Green tea catechin: does it lower blood cholesterol?

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Abstract. Tea is one of the most popular beverages in the world, especially in Asian societies. Green, oolong and black tea are three main types of tea products. Catechin is the principal polyphenol compound in all tea products including four major subgroup compounds, epigallocatechin gallate (EGCG), epicatechin (EC), epigallocatechin (EGC) and epicatechin gallate (ECG). Green tea contains highest amount of catechin compared to oolong and black tea since fermentation process can significantly reduce the amount of catechin in tea product, which polyphenol oxidase can convert catechins to theaflavins and thearubigins during fermentation process. Therefore, green tea catechin is becoming more and more attractive to nutritionists since it can provide several health benefits to human body. Cholesterol lowering effect is one of the health benefits been studied and proposed over decade. There are well documented evidences that suggested green tea catechin, in particular EGCG has the potential to lower blood cholesterol concentrations. Since the pool bioavailability and absorption ability of catechin, researchers believed that green tea catechin may significantly inhibit lipids absorption in intestine. Mechanisms are including inhibition of pancreatic lipase activity, lipids hydrolysis, and emulsification in intestine and precipitation of micellar cholesterol. In vitro studies, animal studies as well as most of human RCT, consistent results been observed that dietary intake of green tea beverages or extracts could significantly lower circulating cholesterol concentration, in particular lower LDL-C and total cholesterol level. However, in 2010, European Food Safety Authority (EFSA) denied the health claim of cholesterol lowering benefits of dietary intake of green tea or green tea catechins. In this presentation, current scientific evidences and EFSA judgment will be reviewed and discussed.

1. Introduction
Tea as known as Camellia sinesis that originates from ancient China with long history for using as beverage and pharmaceutical compounds since 3000 B.C [1]. Tea is now widely cultivated and consumed worldwide, according to the statistical report from USDA, Kenya, Sri Lanka, China, India and Vietnam are the top five tea exporters in the world which represented over one hundred million tons total productivity of tea per annum [2]. People considered that improving attention is one of major benefits from tea consumption; however, more potential health benefits associated with tea consumption being discovered and studied recently [3-5]. Protein, fiber, carbohydrates, lipids, pigments, minerals and phenolic compounds are major ingredients enrich in tea products [6, 7]. However, tea polyphenols are predominant compounds in tea leaves with over 30% enrichment of total composition [7]. Catechins are major polyphenols in tea products, epicatechin (EC),
epigallocatechin (EGC), epicatechin-3-gallate (ECG) and epigallocatechin-3-gallate (EGCG) are four major sub-categories been identified [8]. However, total catechin content can vary between green, oolong and black tea due to fermentation. Fermentation process is the principal reason that can result in degradation of catechins by converting catechins to theaflavins (TF) and thearubigins (TR) through enzymatic activity of polyphenol oxidase. Produced TF compounds can contribute to smooth texture and brown color in oolong and black tea; however, total catechin content can be significantly reduced after this process. Thus, green tea is the richest source of catechins, one cup of green tea can provide 150-200 mg catechins respectively [8]. And over 50% total catechins are EGCG since it is predominant in all tea leaves, and 90 mg EGCG naturally present in one cup of green tea [8].

Cardiovascular disease (CVD) and cancer are two leading causes of death worldwide, and over 1.4 million Canadians have CVD currently [9]. The pathogenesis of CVD involves several factors which go beyond only diet and aging; however, diet is one of the easiest approaches to investigate and control the prevalence of CVD [10]. Increased blood total cholesterol (TC) and LDL cholesterol (LDL-C) concentrations are significantly associated with development of CVD. Studies indicated that every 1% reduction on serum TC contributes to 3% reduction of risk of CVD [11]. In addition to the known benefits of green tea catechins such as improving attention and scavenging free radicals, effect of lowering blood cholesterol also became attractive and been studied recently. Studies indicated that green tea catechins may affect lipids absorption in small intestine, which contribute to cholesterol lowering effect [12]. Possible mechanisms are inhibiting lipids hydrolysis, inhibiting luminal emulsification, reducing micellar solubility and precipitating cholesterol from micelles [12]. In an animal study, dietary intake of EGCG exhibited significant effect on reducing plasma TC and LDL-C concentrations in rats fed by high-fat and cholesterol diet [13]. Meanwhile, authors also observed a significant increase in fecal excretion rate of cholesterol in rats fed by EGCG [13]. These findings suggested that green tea catechins have the potential to lower blood cholesterol by inhibiting cholesterol absorption in small intestine.

Human intervention trials also observed similar results. Studies indicated that a significant reduction on TC and LDL-C and increasing on HDL-C concentration been observed after dietary intake of green tea or extracts [14-16]. However, conclusion of effects of green tea consumption on HDL-C concentration is not always consistent, whereas studies also reported that there were no significant changes of HDL-C after dietary intake of green tea products [17, 18]. Interestingly, one study reported that dietary intake of a combination of green tea catechins, TF and non-catechin polyphenol (150 mg/day, 75 mg/day and 150 mg/day) for 12 weeks showed dramatic changes on TC (-11.3% reduction) and LDL-C (-16.4% reduction) in 120 Chinese subjects [19]. However, even though these well documented evidences demonstrated the beneficial effects of green tea catechins on blood cholesterol control, yet no consistent conclusion has been made due to controversial results obtained. For instance, a randomized and placebo controlled study failed to observe a significant change on neither TC nor LDL-C in 45 subjects, who fed by 3 g green tea extract per day for 4 weeks[20]. Therefore, the debate on how effective of green tea catechins on blood cholesterol reduction is still ongoing and research results are controversial.

2. Evaluation of efsa framework and critical assessment on green tea catechins

The scientific panel of EFSA as known as NDA who is responsible to evaluate and provide scientific opinion to health claims that submitted by member states, and will also give a final judgment within 5 months as requested by European Commission. There are two general categories within EFSA framework, which are Article 13 and Article 14 under EU regulation No. 1924/2006. Article 14 primarily deals with the health claim related to reduction of disease risk and children’s development and health care, whereas Article 13 deals with Health claims other than disease risk reduction [2].Two main subcategories also been described where health claims pursuant to Article 13.1 should refer to the role of the nutrient or substance in foods on body growth, function, development, physiological behavior and/or body weight control purposes, and Article 13.5 should refer to the claims based on newly developed data or that include a request for the protection of proprietary data [21]. Under this
regulatory framework, EFSA NDA panel will initiate a procedure (Fig. 1.) to evaluate the submitted health claim, weigh scientific evidences and provide scientific opinion to European Commission. After evaluation process, a final conclusion usually can be made by EFSA panel, which describe whether a cause and effect relationship has been established and whether the scientific evidences are sufficient or not [22].

![Diagram](image)

**Figure 1.** Key elements addressed by EFSA NDA panel on evaluation process [21].

In 2010, EFSA NDA panel evaluated a health claim pursuant to Article 13 that related to Camellia sinensis, including green tea catechins and black tea tannins, and the panel provided scientific opinion on this claim as requested by European Commission. One of claimed effects of green tea catechins intake is “maintain of normal cholesterol concentration” [23]. The panel took look into two human intervention trials [19, 24], three observational studies [25, 26] and three additional intervention trials which included in Maron’s study [20, 27, 28]. In a randomized placebo-controlled trial, 42 subjects were randomly assigned into control group and treatment group that participants fed by 2 cups green tea per day for 42 days period. However, no significant changes and differences been observed on LDL-C, HDL-C and TC within and between groups after treatment [23]. Similarly, in Van het Hof et al study, 45 subjects were randomized assigned to 3 groups, which required consuming 900 ml mineral water, 3 g green tea extract and 3 g black tea extracts for 4 weeks period. No significant changes on TC, HDL and LDL-C been observed in all three groups. Interestingly, in Maron et al study, a dramatic change of LDL-C and TC concentration been observed; however, a combination of green tea catechins, black tea theaflavins and non-catechin polyphenol was used in the study, which cannot fully represent the effects of green tea catechins. Therefore, after weighing the evidences provided to EFSA, the panel concluded that a cause and effect relationship between green tea catechins and blood cholesterol concentration maintenance has not been established, and the health claim was been rejected. This conclusion basically liberated a sign to public society that the effect of green tea catechins on blood cholesterol cannot be identified and there are insufficient evidences which can support.
consumption of green tea catechins. For instance, a commercial green tea extract product which rich in green tea should also be noted. Hepatotoxicity is one of the most severe adverse effects after high dose Coimbra Suliburska Boganski Hsu Van He Source cholesterol lowering effect associated with green tea consumption. Therefore, it can be d catechins used such as green tea extracts, isolated EGCG compound and green tea infusions. the dose of green tea catechins used in current studies are inconsistent, as well as the form of green tea hence further studies are needed to further clarify mechanisms behi hypercholesterolemic and overweigh people rather than general population remains questionable, system rather than in liver. Therefore, whether green tea catechins are effective to cholesterol synthesis rate is limited due to the poor bioavailability of green tea catechins in animals [11]. Most of vitro, animal and human intervention studies were mainly focused on and explained that green tea catechins can inhibit cholesterol absorption and increase fecal cholesterol excretion in intestinal system rather than in liver. Therefore, whether green tea catechins are effective to hypercholesterolemic and overweigh people rather than general population remains questionable, hence further studies are needed to further clarify mechanisms behind observational results. Moreover, the dose of green tea catechins used in current studies are inconsistent, as well as the form of green tea catechins used such as green tea extracts, isolated EGCG compound and green tea infusions. Therefore, it can be difficult and inaccurate when compare studies and make such a conclusion for cholesterol lowering effect associated with green tea consumption.

| Source                | BMI | TC    | LDL-C | HDL-C   |
|-----------------------|-----|-------|-------|---------|
| Van Het Hof et al, 1997 [20] | 23.89 kg/m² | 5.38 mmol/L | 2.53 mmol/L | 1.53 mmol/L |
| Erba et al, 2005 [24]   | 19.1 kg/m²  | 172 mg/dL   | 56.3 mg/dL  | 110 mg/dL |
| Hsu et al, 2008 [14]    | 30.85 kg/m² | 206.5 mg/dL | 142.5 mg/dL | 43.8 mg/dL |
| Boganski et al, 2012[16] | 33.2 kg/m²  | 5.5 mmol/L  | 3.6 mmol/L  | 1.2 mmol/L |
| Suliburska et al, 2012 [18] | 32.76 kg/m² | /             | 3.62 mmol/L | 1.105 mmol/L |
| Coimbra et al, 2006 [15] | 25 kg/m²    | 210.3 mg/dL | 136.2 mg/dL | 56.4 mg/dL |

Additionally, green tea catechins as the potential functional food, side effects of consumption of green tea should also be noted. Hepatotoxicity is one of the most severe adverse effects after high dose consumption of green tea catechins. For instance, a commercial green tea extract product which rich in
EGCG resulted in 13 reported cases of liver damage in 2003 [31]. Despite studies indicated that the toxicity correlated with the bioavailability of EGCG, whereas catechins bioavailability in human is relative low; however, toxic level of catechins in plasma can also be reached under high dose administration and fasting state [30]. Meanwhile, harmful elements may also naturally present in tea leaves due to environmental pollution. For instance, studies reported that 431-2239 μg/L aluminum been found in green tea and black tea infusions per cup, but the maximum amount of aluminum allowed is 6 mg per day in human [32]. Accumulated aluminum can become toxic and damage to human neurological function which is not reversible. Besides, Lead (Pb) in tea leaves can also be harmful and increase the risk of CVD [8]. Green tea catechins also been found have affinity to Iron and may cause Iron deficiency in human body, thus studies suggested that patients suffering from anaemia should avoid consume tea products [32].

In order to pass the EFSA as well as other health claim regulatory systems in the near future, more high quality trials should be done such as randomized double-blinded long term crossover study. And questions should also be addressed in future studies are: What is the target population? Is cholesterol lowering effect applied to general population? What is the optimal dose of green tea catechins in reducing or maintaining normal blood cholesterol concentration? How to minimize side effects associated with green tea consumption?

3. Conclusion
CVD is one of the leading causes of death worldwide, and green tea consumption has long been considered as one approach to reduce the risk of CVD, in particular lower circulating cholesterol concentrations. Possible proposed mechanisms are inhibiting dietary lipids hydrolysis, reducing micellar solubility and precipitating cholesterol from micelles in intestinal lumen, as well as inhibiting HMG-CoA reductase in liver. After critical review of current scientific evidences, the conclusion appears controversial and inconsistent; genetic variations, life-style differences and different form and dose of green tea catechins used can possibly affect results obtained. Most of human intervention trials and animal studies showed positive effects, which suggest that green tea catechins may have the potential to maintain normal blood cholesterol level. Therefore, health claim of green tea catechins on cholesterol lowering deserve to have a second chance for assessment.

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