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Original Article

Effect of *Camellia sinensis* on Fat Peroxidation and Ox-LDL in Rats

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Abstract

Green tea (GT) is believed to have antioxidant properties and beneficial effects on the treatment of some diseases. However, few findings were found concerning the impact of GT on oxidative stress. In the present study, the protective influence of GT against the oxidative stress caused by hydrogen peroxide (H_2O_2) in rats was evaluated. The research groups included a control (Con) group and five groups supplemented with 10g GT(G1), 20g GT(G2), 1% H_2O_2(P), 1% H_2O_2and10g GT (GP1), as well as 1% H_2O_2 and 20g GT(GP2). The effects of GT and H_2O_2 administration on serum biochemical parameters, such as lipid profile, malondialdehyde (MDA), and oxidized low-density lipoprotein (Ox-LDL) were assessed. The findings of this research revealed that the usage of GT lowered the level of cholesterol, triglyceride, LDL, MDA, Ox-LDL and coronary risk index. Moreover, an increase in high-density lipoprotein and very-low-density lipoprotein (VLDL) was observed in subjects who received GT, compared to the rats of the P group. The baseline lipid profile and GT consumption with or without H_2O_2 were the same between the Con and GT-treated groups. Therefore, GT usage was found to be advantageous in reducing Ox-LDL and lipid peroxidation in rats. These results confirm the traditionally claimed benefits of GT for protection against lipid peroxidation and atherosclerosis.

Keywords: *Camellia sinensis*, Green tea, Lipid peroxidation, Ox-LDL, Rat

1. Introduction

Diet and beverages play an essential role in the protection mechanisms of the body against oxidative damage, which is linked to various diseases. Tea is the beverage consumed widely by humans globally and has received considerable attention for its potential protective effects against coronary artery disease, tumor progression, cardiovascular disease, diabetes, and hypertension. In addition, it can be beneficial in the development of vascular resistance (1). All types of tea, namely green, oolong, and black tea are the dried leaves of *Camellia sinensis* vine, which belongs to the *aceae sp.* (2, 3). Green tea (GT), unlike black and oolong tea, is not fermented causing the active constituents in the plant to stay untouched (4, 5). The main GT components are polyphenols, particularly cate chin (6). The polyphenols of *Camellia sinensis* have been shown to minimize plaque formation and lipid oxidation suggesting an anti-atherosclerotic effect (7). Many studies have indicated the effect of GT compounds on the removal of reactive oxygen species (ROS), as well as the inhibition of free radicals (8-10). It is now possible to measure oxidized low-density lipoprotein (Ox-LDL) in blood circulation by several methods (11, 12). The Ox-LDL in peripheral blood could be considered a valuable p redactor for

atherosclerosis and coronary heart disease (13, 14). Although GT has numerous antioxidants (15), few studies have been conducted on the impact of antioxidants on circulating Ox-LDL levels (16). Antioxidants help minimize oxidative stress and affect free radicals to prevent the progression of oxidation reactions (15, 17). Drinks rich in antioxidants can assist in preventing chronic diseases. The GT, a common antioxidant beverage among Orientals, is one of the most well-known antioxidant beverages (18).

Given the limited research on the effect of increased antioxidants due to GT consumption, we aimed to clarify the impact of GT antioxidants on the circulatory Ox-LDL. Furthermore, we investigated the influence of GT intake on blood lipid profile, oxidative stress markers, and Ox-LDL.

2. Material and Methods

2.1. Animals

Thirty-six male Sprague-Dawley albino rats with a weight range of 250-300 g were randomly divided into six groups. The animals were housed in a polypropylene cage and were held under normal controlled conditions (i.e., the temperature of 25°C±2°C and natural light-dark cycle) in Veterinary Faculty, the University of Kirkuk, Iraq. The rats were supplied with food and water ad libitum, and were divided into the following groups after seven days:

Group 1: one month regular distilled water (Control, N=6),

Group 2: one month 10g GT prepared solution/1L distilled water (G1, N=6),

Group 3: one month 20g GT prepared solution/1L distilled water (G2, N=6),

Group 4: one month 1% hydrogen peroxide (H_2O_2) (P, N=6),

Group 5: one month 1% H_2O_2 and10gGT/1L distilled water (GP1, N=6).

Group 6: one month 1% $H_2O_2$and 20g GT/1L distilled water (GP2, N=6).

2.2. Sample Investigations

The GT was purchased from a local farmer's market in Konya, Turkey. The GT solutions (10-20 g) were boiled in 1 L of distilled water to extract different concentrations. After cooling, the solutions were filtered by filter paper and were given to rats as a drinking water source (19, 20). The H_2O_2 was obtained from Sigma Company (St. Louis, MO, USA).

2.3. Blood Sample Collection

After the experimental duration of 30 days, under ether anesthesia, the cardiac blood sample was taken using 5 cc syringes following the principles of research ethics. Next, the specimens were collected in tubes without coagulant for biochemical examination. The samples were centrifuged for 10 min at 3000rpm, and the sera were harvested, numbered and frozen at -20˚C to measure the biochemical parameters.

2.4. Biochemical Parameters

Cholesterol (CHO), triglyceride (TG), high-density lipoprotein (HDL), and LDL were measured using commercial kits (BIOLABO, SA, France) according to the instructions of the manufacturer. The concentration of very low density-lipoprotein (VLDL) was calculated as TG/5.In addition, the coronary risk index (CRI)was also calculated (21, 22). The Ox-LDL was measured using a commercial sandwich enzyme-linked immunosorbent assay (ELISA) (Mercodia, Uppsala, Sweden) and malondialdehyde (MDA) was determined based on thiobarbituric acid reactivity substances (23).

2.5. Statistical Analysis

All results of descriptive statistics are expressed as mean ±standard deviation (SD). The data were analyzed by one-way analysis of variance (ANOVA) and Duncan's multiple range test (DMRT) using the SPSS software version 18 (SPSS, Cary, NC, USA) (24). $P \leq 0.05$ was considered significant for all tests.

3. Results

According to the results shown in table 1, the effects of GT extracts on serum lipid profiles and serum concentrations of CHO, TR, HDL, LDL, VLDL, and

CRI in rats that drink GT for four weeks versus the control group, there were no significant difference (P≤0.05) in CHO, TR, HDL, LDL, VLDL, CRI between the control and GT groups G1 and G2. A significant increase was reported in the CHO, TR, LDL, VLDL, and CRI levels of the H_2O_2-treated group (P≤0.05) compared to the control group. On the other hand, HDL decreased significantly in the P group (P≤0.05), compared to the control, G1, G2, and GP2 groups. However, the GP1 and GP2 were not significantly different with other groups. Moreover, CHO, TG, LDL, VLDL, and CRI were significantly lower in the GP1 and GP2 groups, in comparison with the H_2O_2-treated group P≤0.05).

Table 1. Effects of GT extracts on serum lipid profile in treatment groups

Parameters	Con	G1	G2	P	GP1	GP2
CHO	82.5±5.2^{a,c}	80±7.4^{a}	75.8±3.9^{a}	173.3±11.6^{b}	116.3±12.5^{c}	99.8±10.3^{c}
TG	71.3±8.5^{a}	76±7.4^{a}	70.5±2.6^{a}	123.3±10.4^{b}	98.5±9.8^{c}	94.3±5.9^{c}
HDL	47.3±6.1^{a,b}	52.8±9.1^{a}	60.0±9.5^{a}	32.5±6.3^{b}	44.5±6.7^{a,b}	50.8±6.5^{a}
LDL	49.5±10.7^{a,c}	42.5±7.3^{a,c}	29.9±8.9^{a}	162.2±13.9^{b}	91.45±16.7^{d}	67.9±14.7^{cs,d}
VLDL	14.3±1.7^{a}	15.2±1.5^{a}	14.1±0.5^{a}	24.7±2.1^{b}	19.7±1.9^{c}	18.9±1.2^{c}
CRI	1.1±0.3^{a}	0.8±0.25^{a}	0.5±0.2^{a}	4.6±0.8^{b}	2.1±0.7^{c}	1.4±0.4^{a,c}

*The different letters in each column indicate significant differences (P≤0.05)

Figure 1 shows the impacts of GT extracts on serum Ox-LDL in distinct groups (Table 2). It was found that exclusively the H_2O_2-treated group had a significant difference with the G1, G2, and GP2 groups (P≤0.05) with no statistically significant difference between other treatment groups.

As shown in figure 2, a significant elevation in serum MDA was observed in GP1 GP2 groups (P≤0.05), while no significant difference (P≤0.05) was found between GP2 and Gp1 (Table 2). Moreover, the GP2 group was not significantly different from the control group in this regard.

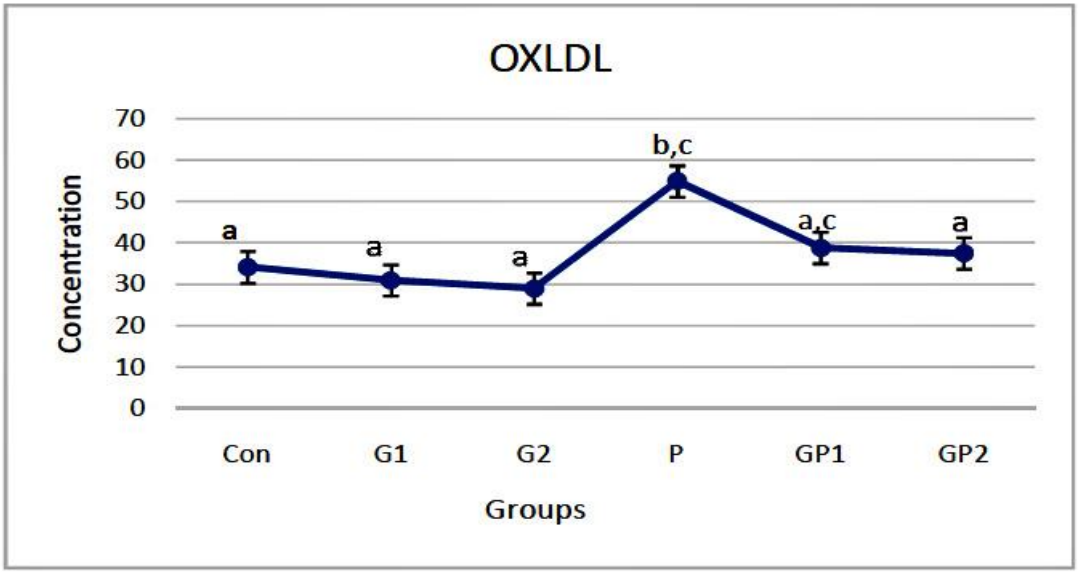

Figure 1. Level of Ox-LDL in the serum of treatment groups

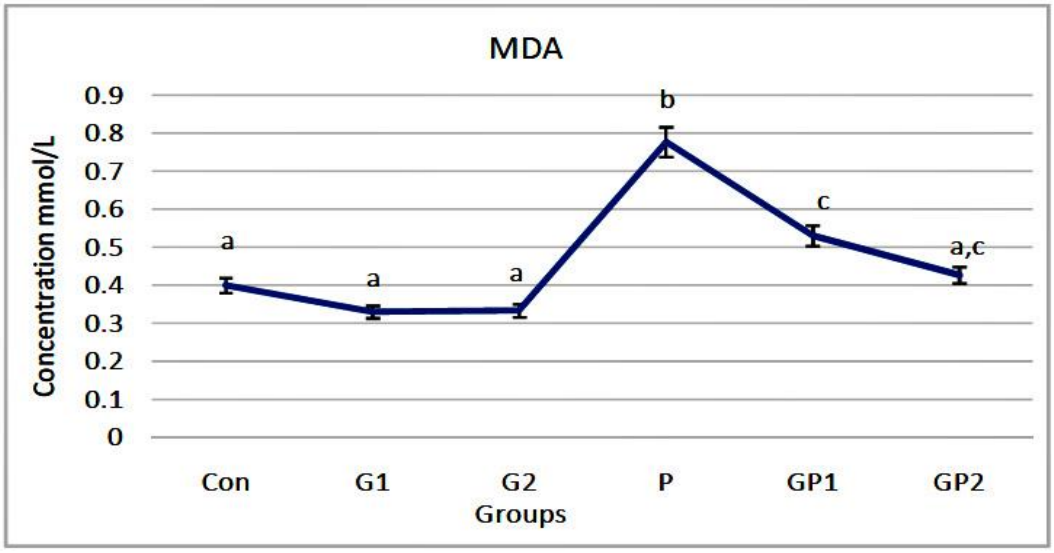

Figure 2. Level of MDA in the serum of treatment groups

Table 2. Effects of GT extracts on serum MDA and Ox-LDL in treatment groups

Parameters	Con	G1	G2	P	GP1	GP2
MDA (mmol/L)	0.4±0.03[a]	0.3±0.01[a]	0.3±0.6[a]	0.8±0.07[b]	0.5±0.1[c]	0.43±0.07[a,c]
OXLDL (ng/mL)	34.1±1.3[a]	30.9±6.1[a]	28.9±9.0[a]	54.9±7.4[b,c]	38.8±10.8[a,c]	37.4±3.6[a]

*The different letters in each column indicate significant differences (P≤0.05)

4. Discussion

Oxidative stress caused by H_2O_2 is associated with potent ROS and nitrogen reactive species in laboratory animals (25). Copper and iron catalyze oxidative reactions via the Fenton reaction in cells, which is responsible for most of the harmful effects of medications on tissues, such as lipid peroxidation (26). Whenever the amount of free radicals exceeds cellular ability to eliminate them, oxidative stress may occur, which causes severe cell toxicity. Exposure to excessive oxidative stress leads to damages to DNA, enzymes, and proteins, as well as lipid peroxidation (27, 28). This degeneration results in dead cells and various pathological conditions (26). Medicinal plants are an important part of the pharmaceutical industry that extracts medicinal compounds directly and indirectly from herbs (29).

Tea is a common beverage throughout the world. In the current investigation, it was found that GT has an antioxidant effect in rats (30, 31). Our findings demonstrated that GT intake reduced MDA concentration in addition, the results suggested that treatment with GT diminished lipid peroxidation and oxidative stress in experimental rats. The level of lipid peroxidation is generally assessed by measuring MDA. These findings are compatible with the theory that antioxidants can reduce the markers of oxidative injury (32). Lipid peroxides are the products of lipid peroxidation reactions caused by biological processes and impose harmful influences on cell membranes and DNA (33). Several potential pathways have been suggested for the anti-oxidative activity of GT. The GT possibly inhibits iron-induced lipid peroxidation by chelating iron. The Ox-LDL of oxidative phase rises in net negative charge and increases in buoyant mass. The concentration of MDA in blood circulation is used as a marker of Ox-LDL (33).

The efficiency and performance of the circulating Ox-LDL are still uncertain. LDL is the main lipoprotein carrier in the blood with three-quarters of the total CHO being in LDL. Circulatory LDL is vulnerable to oxidation. Researchers believe that Ox-LDLs play a highly important role in the initial vascular endothelial attack before lesion formation. Pathophysiological findings have revealed that Ox-LDL is involved in atherosclerotic lesions (34). It is also conceivable that LDL-Cholesterol (LDL-C) is transformed to Ox-LDL by free radicals or many other compounds in the blood. The Ox-LDL exerts several results that may be atherogenic, including monocytes chemotaxis, the up-regulation of endothelial adhesion molecules, growth factor activation, chemokine expression, as well as proliferative influence on smooth muscle cells and monocytes (35, 36). The present study reports the inhibitory effects of GT on circulating Ox-LDL, which is in line with the results of Inami, Takano (37), who found that Japanese GT usage (500 mg/day) resulted in an 11.7% reduction in plasma Ox-LDL concentration.

The GT produces excellent metal-chelating structures. Researches have demonstrated that GT possesses antioxidant activities and effectively inhibits LDL oxidation and lipid peroxidation in vitro. The polyphenols of GT are poorly absorbed leading to the emergence of small portions of orally administered GT in the blood of rats. Therefore, more GT accumulates in the intestinal lumen, and the lipid-lowering effect of GT is likely to be mediated largely by the intestinal processes involved in the digestion and absorption of lipids. According to available data, GT interacts with lipid luminal emulsification, hydrolysis, and micellar solubilization (38). The GT can potentially affect the absorption and intracellular metabolism of lipids, as well as the assembly and release of chylomicrons. The polyphenols of GT are quickly absorbed into LDL particles and play a role in reducing LDL oxidation, which means that taking GT is beneficial in reducing atherosclerosis risk associated with oxidative stress (39). The latter result is consistent with our findings that GT specifically contributed to the defense against LDL oxidation. Importantly, the hypocholesterolemic behavior of GT has also been identified in laboratory animals and humans. Previous studies and our findings indicate that GT can prevent the progression of Ox-LDL-triggered atherosclerosis by synergistic action between both the cholesterol-lowering effect and anti-oxidative property in humans (40). The results of the present study revealed significant rise in CRI in the peroxidation group, compared to the other groups, which is in line with a study showing that CRI-1 or CRI-2 are significant indicators of vascular risk with their predictive value being better than independent parameters (41). On the other hand, GT has been demonstrated in animal experiments to reduce plasma CHO and TG levels in CHO-fed hamsters, rats, and mice (42).

The GT was found to have an anti-oxidative impact on rats (43). The results indicated that GT administration diminished lipid peroxidation and oxidative stress in experimental rats. Lipid peroxides are a combination of highly reactive components of lipid peroxidation, a natural mechanism in all biological processes, and negative consequences for cell membrane and DNA (44).

In conclusion, the present investigation has shown that providing GT extract in the drinking water of rats for four weeks with or without H_2O_2 reduces the concentration of lipid peroxidation products in serum. Bioactive ingredients in GT play a significant role against lipid peroxidation. Therefore, GT may be highly beneficial as an alternative therapeutic agent in atherosclerotic cases.

Authors' Contribution

Study concept and design: A. A. A.
Acquisition of data: E. M. M.
Analysis and interpretation of data: O. M. A. S.
Drafting of the manuscript: A. A. A.
Critical revision of the manuscript for important intellectual content: E. M. M.

Statistical analysis: O. M. A. S.
Administrative, technical, and material support: A. A. A.

Ethics

Ethical principles of working with laboratory animals in the present study were approved by the Ethics Committee of the University of Kirkuk.

Conflict of Interest

The authors declare that they have no conflict of interest.

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