dental caries. Cabrera et al. (2006) reported that green tea extract is a powerful herbal that can reduce the gingival inflammation that may be created by periodontal structures such as dentures. Furthermore, they pointed out that the antibacterial impacts of green and black tea extracts are comparable with those of amoxicillin, cephradine, and eugenol. Wu and Wei (2002) reported that frequent intake of green tea can significantly diminish caries formation, even in the presence of sugars in the food regimen. Aside from their polyphenol content, both green and black tea are a natural source of fluoride and a powerful vehicle for fluoride delivery to the oral cavity (Cabrera et al., 2006). According to Cabrera et al. (2006), green tea polyphenols can inhibit *Streptococcus mutans*, dental plaque bacteria, and glucosyltransferase enzyme activity. In consequence, Cabrera et al. (2006) stated that green tea is considered a useful food for oral health and has been broadly utilized as a part of toothpaste formulation.

Awadalla et al. (2011) assessed green tea as a protective factor on human oral health. They used different measurements such as *Streptococcus mutans* count in saliva, *Streptococcus mutans* count in plaque samples from margins of composite restorations, and gingival bleeding

index (GBI). Sixty individuals were divided equally into two groups. The first group (control group) used the regular oral hygiene measurements. However, the second group (study group) was given 2% green tea 3 times daily for 7 days. Their results showed that the means of *Streptococcus mutans* count in saliva (1.74 vs 0.64), *Streptococcus mutans* in plaque (2.52 vs 0.80), and GBI (10.7 vs 4.0) were significantly lower in the green tea group than the control group. Authors suggested that green tea effects on *Streptococcus mutans* may be due to catechins ability to reduce plaque acidity and preserving saliva and plaque pH toward neutrality and therefore creating unfavorable conditions for *Streptococcus mutans* growth. Authors concluded that using green tea solution improved oral health by inhibiting *Streptococcus mutans*, which is the main causative bacteria for caries.

Ooshima et al. (2010) examined 35 human volunteers to evaluate the inhibitory effect of green tea extract (GTE) on plaque. All volunteers were 18 to 29 years old. Volunteers were asked to do the oral prophylactic procedures, to avoid all oral hygiene procedures for 4 days, and to rinse their mouths with 0.5 mg/ml GTE solution in 0.2% ethanol before and after every intake of food and before sleeping at night. During the study period, the authors did not give any restrictions for meals except to avoid drinking tea or coffee. At the end of the study, they evaluated the plaque deposition after revealing the teeth with Erythrocin. After 1 week of the first test, they repeated the study for the second trial with giving 0.2% of ethanol solution, but without GTE for mouth rinsing. Their results showed that GTE significantly inhibited plaque deposition in volunteers although there was no significant impact on the *streptococci mutans* in saliva when the GTE solution was used in mouth rinsing.

Otake et al. (2006) investigated the inhibition of acid production from dental plaque and *streptococci mutans* by using one of green tea catechins compounds (epigallocatechin gallate;

EGCg). Fifteen volunteers were used in this study and their mouths were cleaned with 2 mg/ml of EGCg solution. After 30 minutes of waiting, they cleaned the participants' mouths with 10% sucrose. Then, after 20 minutes, they collected the plaque samples` and measured the pH. The results showed that the pH values of plaque samples from 15 volunteers were significantly higher after treatment with catechin than after treatment with water. In addition, when cariogenic bacteria grown in medium with sucrose were incubated with sugar, green tea catechins addition inhibited the pH fall. Authors suggested that EGCg is an effective compound that can decrease the acid production in dental plaque.

Comparing with chlorhexidine and plain water, Linke and LeGeros (2003) evaluated the effect of cleaning mouths with green tea on *Streptococcus mutans* count. The study included 30 participants aged 20 to 25 years. Participants were divided into three groups: group 1 had green tea, group 2 had chlorhexidine, and group 3 had plain water. Participants cleaned their mouths with 10 ml of treatment solutions for one minute under a respective examiner. Five minutes after cleaning, plaque samples were collected and compared to baseline plaque samples collected before cleaning with solutions. Their results showed that both the chlorhexidine and green tea significantly reduced *Streptococcus mutans* colony counts compared to plain water. Authors concluded that green tea and chlorhexidine mouth solutions proved to be equally effective in reducing *Streptococcus mutans* counts in mouth.

Zhang et al. (2012) carried out a study to determine if tea decoctions would delay the release of maltose in food particles that became entrapped on the dentition or not. In their study, 25 subjects of both sexes were divided into three groups and fed salted crackers. Participants then rinsed their mouths for 30 second with black, green tea decoctions, or water. Their results showed that maltose release was reduced by more than 70% after rinsing with both the black and

green tea. However, black tea decoction was more effective than green tea. Authors concluded that tea consumption can reduce the tendency for starch foods to serve as slow-release sources of fermentable carbohydrate.

In summary, green tea has some powerful effects on oral health as it was shown to reduce dental caries, gingival inflammation, and caries formation. Additionally, green tea inhibited the growth *Streptococcus mutans* responsible for most cases of caries.

Arthritis

A study presented by Haggi et al. (1999) deduced that an antioxidant-rich polyphenolic fraction isolated from green tea possess anti-inflammatory properties in laboratory animals. Haggi et al. (1999) conducted a study to determine the effect of oral consumption of green tea polyphenols (GTP) on collagen that persuaded arthritis in mice. In their study, three independent experiments mice were given GTP in water or just water. Compared with mice that received only water, authors found that mice received GTP had significantly less occurrence of arthritis by 33 to 50%. Additionally, a marked reductions in the representation of inflammatory mediators such as, cyclooxygenase 2, interferon (IFN), and tumor necrosis factor (TNF) in the arthritic joints of the mice fed green tea polyphenols were observed. Moreover, total IgG and sort II collagen-particular IgG levels were lower in the serum and the arthritic of mice received the GTP. Authors concluded that green tea polyphenols are very useful and helpful in the protection of acute and sever arthritis.

Kim et al. (2014) investigated the ability of polyphenolic green tea (PGT) to protect against autoimmune arthritis mice adjuvant arthritis (AA) as a model of human rheumatoid arthritis (RA). In their experiment, the mice were given 2-12 g/L of green tea in their drinking

water for one to three weeks and then vaccinated with Mycobacterium tuberculosis H37Ra (Mtb) to persuade disease. Mice were then killed to harvested and test their draining lymph node cells and sera for T cell proliferative, cytokine responses, and for anti-Bhsp65 antibodies. Their results showed that mice received 8 g/L of PGT for nine days had significantly less cute arthritis. Additionally, mice fed PGT had a lower concentration of the proinflammatory cytokine interleukin (IL)-17 and a higher concentration of the immunoregulatory cytokine IL-10. Furthermore, PGT inhibited the anti-Bhsp65 antibody response. Authors concluded that green tea persuade some changes in arthritis that related to immune responses and suggested more methodical examination of PGT dietary supplementation as an adjunct nutritional strategy to manage rheumatoid arthritis.

In summary, green tea has some positive impacts on arthritis as it can reduce the severity of cute arthritis. Green tea reduced the production of inflammatory mediators such as, cyclooxygenase 2, interferon (IFN), and tumor necrosis factor (TNF). Additionally, green tea persuade some changes in arthritis that related to immune responses.

Over Consumption of Green Tea

Although green tea has several beneficial effects on health, the effects of green tea and its components may be beneficial up to a certain dosage; yet higher doses may cause some adverse effects. According to Chacko et al. (2010), although the consumption of herbs, such as green tea, is intended to strengthen the body and treat diseases, they also contain active substances that can trigger side effects and interact with other herbs, supplements, or medications. Moreover, adding green tea to diets at high levels may cause serious health complications.

Chacko et al. (2010) indicated that the effects of green tea catechins may not be similar in all individuals. In fact, they said that EGCG of green tea extract is cytotoxic, and at high consumption levels, green tea can exert acute cytotoxicity and hepatotoxicity in liver cells and in major metabolic organs in the body. Emoto et al. (2014) investigated the responsible mechanism of green tea extract hepatotoxicity in mice. Both sexes of mice, 6 weeks old, were vaccinated with single intraperitoneal and 200 mg/kg green tea extract. Using blood-chemistry, histopathology and immunohistochemistry to notice cell death and proliferative activity, they evaluated liver damage at different times (8, 24, 48 and 72 hours), then after 1 and 3 months. Moreover, by using immunohistochemistry, they analyzed the malondialdehyde in the serum and liver, and placental glutathione S-transferase, which is a sign of hepatocarcinogenesis by immunohistochemistry. Authors also examined the toxicity at older ages of mice (18 weeks old female mice) when fed 200 mg/kg green tea extract. In their results, they reported that 12% of males and 50 % of females, which were 6 week old, and 88% of 18 weeks old died within 72 hours of receiving the green tea extract. The aspartate aminotransferase, alanine aminotransferase, and total bilirubin serum levels increased in both sexes of mice. From 8 hours and up, they noticed positive signs in perilobular hepatocytes of single-cell necrosis, TUNEL, and caspase-3 in all lobular areas. At 48 hours, the positive hepatocytes and malondialdehyde increased in the serum and liver. Authors concluded that a single injection of green tea extract induced acute hepatotoxicity.

Based on Yun et al. (2006) study, higher intake of green tea might cause oxidative DNA damage to a hamster's pancreas and liver. Yun et al. (2006) clarified that green tea polyphenol (EGCG) have two activities, which are antioxidant and pro-oxidant. In their study, Yun et al. (2006) evaluated the effects of nanomolar concentrations of EGCG on beta cell survival and the

response to high glucose loading in streptozotocin-induced diabetic mice. The mice were treated with 5 mg/kg/day of EGCG for 4 days. Their results showed that beta cell increased blood glucose rates in diabetic mice. In addition, in beta cells, EGCG increased the damage of cell mass and insulin-immunoreactivity. From these results, Yun et al. (2006) suggested that green EGCG can act as a pro-oxidant and as an antioxidant, especially in pancreatic beta cells.

Sakamoto et al. (2001) determined the effects of green tea extract catechins on mice thyroid. Green tea catechins source, called polyphenon-60 (p-60), was added at different concentrations (0 (control), 0.625, 1.25, 2.5 and 5.0%) to the diets of mice and fed for 13 weeks. Their results showed that the mean thyroid weight in male mice fed the diet containing 5% P-60 was significantly heavier than in female mice. Additionally, in the thyroid of the 5% group, they have found also some noticeable impacts such as hypertrophy and hyperplasia of the follicles, depletion and/or rich colloid, and formation of a fibrous capsule. However, in male mice group fed the 1.25% P-60 and in female mice fed the 2.5% P-60, they observed a slight hypertrophy of follicular cells in both groups. In all groups, male mice had a higher degree and occurrence of thyroid lesions than female mice. In week 13, they did not observe any impacts level of green tea extract catechins in female mice fed 1.25% p-60 diet, and in males fed 0.625% p-60 diet. In short, they concluded that because of the antithyroid effects of catechins, the dietary supplements of green tea extract catechins at high doses can persuaded goiters in mice.

Moreover, Chacko et al. (2010) claimed that the harmful impacts of black or green tea overconsumption are because of three primary elements, caffeine, aluminum, and tea polyphenols effect on iron bioavailability. Hamdaoui et al. (2003) have shown that black tea inhibits the bioavailability of non-heme iron by 79 to 94% when both are consumed concomitantly. Authors suggested that green tea catechins may have an attraction for iron

causing a significant decrease in iron bioavailability from the diet. However, the effect of this activity relies on iron intake and iron status of the person. Hamdaoui et al. (2003) evaluated the green tea catechins effects on iron bioavailability and the weight gains in mice fed a Tunisian meal (bean seeds ragout), with or without beef, and with black or green tea decoction. By using the hemoglobin repletion method, they evaluated iron bioavailability and the storage of iron in the liver in iron-deficient mice. When they added the beef to the Tunisian meal (control group), they reported a significant increase in iron bioavailability by 147%, and a 77% increase in iron storage in the liver. However, iron bioavailability and the storage of iron in the liver were significantly decreased in both black and green tea decoctions groups relative to that of the control group.

In addition, Cabrera et al. (2006) affirmed that tea should not to be consumed by patients experiencing anemia. Case in point, iron deficiency anemia among kids or people, such as those in Saudi Arabia and the United Kingdom, who drink tea with meals, may be exacerbated by the regular consumption of tea. On the other hand, this impact may be more beneficial to patients who are diagnosed with genetic hemochromatosis. Cabrera et al. (2006) pointed out that it is important to note that the interaction between tea and iron can be alleviated by adding lemon to tea or drinking tea between meals. For example, Marouani et al. (2007) investigated the aluminum (Al) absorption from green tea decoction and its influence on iron status and hematological parameters in mice. In their study, a group of mice fed a simple dose of Al sulfate, a second group fed diet with doses of green tea decoction (25, 50 and 100 g/l), and a third group fed diet without green tea decoction dose. They assessed Al absorption, hemoglobin, and hematocrit in the mice serum, and assessed iron status via iron concentration in mice liver, kidney, spleen and femur. Authors found that depending on green tea doses, there was a

significant increase in Al serum level. In all tested organs, the reserve of iron reduced by Al sulfate, and in groups fed green tea decoction alone, or fed Al with doses of green tea. When mice fed Al alone or with doses of green tea, the concentrations of hemoglobin and hematocrit were significantly reduced. Authors concluded that there was more absorption of Al with green tea decoction than Al sulfate in the mice bloods. The absorption of Al can decrease iron status, hemoglobin, and hematocrit. They assumed that the negative impacts of green tea on iron status are not only from polyphenols iron complexes but also from Al in green tea decoction.

Costa et al. (2002) compared the heating extraction process for Al, calcium (Ca), magnesium (Mg), and manganese (Mn) in tea samples. They adopted a focused-microwave-assisted process for the extraction of Al, Ca, Mg, and Mn in tea leaves. They evaluated the efficiency of extraction by using diluted acids and a water-soluble alkaline tertiary-amines solutions. The extraction process was applied every five minutes. In their results, they noticed that black tea contains almost six-fold more Al than green tea, and the extraction of Al in black tea was higher than the observations noticed in green tea. Furthermore, authors pointed out that the differences between different samples might be because of the differences in soil conditions, harvesting periods, and water quality. Following this line of study, they considered that Al did not appear to be substantially more bioavailable in tea than in other dietary sources. At this respect, Costa et al. (2002) reported that the composition of Al species could differ relying on the method of tea production. For non-fermented tea, most of the leached Al is mainly found in large or small organic compounds such as citrates. However, they found that Al complexes are more bioavailable than inorganic complexes, such as hydroxide. But in general, the absorption of Al by the body is rather poor.

Cabrera et al. (2006) suggested that although caffeine content in green tea is low, its consumption is not advisable in instances of exceptional sensitiveness to xanthic bases as high consumption of caffeine from green tea may cause nervousness sleep disorders, vomits, headaches, epigastric pain, and tachycardia. Furthermore, high consumption of green tea or green tea extract may interact with some medications. A study by Steven (2011) found that green tea caffeine might reduce the sedative effects of medications, such as Benzodiazepines, which is used to treat anxiety, including diazepam (Valium) and lorazepam (Ativan). Green tea caffeine may also increase blood pressure in people taking medications such as Beta-blockers, Propranolol (Inderal), and Metoprolol (Lopressor, Toprol XL). In Chemotherapy treatment, Steven (2011) emphasized that the combination of green tea and chemotherapy medications, specifically (doxorubicin and tamoxifen), increases the effectiveness of these medications in laboratory tests. However, the same results have not been matched in humans' studies. On the other hand, Steven (2011) stated that there have been reports of both green and black tea extracts affecting a gene in prostate cancer cells that may make them less sensitive to chemotherapy drugs. Additionally, with birth control pills, taking oral contraceptives can prolong the amount of time caffeine stays in the body, which may increase its stimulating effects. Lastly, medication with a combination of caffeine from green tea and phenylpropanolamine, which are used in cough and cold medications and weight loss products, may cause mania and a severe increase in blood pressure.

CHAPTER THREE

CONCLUSION

To surmise, green tea has been consumed in China and other Asian countries since ancient times in order to maintain and improve human health. Nowadays, green tea is considered to be one of the most promising dietary agents for the prevention and treatment of many diseases and is consequently being studied extensively worldwide. Numerous studies in humans and a variety of experimental animal models have demonstrated that the aqueous extract of green tea designed as catechins (EGCG, EGC, ECG and EC) possess antioxidant, antimutagenic, antidiabetic, anti-inflammatory, antibacterial, antiviral, and anticarcinogenic effects. Furthermore, green tea consumption has been reported to act positively against cardiovascular diseases, obesity, insulin sensitivity, oral infections, and arthritis.

On the other hand, excess consumption of green tea can cause several health complications as well. For example, EGCG of green tea extract is cytotoxic, and at high consumption levels, it can exert acute cytotoxicity and hepatotoxicity in liver cells and in major metabolic organs in the body. Moreover, it can also cause oxidative DNA damages to pancreas and liver cells. Due to the antithyroid effects of catechins, the dietary supplements of green tea extract catechins at high doses can also cause goiters due to reductions in iron bioavailability. Finally, overconsumption of caffeine from green tea may cause nervousness sleep disorders, vomits, headaches, epigastric pain, and tachycardia. Additionally, several studies have reported that green tea may interact with some supplements and medications.

The green tea beneficial health impacts have resulted in recent recommendations by many nutritionists to support the regular consumption of 2-3 cups of green tea per day (a total of

240-320 mg polyphenols, or 100-750 mg per day of standardized green tea extract) as a useful alternative to other beverages. However, since human clinical evidence is still limited, future research is still needed to implement a system, which defines the actual size of health benefits, founds the safe and right amounts of tea consumption and clarifies the mechanisms of actions.

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APPENDICES

1/ Catechin: a type of natural phenol and antioxidant. It is a plant secondary metabolite, and belongs to the group of flavan-3-ols (or simply flavanols), which is part of the chemical family of flavonoids.

2/ EGCG: is a catechin compound. It includes catechin, gallaogatechin, epicatechin, epigallocatechin, epicatechin gallate, and apigallocatechin gallate.

3/ Al: Aluminum.

4/ Ca: Calcium.

5/ Mg: Magnesium.

6/ Mn: Manganese.

7/ Oolong Tea: is a type of tea that is similar to green tea. The word oolong is an English name. In China it is called Black Dragon tea.

8/ Free Radicals: are atoms or groups of atoms with an odd number of electrons and can be formed when oxygen interacts with certain molecules. Once formed these highly reactive radicals can start a chain reaction, like dominoes.

9/ CVD: Cardiovascular disease.

10/ Vitro: refers to the technique of performing a given procedure in a controlled environment outside of a living organism.

11/ Vivo: refers to experimentation using a whole, living organism as opposed to a partial or dead organism. Animal studies and clinical trials are two forms of in vivo research.

12/ AMPc: it is the first bacterial enzyme reported to destroy penicillin was the AMPc β-lactamase of Escherichia coli.

13/ GTE: green tea extract.

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