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Effect of Green Tea Intake on some Inflammatory and Physiological Markers in Men

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تأثير تناول الشاي الأخضر على بعض العلامات الالتهابية والفسيولوجية عند الرجال

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ABSTRACT

Background:

The daily consumption of green tea is one of the most important beverages that contains many bioactive compounds, such as polyphenols and flavonoids, in large proportions. It has important health and disease prevention benefits and has antioxidant and anti-inflammatory properties and plays an important role in preventing and preserving the structure and function of body cells. Our study was designed to investigate the effect of daily green tea intake on inflammatory markers, including IL-2, IL-6, and IL-12, as well as TNF-α, C-reactive protein, lipid profile, glucose status, and markers of liver, kidney, and heart function in men in Erbil.

Materials and Methods:

The study involved 21 healthy male volunteers, aged between 21 and 40 years, who consumed two cups of green tea daily and assessed inflammatory markers and physiological and biochemical tests by comparing the results before and after four weeks of daily intake of green tea.

Results:

Serological results of blood samples after 4 weeks of daily intake of green tea revealed a significant reduction ($P < 0.001$, $P < 0.005$) in IL-2, IL-6, IL-12, TNF-α, and C-reactive protein, and showed a significant reduction in blood glucose, HbA1c, TG, TC, and LDL cholesterol. It also showed significant reductions in liver, kidney and cardiac function.

Conclusion: Our findings suggest that daily intake of green tea reduces the levels of inflammatory markers, reduces the blood lipid and sugar profiles, improves the physiological functions of the liver, kidneys and heart, and increases the effectiveness and activity of the body's immune system.

Key words: Green tea, physiological markers, inflammatory parameters, bioactive compounds.

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INTRODUCTION

Green tea is the leaves of the tea plant *Camellia sinensis*, which are rich in bioactive compounds, such as polyphenols with antioxidant and anti-inflammatory properties, pathophysiological protective effects and health benefits [1,2,3 and 4], a potent anti-inflammatory by reducing nuclear factor-κB gene expression and the production of pro-inflammatory cytokines [5], and its protective effect and pathophysiological benefits are mainly due to bioactive polyphenolic compounds such as catechins, epicatechin (EC), epigallocatechin (EGC), epicatechingallate (ECG), and epigallocatechin gallate (EGCG) [3,4 and 6].

Daily consumption of green tea leads to a reduction in pro-inflammatory cytokines, C-reactive protein, and inflammatory and pathological growth factors. Several studies have shown that green tea catechins limit and reduce the secretion of inflammatory cytokines and CRP through inhibition of nuclear factor kappa (NF-κB) of activated B cells and regulation of immune responses [7and 8]. Inhibition of NF-κB by green tea catechins reduces the production of tumor necrosis factor-α (TNF-α), interleukin IL-6 and other inflammatory cytokines affecting C-reactive protein which is a marker of systemic inflammation and high levels are associated with an increased risk of metabolic syndrome and cardiovascular disease[9].

Green tea polyphenols, especially EGCG, enhance insulin sensitivity in cells and increase glucose entry and oxidation, as well as reduce glucose production in liver cells by activating the MP-activated protein kinase (AMPK), which plays a key role in regulating cellular energy and glucose metabolism, leading to improved blood glucose control. The activation and stimulation of protein kinase facilitates the uptake and absorption of glucose by cells by promoting the translocation of glucose transporter type 4 (GLUT4) receptors to cell membranes, thereby lowering blood glucose levels [10 and 11]. Studies have confirmed that green tea catechins reduce carbohydrate digestion by inhibiting alpha-amylase and alpha-glucosidase enzymes, thereby limiting post-meal glucose spikes [12 and 13].

Some human clinical studies and in vitro animal experiments have shown that green tea catechins lower levels of neutral triglycerides (TG), total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol [16,17 and 18]. Daily tea intake increases the gene expression of the translocase/CD36 and acyl-CoA dehydrogenase enzymes involved in fatty acid transport and oxidation, and reduces

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malonyl CoA metabolism, which leads to an increase in the activity and potency of the enzyme carnitine palmitoyl-transferase involved in lipid metabolism [19 and 20]

Several studies have shown that green tea has hepatoprotective effects, as it reduces liver damage caused by alcohol, viral hepatitis, free radicals, heavy metal elements, toxins, drugs and accumulated fats [21 and 22].

Green tea has an effective protective effect on liver cells, improving their function by reducing the levels of liver enzymes (ALP, ALT, and AST) and restoring the normal levels of these enzymes, as well as total protein and albumin in blood plasma [23,24,25,26,27 and 37].

Experimental studies have concluded that consuming green tea has protective effects on kidney function and has no negative effects on the structure and function of kidney cells and nephrons, reduces the levels of blood urea, serum creatinine and albumin in the urine and maintains normal levels of renal function indicators in blood and urine [28,29,30 and 31]. Experimental studies have also demonstrated that green tea offers protective benefits for cardiac activity and the health of cardiomyocytes, maintaining normal levels of cardiac health indicators such as CK-MB and LDH enzymes [32,33,34,35,37 and 38]. The protective effects and health benefits of green tea on the heart and other vital organs are mainly due to the antioxidant and anti-inflammatory properties of polyphenols and catechins that work by stimulating antioxidant enzymes, inhibiting oxidative enzymes, eliminating free radicals, reducing inflammation, reducing total and LDL cholesterol and increasing lipid peroxidation [39,40,41,42,43,44,45,46,47,48 and 33].

Therefore, the current study was designed to investigate and determine the effects of daily intake of green tea on inflammatory markers such as cytokines IL-2, IL-6, IL-12, TNF-α, C-reactive protein (CRP), glucose status, lipid profile, and biomarkers of liver, kidney and heart functions in men in Erbil city.

MATERIALS AND METHODS

- Study participants

The current study was conducted on healthy men, aged between 21 and 40 years, and the green tea (Chihan®) used in this study was chosen due to its easy accessibility and availability to the participants. The concentration of flavonoids was reported to be between 100 and 200 mg per tea bag, according to the manufacturer's estimates. Each participant consumed two cups of green tea per day, each cup was prepared with a green tea bag (2 g, Chihan®) in 250 ml of warm water

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at 70 °C. Data were obtained from study participants, and venous blood samples were collected before and after 4 weeks of daily green tea intake to assess inflammatory markers and physiological and biochemical parameters.

- Blood sample Collection

Venous blood samples were collected in the morning after fasting for 12 hours overnight the day before the experiment and after 4 weeks of green tea intake. Blood samples were placed in collection tubes for biochemical and physiological analysis, blood samples were transported directly to the laboratory and serum was separated by centrifugation at 3000 RPM for 10 minutes, and analyses of inflammatory markers, lipid profile tests, glucose, liver, kidney and heart functions were performed in blood plasma.

- Inflammatory markers assessment

Serum concentration of IL-6, IL-12, IL-2, TNF-α, and CRP were measured by enzyme-linked immunosorbent assay (EILISA) and Beckman Coulter AU systems before and after 4 weeks of green tea intake [23 and 24].

- Assessment of lipid profiles and glycemic status

The lipid profile was analyzed using the Cobas Integra 400 Plus (Roche Diagnostics, Mannheim, Germany) and using specialized lipid profile analysis kits, total cholesterol (TC), neutral triglycerides (TAGs), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were evaluated [50,51]. Blood glucose concentration and HbA1c were measured using a Cobas Integra 400 Plus automatic analyzer (Roche Diagnostics, Mannheim, Germany) and using specialized kits for this analysis [52].

- Assessment of liver, renal and cardiac functions

Liver, renal and cardiac function tests were analyzed using a Cobas Integra 400 Plus (Roche Diagnostics, Mannheim, Germany) and using specialized kits for these tests, where total protein concentration was measured

- Statistical analysis

Data were represented in tabular form, and variables were presented as mean ± SD. Inferential statistics and a paired t-test were used to analyze the data through SPSS version 22, and a P value of ≤ 0.05 was considered statistically significant.

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RESULTS AND DISCUSSION

- Effect of green tea on inflammatory markers:

In the current study, statistically significant reductions ($P < 0.01$, $P < 0.05$) were observed in the levels of inflammatory cytokines IL-2, IL-6, IL-12 and TNF-α. and C-reactive protein (CRP) in blood plasma after four weeks of daily consumption of green tea when compared to pre-treatment samples in healthy men (Table 1), the results were considered statistically significant at ($P < 0.05$) using paired t test as in Table 1.

The results of the current study are consistent with the results of several previous studies on the effect of green tea intake on reducing pro-inflammatory markers such as cytokines IL-2, IL-6, IL-12, TNF-α, and CRP in the body [3,5,9,24,54 and 55]. The mechanisms of action of the anti-inflammatory property of green tea polyphenols are due to the inhibition of gene expression and chemical pathways of nuclear factor-κB, reduction of pro-inflammatory cytokine production through inhibition of gene expression and MAPK pathway, and inhibition of STAT1 , AP-1 pathway activity and COX cyclo-oxygenases pathway of inflammation in the body [56,57,58,59 and 60].

Table 1: Effect of green tea intake on inflammatory markers in male participants

inflammation markers	**Pre-green tea consumptions** mean ± SD	**Post-green tea consumptions** mean ± SD	**p value***
IL-2 pg/Ml	3.63 ± 0.573	2.94 ± 0.489	0.0481
IL-6 pg/mL	9.83±2.89	7.68±3.95	0.0876
IL-12 pg/mL	7.62± 0.811	5.74± 1.42	0.0998
TNF-α pg/mL	4.72 ± 2.13	3.79 ±1.39	0.0396
CRP mg/mL	3.15 ± 1.03	2.37 ±1.33	0.0475

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- Effect of green tea on Lipid profile

The results of the current study showed conclusive data on the effects of daily intake of green tea on lipid levels in healthy participants. Our study revealed that daily consumption of green tea led to a significant reduction in the levels of neutral triglycerides, total cholesterol, LDL cholesterol and a slight non-significant increase in HDL cholesterol (Table 2). The results of our study are similar to the results of some previous studies that showed a significant decrease ($P<0.05$) in the levels of neutral triglycerides, total cholesterol and LDL cholesterol and an increase in the level of HDL cholesterol within normal levels [28,39,50,61,62 and 63].

Table 2: Effect of green tea intake on serum lipid levels in male participants

Lipid profile	**Pre-green tea consumption** mean ± SD	**Post-green tea consumption** mean ± SD	**p value***
TG mg/dL	129.42 ± 8.71	119.83 ± 5.17	0.0439
TC mg/dL	167.38 ± 6.23	158.41 ± 4.87	0.0327
LDL -Cholesterol mg/dL	69.89 ± 7.13	57.19 ± 3.43	0.0441
HDL-Cholesterol mg/dL	42.278 ± 3. 39	**43**.375 ± 2.58	0.0508

- Effect of green tea on glycemic status

Daily consumption of green tea led to a significant decrease in fasting blood glucose (FBS) level and cumulative blood glucose (HbA1c) level after four weeks of green tea consumption compared to their levels before starting to consume them (Table 3), the results of our study are very similar to those of previous studies [28,53,64]. The antidiabetic effect of green tea polyphenols comes through inhibition of alpha-glucosidase and alpha-amylase, inhibition of hepatic gluconeogenesis and increased insulin sensitivity of cells [10,11,12,13,56 and 57].

Daily consumption of green tea reduces blood glucose levels and cumulative hemoglobin (FBS, HbA1c), and led to decrease TG, TC and LDL cholesterol, and an increase in HDL. This demonstrates the effects of green tea that reduce the risk of metabolic syndrome and cardiovascular disease.

Table 3: Effect of green tea intake on blood glucose levels in male participants

Glycemic status	Pre-green tea consumptions mean ± SD	Post-green tea consumptions mean ± SD	P value*
FBC mg/dL	87.73 ± 6.91	83.42 ± 6.81	0.0435
HbA1c (%)	5.21 ± 1.19	4.58 ± 1.24	0.0395

- Effect of green tea on liver function tests

The results of the current study showed positive data on the protective effect of daily intake of green tea on the levels of liver function markers in healthy participants, as our study revealed that daily consumption of green tea led to a statistically significant reduction in the levels of liver function enzymes such as ALP, ALT and AST and an increase in the level of total protein and serum albumin Table 4. These results are supported by the several previous studies that showed a significant decrease ($P<0.05$) in liver function enzyme levels (ALP, ALT AST) and an increase in the level of total protein and albumin within normal levels [23,24,25,26,27 and 37]. The protective effect of green tea is attributed to its antioxidant and anti-inflammatory properties, which preserve the structure and physiological functions of cells from oxidative and inflammatory damage.

Table 4: Effect of green tea intake on serum levels of liver function tests in male participants

liver function tests	Pre-green tea consumption mean ± SD	Post-green tea consumption mean ± SD	P value*
Total protein TP g/dL.	4.26 ± 1.29	5.56 ± 1.38	0.0481
Albumin g/dL.	3.67 ± 0.97	5.39 ± 1.05	0.0392
ALT (IU/L)	21.71 ± 5.63	18.52 ± 3.54	0.0419

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AST (IU/L)	14.82 ± 6.82	11.93 ± 3.41	0.0501
ALP (IU/L)	45.49 ± 3.77	.39 ± 5.24	0.0392

- Effect of green tea on renal function tests

The results of the current study provided significant data on the protective effect of daily intake of green tea on the levels of kidney function markers in healthy participants. Our study revealed that daily consumption of green tea led to a statistically significant reduction in serum creatinine and urea levels Table 5. These results were consistent with the results of several previous studies that showed a significant reduction (P< 0.05) in serum creatinine and urea levels [28,29,30 and 31]. The protective effects of green tea are attributed to its antioxidant and anti-inflammatory properties as it preserves the structure and physiological functions of cells from oxidative damage and inflammation as well as maintaining a normal lipid and blood sugar profile which protects the kidneys from the complications of diabetes, hypertension and cardiovascular disease.

Table 5: Effect of green tea intake on blood levels of renal function tests in male participants

Renal function test	**Pre-green tea consumption** mean ± SD	**Post-green tea consumption** mean ± SD	**P value***
Serum Creatinine mg/dL	0.39 ± 0.21	0.23 ± 0.18	0.0438
Urea mg/dL	14.28 ± 2.47	8.79 ± 3.69	0.0392

- Effect of green tea on cardiac function tests

The results of the current study show a significant data on the protective effect of daily intake of green tea on the levels of cardiac function enzyme markers in healthy participants. Our study revealed that daily consumption of green tea led to a significant reduction in serum levels of creatine kinase and dehydrogenase (CK-MB and LDH) (Table 6). These results were similar to the results of previous studies that showed a significant reduction (P<0.05) in serum CK-MB and LDH levels [32,33,34,35,37 and 38]. The protective effect of green tea is attributed to its antioxidant and anti-inflammatory properties as it preserves the structure and physiological functions of cardiomyocytes from oxidative damage and inflammation as well as maintaining a

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normal lipid and blood sugar profile which protects the heart and blood vessels from the complications of hyperglycemia and hypertension and reduces the risk of cardiovascular disease.

Table 6: Effect of green tea intake on blood levels of cardiac function tests in male participants

Cardiac function enzymes	**Pre-green tea consumptions** mean ± SD	**Post-green tea consumptions** mean ± SD	**P value***
LDH IU/L	118.37 ± 7.81	109.69 ± 8.52	0.0302
CK-MB IU/L	7.36 ± 0.13	5.8 ± 0.21	0.0511

CONCLUSIONS

We conclude from the data of our study results that daily drinking of green tea reduces the levels of inflammatory and pathophysiological indicators in the blood such as cytokines, chemokines and inflammatory proteins, and that it has anti-diabetic, anti-hyperlipidemic and anti-cholesterol effects, It has protective effects and great health benefits on vital organs such as the liver, kidneys and heart, as it preserves the cellular structure and cell functions, and reduces the risk of metabolic diseases such as diabetes, cardiovascular disease, liver and kidney dysfunction.

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Conflict of interests.

There is no conflict of interest, according to the authors.

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الخلاصة

المقدمة: يعد تنازل اليومي للشاي الاخضر Green tea من أحد اهم المشروبات اليومية Daily consumption والتي تحتوي علي العديد من المركبات الحيوية الفعالة Bioactive compounds بتركيزات كبيرة مثل الفينولات Polyphenols وفلافونويدات Flavonoids , والتي لها فوائد صحية ووقائية مرضية مهمة وتأثيرات فيسيولوجية وأيضية ومناعية ايجابية كبيرة, ولها خصائص مضادة للاكسدة والالتهابات وتلعب دورًا مهمًا في وقاية وحفظ بنية ووظائف خلايا الجسم. صممت دراستنا للتحقق من أثر تناول اليومي للشاي الاخضر على مؤشرات الألتهاب كالسيتوكينات IL−2 وIL−6 وIL−12 وTNF−α وبروتين سي التفاعلي CRP ، وأختبارات بروفايل الدهون و السكر و وأختبارات وظائف الكبد والكلية والقلب لدى الرجال في مدينة أربيل.

طرق العمل: شارك في الدراسة 21 متطوعاً من الرجال الذين تتراوح أعمارهم بين 21 و 40 عامًا, تناول المشاركون يوميا كوبين من الشاي الاخضر , وتم تقييم مؤشرات الالتهابات والاختبارات الفيسيولوجية والكيموحيوية من خلال أخذ الدم الوريدي قبل وبعد اربعة أسابيع من تناول اليومي للشاي الاخضر .

النتائج: أظهرت نتائج الدراسة لتحليل ملف الدهون والسكر انخفاضا ملحوظا معنويا ($P<0.005$) في معدل كلوكوز الدم والسكر التراكمي HbA1c وفي الدهون االثلاثية المتعادلة واجمالي الكوليسترول و كوليسترول منخفض الكثافة LDL في الدم الوريدي بعد اربعة اسابيع من تناول الشاي الاخضر . وكشفت الاختبار المصلي لعينات الدم الوريدية بعد 4 اسابيع من تناول اليومي للشاي الأخضر انخفاضًا ملحوظًا ($P <0.001, P <0.005$) في سايتوكينات IL−2 و IL−6 و IL−12 و TNF−α و بروتين سي التفاعلي CRP. وأظهرت أيضا انخفاضا ملحوظا معنويا لنتائج تحليل وظائف الكبد ووظائف الكلى و والإنزيمات الوظيفية للقلب.

الاستنتاجات: نستنتج من نتائج الدراسة أن تناول الشاي الأخضر يوميًا يقلل من مستويات العلامات الالتهابية مثل السيتوكينات والكيموكينات والبروتينات الالتهابية، ويقلل من نسبة الدهون والسكر في الدم، ويحسن الوظائف الفسيولوجية للكبد والكلى والقلب، ويزيد من فعالية ونشاط الجهاز المناعي للجسم.

الكلمات المفتاحية: الشاي الاخضر , المؤشرات الفسيولوجية, العلامات الالتهابية, المركبات الحيوية.

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