

LIPID AND CHOLESTEROL LOWERING EFFECT OF GREEN VS BLACK TEA – HOW MUCH, HOW FREQUENT: A LITERATURE REVIEW

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Abstract: Green tea, unfermented leaves are rich in catechins. Catechins are known to lower the lipid level by un-regulating lipid-metabolizing enzyme via NF-KB and thereby stimulating fat oxidation. Black tea results from the fermentation of green tea in which catechins of green tea is converted to theaflavin and thearubigin, which has some significant health benefits of their own. Theaflavin is responsible for reduced lipid accumulation, suppressed fatty acid synthesis, and stimulated fatty acid oxidation by inhibiting acetyl-coenzyme-A-carboxylase activities.

A literature review of a total of 8 Randomized Controlled trials (RCTs), 5 Meta analyses consisting of 75 peer-reviewed Randomized Controlled trials (RCTs) on 5319 subjects and 6 population based studies were selected for this study. The research related to Green tea effect on the cholesterol and lipid lowering effect shows promising results with high dose of intake for long term. Studies and meta-analyses of CCTs in most cases showed improved low density lipoprotein (LDL)-cholesterol and total cholesterol level. Green tea consumption was unrelated to serum HDL- cholesterol and triglycerides level in most of the studies. Studies revealed that the theaflavin and thearubigin of black tea significantly reduced the serum concentrations of total and HDL cholesterol on long term use. Though the use of green and black tea was responsible for reducing the triglyceride level in the animal studies but most studies done on human being did not find any significant reduction of serum triglyceride level. Green tea has also been proved to be a natural therapeutic alternative for normalizing the lipid profile found in subjects exposed to DMPA.

Key Words: Green Tea, Catechins, black Tea, Theaflavin, Lipid lowering effect.

INTRODUCTION:

Green tea (*Camellia Sinensis*), which contains powerful antioxidants, is one of the most popular beverages consumed around the world. It differs from black tea since it is made from unfermented leaves and reportedly contains the highest concentration of powerful antioxidants called polyphenols which constitute 30-35% of its dry weight and is popularly known as catechins [1]. The compound (–)-epigallocatechin-3-gallate (EGCG) is the major catechin which constitutes 63% of the total catechins. A cup of green tea typically provides 60 to 125 mg catechins, including EGCG [2].

Other primary catechins present in green tea include epicatechin (EC), epicatechin gallate (ECG), and epigallocatechin (EGC). The catechins are mainly absorbed by small intestine after ingestion. They are metabolized by Phase II enzymes including sulphotransferases (SULTs), UDP-glucuronosyltransferases (UGTs), and catechol-O-methyltransferase (COMT), with further metabolism occurring in the liver [3].

Catechins lower the lipid by un-regulating lipid-metabolizing enzyme via NF-KB and thereby stimulating fat oxidation. They also inhibit neither COMT which leads to an increase in nor epinephrine and acdenyl cyclase, thereby decreasing the glucose uptake and enhancing the biolysis. Furthermore, they decrease fat absorption by inhibiting pancreatic lipases and gastric lipases [4].

Fermentation of green tea results in the formation of black tea. When green tea is fermented, some of the most beneficial chemical compounds it contains are partially or completely destroyed. The most notable of these health-giving compounds is EGCG (epigallocatechin gallate). The catechins in green tea polymerizes resulting in

polyphenolic pigments in black tea called **theaflavin** and thearubigin, which have some significant health benefits of their own. Thus, as catechin levels in tea go down in the progression from green to oolong to black, theaflavin and thearubigin levels go up. Researches show that theaflavins is responsible for reduced lipid accumulation, suppressed fatty acid synthesis, and stimulated fatty acid oxidation by inhibiting acetyl-coenzyme A carboxylase activities thereby stimulating AMP-activated protein kinase (AMPK) through the LKB1 and reactive oxygen species pathways [5].

Articles included in the study covered the following effects of green tea and black tea (1) the lipid and cholesterol lowering effect of green tea and black tea in humans and animals, (2) quantity and frequency of green tea and black tea to be consumed to get the optimal result of lipid lowering effect

Hypotheses:

Extracellular Mechanism:

The potent inhibitory effect of EGCG appears to be associated with its ability to form complexes with lipids and lipolytic enzymes (Gastric Lipase, Pancreatic lipase), thereby interfering with the luminal processes of emulsification, hydrolysis, micellar solubilization, and subsequent uptake of lipids. EGCG appears to be more effective in lowering the absorption of lipids of extreme hydrophobicity, such as cholesterol and α -tocopherol, with little or a moderate effect on less hydrophobic lipids such as retinol and fatty acid. Likewise Theaflavin of Black tea has mechanisms to inhibit lipid (fatty acid) absorption from the diet following oral administration, which could result in less bioactivities of those fatty acids in the body if they are not absorbed.

Intracellular Mechanism:

Catechins lower the lipid by un-regulating lipid-metabolizing enzyme via NF-KB and thereby stimulating fat oxidation. They also inhibit COMT which leads to an increase in nor epinephrine and acdenyl cyclase. AMPK is a critical component of decreased hepatic lipid accumulation. Both EGCG and theaflavins cause increased AMP-kinase phosphorylation and HMG-CoA reductase phosphorylation by 2.5- to 4-fold, but with different time courses: maximal phosphorylation with EGCG tea is evident within 30 min of treatment, whereas with theaflavins phosphorylation is slower to develop, with maximal phosphorylation occurring ≥ 3 hours after ingestion.

SEARCH METHODS:

The authors searched following databases on 25th September 2016 without language restrictions in *The Cochrane Library*, MEDLINE, Google, Medscape EMBASE (OVID) and Web of Science (Thomson Reuters). We also searched trial registers, screened reference lists and contacted authors for additional information where necessary.

SELECTION CRITERIA:

The authors read full articles and reached consensus after discussion. A total of 8 Randomized Controlled trials (RCTs), 5 Meta analyses consisting of 75 peers reviewed Randomized Controlled trials (RCTs) on 5319 subjects and 6 population based studies were selected for this study. The eight RCTs included in this study were not part of studies in the mentioned 5 Meta analysis. However 7 experimental studies on animals were also included. In these studies the comparison group was no intervention, placebo or minimal interventions. The outcome of the interest was the effect of green and black tea drinking on the level of lipids and cholesterol. Any trials involving multifactorial lifestyle interventions were excluded to avoid confounding. The studies selected for this research were not more than one decade old.

DATA COLLECTION AND ANALYSIS:

The researcher of Biochemistry department of the King Saud University of Nursing College has selected trials, population studies and systemic reviews for inclusion, abstracted data and assessed the effect of green and black tea drinking on the lowering effect of cholesterol and lipids.

RESULTS:

We searched on Google and found about 320000 results on lipid lowering effect of green tea and 33000 results on the black tea's effect on blood lipid level. Medline fetched 4786 results (2434 on green tea and 2352 on black tea)

while Cochrane Library and Medscape searched 19 and 1713 papers respectively. However in Google search we found many repeated same articles and many were not research papers.

Experimental studies on animals:

Yang TT and Koo MW, 1995 [6] and Onuoha, H.C et al, 2012 [7] have found significant serum and liver cholesterol lowering effects of Chinese Green Tea Extracts (GTE) on diet-induced hypercholesterolemic rats. The same result was found in a research conducted by Raederstorff DG et al ,2003 [8] , who found the cholesterol lowering effect of green tea on diet-induced hypercholesterolemic mice which was mainly elicited by EGCG and the underlying mechanism was suggested to be the interference with the micellar solubilization of cholesterol in the digestive tract, which then in turn decreased cholesterol absorption.

In a similar study on West African green tea's effect on the rats the researchers have found a significant lowered serum and liver cholesterol (30% and 10% respectively) and increased serum HDL cholesterol (30%) after 6 weeks. In this study a, marked increase in fecal total lipids, cholesterol (60%), and bile acids (50%) was observed in rats that consumed west African green tea compared to the control group [9]. Mustafa. A. Hussein, 2011 [10], in his study has also found a significant increase of HDL apart from a significant decrease of total serum cholesterol and LDL. But in this study the researcher injected the Green Tea Extract intraperitoneally to the mice subjects. In a case control trial on diabetic rats Usama El-Sayed Mostafa, 2014 [11], has found that green tea plus 30 mg of powder catechin and green tea plus 100 mg of powder catechin led to a significant decrease in the mean value of serum cholesterol, triglyceride, LDL and VLDL as compared to the positive control group. The group ingested with 100mg of catechin powder also showed fastest decrease of blood glucose level.

In a very recent study done on rats the researchers have found a very encouraging result which shows that: Green tea extract inhibited the increase in LDL-c and cholesterol/HDL-c ratio induced by depot medroxyprogesterone acetate (DMPA). This may provide a natural therapeutic alternative for normalizing the lipid profile found in subjects exposed to DMPA [12].

Researchers have found the lipid lowering effects of Black Tea Extract (BTE) as well on high-fat diet (HFD) induced obese rats. Serum levels of total cholesterol (TC), triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) ($p < 0.05$) were significantly reduced in the high-fat diet (HFD) induced obese rats as the control group [13]. The same result was achieved on Hamsters who were fed high cholesterol diet for 2 weeks and drank green or black tea ad libitum. The plasma lipid profile was significantly improved by both teas compared to controls [14].

In a comparative study where the Sprague-Dawley rats **were fed green and black tea for 30 weeks, the researchers have found that** green tea were more efficient than black tea in lowering the level of total cholesterol while black tea leaves were more effective on their growth suppressive and hypolipidemic effects as compared to the non fermented green tea leaves [15].

Human Studies:

Cross sectional surveys:

Suminori Kono et al, 1992 [16], has found that the serum total cholesterol levels were inversely related to the consumption of green tea while no association was noted with serum triglycerides and high-density lipoprotein cholesterol. However later on in a cross sectional study on 1371 Japanese adult over 40 years of age, increased consumption of green tea was found to be associated with decreased serum concentration of total cholesterol and triglycerides [17]. In a larger cross sectional survey which involved 13,916 Japanese workers (8476 men and 5440 women) aged 40-69 years at over 1000 workplaces in Nagano prefecture, central Japan, the researchers have found that consumption of green tea was associated with lower serum concentration of total cholesterol. However, green tea consumption was unrelated to serum HDL-cholesterol and triglycerides in this study. The data in this study were analyzed with multivariate linear model [18]. A study as quoted by Dr Brian Davies [19] in a Post on 13th July, by West coast Integrative Health in Gastroenterology - Healthy guts (13th July 2012) has found that there was 7.2 milligrams per deciliter (mg/dL) reduction in total cholesterol among the green tea drinker in few weeks to three months as compared to the participants who did not consume green tea . The researchers conducted 20 trials over the course of 24 weeks and have found a significant lower LDL cholesterol levels.

Specifically, the participants showed a five to six point reduction in their levels. Tomonori Nagao et al. 2005 [20], in his study has found that daily consumption of green tea containing 690 mg catechins for 12 weeks has significantly reduced LDL and the body fat. Jarosław Walkowiak et al, 2013 [21], in their study have found that even a single dose of green tea extract of 4 gm (equivalent to more than 10 cups per day) was responsible for significant decrease in lipid digestion and absorption. In a very recent prospective study done on middle-aged and older Chinese populations, green tea consumption was associated with improved total cholesterol, HDL-cholesterol and triglycerides [22]. However a study conducted on a small study group(15 subjects), the daily consumption of 1200 mL of green tea for 30 days promoted the decrease of cholesterol and LDL levels after 15 days, but this effect was not persistent after 30 days [23].

Randomized controlled clinical trials study:

Double blind randomized, controlled studies where the subjects ingested between 575-583 mg of catechins (catechin group) or 75 to 96 mg of catechins (control group) per day over 12-week, the researchers have found decreased low-density lipoprotein (LDL) cholesterol in the catechin group (Nagao T, Hase T and Tokimitsu I, 2007 [24] and Matsuyama T et al, 2008 [25] and Batista et al, 2009 [26]). Similarly in a randomized, double-blind, placebo-controlled intervention study on postmenopausal women, the researchers have found a significant decrease of low density lipoprotein (LDL)-cholesterol. This result was found when the subjects were administered green tea (400 and 800 mg EGCG as PPE; ~5–10 cups) supplementation for 2 months [27]. Norie Suzuki-Sugihara et al, 2015 [28] in a randomized, placebo-controlled, double-blind but crossover trial, has found that catechins are rapidly incorporated into LDL particles and play a role in reducing LDL oxidation in humans.

Drinking of black tea has also been found effective in reducing the blood cholesterol level. In a 3-month double-blind randomized group comparison study in borderline hypercholesterolemic human subjects, long-term ingestion of Chinese black tea extract (BTE) (333 mg) significantly reduced blood cholesterol level. There was significant reduction in total cholesterol, LDL cholesterol and triglycerides with time i.e after 3 months of ingestion [29]. Similarly a prospective randomized controlled clinical trial has revealed that consumption of 9 gm of black tea daily for 12 weeks in a normal population was very effective in reducing not only LDL/HDL plasma cholesterol level (16.6%; $p < 0.05$) but also fasting triglyceride level (35.8%; $p < 0.01$) [30]. In a double-blind, 4 weeks randomized crossover trial, the researchers did not find a clinically significant reduction of lipid profile of borderline hypercholesterolemic subjects when ingested 5 cups of black tea per day [31].

Combination of black and green tea has shown a promising result in a randomized, double-blind, placebo-controlled study where 220 individuals with mild to moderate hypercholesterolemia were given daily supplement of a capsule containing 150 mg of green tea catechins, 75 mg of black tea theaflavins, and 150 mg of better polyphenols for six months. The subjects showed a significantly lowered level of Plasma LDL-cholesterol concentration and the ratio total cholesterol: HDL [32].

Systematic reviews:

The systematic review and meta-analysis of 20 randomized controlled trials involving 1415 study subjects, Amie Kim et al, 2011 [33], has found that the consumption of GTCs is associated with a statistically significant reduction in total and LDL cholesterol levels; however, there was no significant effect on HDL cholesterol or triglyceride levels. In another Meta analysis study which included 14 eligible randomized controlled trials with 1136 subjects, the researchers have found that the administration of green tea beverages or extracts resulted in significant reductions in serum TC and LDL-cholesterol concentrations, but no effect on HDL cholesterol was observed [34]. Louise Hartley et al, 2013 [35], in his systemic review which involved 11 RCTs with a total of 821 participants, has concluded that green tea produce statistically significant reductions in total cholesterol (MD -0.62 mmol/L, 95% CI -0.77 to -0.46) and LDL cholesterol (MD -0.64 mmol/L, 95% CI -0.77 to -0.52). A recently concluded Meta analysis involving 20 RCTs comprising 1536 participants has revealed a moderate lowering effect of green tea consumption on total and LDL cholesterol [36].

Meta analysis of 10 RCTs comprising 411 subjects has found that black tea consumption significantly lowered serum concentration of LDL cholesterol, especially in subjects with higher cardiovascular risk. However, black tea intake did not impose obvious effect on serum concentrations of total and HDL cholesterol [37].

CONCLUSIONS AND FUTURE DIRECTIONS:

The research related to Green tea effect on the cholesterol and lipid lowering effect shows promising results with high dose of intake for long term. Studies and meta-analyses of CCRTs in most cases showed improved low density lipoprotein (LDL)-cholesterol and total cholesterol level. Green tea consumption was unrelated to serum HDL- cholesterol and triglycerides level in most of the studies. However Green Tea Extract of 4 gm (Equivalent to 10 cups of green tea a day) was found responsible for significant decrease in lipid digestion and absorption in one study. Many studies revealed that the theaflavin and thearubigin of black tea significantly reduced the serum concentrations of total and HDL cholesterol on long term use. Though the use of green and black tea was responsible for reducing the triglyceride level in the animal studies but most studies done on human being did not find any significant reduction of serum triglyceride level. However animal studies showed that green tea were more efficient than black tea in lowering the level of total cholesterol while black tea leaves were more effective on their growth suppressive and hypolipidemic effects as compared to the non fermented green tea leaves.

The encouraging result of green tea on rats exposed to DMPA may provide a natural therapeutic alternative for normalizing the lipid profile found in subjects exposed to DMPA. As far as the dose and duration is concerned, most studies suggest 5-10 cups of black or green tea per day for at least 3 months are needed to get the beneficial effect. The result of one CCRT where theaflavin rich green tea was used, suggests combination of green and black tea is an effective adjunct to low saturated fat diet to reduce LDLC in hypercholesterolic adults and is well tolerated.

Although these studies are promising, there is currently not enough evidence to recommend tea or tea extract for treatment of hyperlipidemia. However long term use of green tea alone or in combination with black tea has been proven effective dietary adjunct to help dyslipidemic patients for supporting effect of anti-dyslipidemic drugs and may be used to prevent dyslipidemia in the group of hyperlipidemic persons that need to modify their life style for long term prevention.

Most of the studies of beneficial effect of green and black tea have been conducted in china and Japan and a very few or no study from Middle East and India. It is recommended to conduct studies in these geographical areas to see their effects on the population of these areas. The studies reviewed are summarized in table 1.

Table 1: Showing the results of the studies reviewed article on lipid lowering effect of green and black tea ingestion.

Authors	Year of publication	Results
Animal Studies		
1. Yang TT and Koo MW [6]	1995	Cholesterol lowering effect of green tea on diet-induced hypercholesterolemic mice with possible mechanism of interference with the micellar solubilization of cholesterol in the digestive tract which decreased cholesterol absorption
2. Raederstorff DG et al [8]	2003	
3. Djaafar Rehras, et al [9]	2007	
4. Onuoha, H.C et al [7]	2012	
5. Duiyan Jin et al [13]	2013	
6. Joe A Vinson and Yousef A Dabbagh [14]	2014	Lipid lowering effects of Black Tea Extract (BTE) on high-fat diet (HFD) induced obese rats.
7. Susilawati E et al [12]	2015	Green tea extract inhibited the increase in LDL-c and cholesterol/HDL-c ratio induced by depot medroxyprogesterone acetate (DMPA).
8. Kuo KL et al [15]	2005	Green tea was more efficient than black tea in lowering the level of total cholesterol while black tea was more effective on its hypolipidemic effects as compared to the green tea.
Human Studies		
Cross Sectional		

1. Suminori Kono et al [16]	1992	Consumption of green tea in moderate amount for long duration was associated with lower serum concentration of total cholesterol but was unrelated to serum HDL-cholesterol and triglycerides in most of these studies.
2. K Imai and K Nakachi [17]		
3. Tokunaga S et al [18]	1995	
4. Tomonori Nagao at el [20]	2002	
5. J. Walkowiak et al [21]		
6. Reto, M. et al [23]	2005 2013	
7. ChongTian [22]	2014	
	2016	
Human studies		
CCT		
1. Maron DJ, et al [32]	2003	Ingestion of 75 mg of black tea theaflavins and 150 mg of better polyphnols for six months showed a significantly lowered level of Plasma LDL- cholesterol concentration and the ratio total cholesterol: HDL.
2. Nagao T, Hase T and Tokimitsu I [24]	2007	A moderate amount of green tea ingestion for more than 2 months caused clinically significant decreased low-density lipoprotein (LDL) cholesterol.
3. Matsuyama T et al [25]	2008	
4. Fujita H and Ya magami T [29]	2008	
5. Batista et al [26]	2009	
6. Anna H. Wu et al [27]	2012	
7. Bahorun T et al [30]	2012	
8. Norie Suzuki-Sugihara et al [28]	2016	
9. Rasa Troup et al [31]	2015	
Meta Analysis:		
1. Amie Kim et al [33]	2011	Meta-analysis of 20 randomized controlled trials involving 1415 study subjects has found that GTCs was associated with a statistically significant reduction in total and LDL cholesterol levels; however, there was no significant effect on HDL cholesterol or triglyceride levels
2. Zheng XX et al [34]	2011	Meta –analysis of 14 randomized controlled trials with 1136 subjects have found that the administration of green tea beverages or extracts resulted in significant reductions in serum TC and LDL-cholesterol concentrations, but no effect on HDL cholesterol was observed. 11 RCTs with a total of 821 participants, , has concluded that green tea produce statistically significant reductions in total cholesterol and LDL cholesterol.
3. Louise Hartley et al [35]	2013	20 RCTs comprising 1536 participants has revealed a moderate lowering effect of green tea consumption on total and LDL cholesterol.
4. Onakpoya I et al [36]	2014	Meta analysis of 10 RCTs comprising 411 subjects has found that black tea consumption significantly lowered serum concentration of LDL cholesterol, especially in subjects with higher cardiovascular risk. However, black tea intake did not impose obvious effect on serum concentrations of total and HDL cholesterol
5. Zhao Y, et al [37]	2014	

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