

RAISED SERUM CHOLESTEROL; EVALUATION OF HYPOCHOLESTEROLEMIC EFFECT OF GREEN TEA (CAMILLIA SINENSIS)

ORIGINAL
PROF-1895

DR. SADIA AHMAD

PhD Scholar,
University of Birmingham

DR. FARAH DEEBA

Biochemistry Deptt,
UCMD, University of Lahore

DR. MAZHAR MUSHTAQ

Assistant Professor
Biochemistry Deptt, SMDC

Dr Ghazala Irshad

Biochemistry Deptt,
UCMD, University of Lahore

Dr Samra Hafiz

Biochemistry Deptt,
UCMD, University of Lahore

ABSTRACT... Introduction: Hypercholesterolemia has a strong association with Atherosclerosis and coronary artery disease (CAD). It is a major worldwide health problem and the incidence is rising in Pakistan. Hypocholesterolemic effect of green tea (GT) has been proven in various research studies in the world. **Objective:** Present study aims to evaluate this effect in Pakistani population in the context of specific dietary and social habits prevailing here. **Setting:** The university of Lahore. **Methodology:** Sixty subjects were included in the study comprising of thirty healthy subjects and thirty hypercholesterolemic individuals who were not taking any medication to control their serum cholesterol. They were all given GT in a dose of 3 gm twice daily for sixty days. Serum cholesterol levels were estimated at day 1 and then every 2nd week till the 60th day. **Results:** Significant lowering of serum cholesterol was observed ($p < 0.001$) in hypercholesterolemic individuals after 60 days. There were no side effects reported of GT intake. **CONCLUSIONS:** Our results suggest that GT can safely reduce the raised serum cholesterol level in Pakistani population.

Key words:Hypercholesterolemia, Atherosclerosis, Coronary Artery Disease (CAD), HMG Co A reductase inhibitors, green tea (GT), Catechins, Polyphenols.

INTRODUCTION

Cardiovascular diseases are becoming a major health burden in developing countries. The incidence of hypercholesterolaemia, obesity and cardiovascular diseases has increased remarkably in Pakistani population but published data for prevalence or incidence of CAD and relations between risk factors and disease have not been established^{1,2}.

Amongst all the serum lipids, namely TAG, VLDL, LDL and HDL, cholesterol is most often singled out as being chiefly concerned with incidence of Atherosclerosis and CAD³. Atherosclerosis is a progressive inflammatory disorder of the arterial wall that is characterized by deposition of cholesterol and cholesterol esters from the plasma lipoproteins into the artery walls especially the coronaries⁴⁻⁶.

Patients with high serum cholesterol are often prescribed one or more of the cholesterol lowering drugs from Statin group: Zocor (Simvastatin), Lescol (Fluvastatin) and Lipitor (Atorvastatin) which lower serum cholesterol by blocking the rate limiting step of cholesterol biosynthesis

(competitive inhibitor of HMG Co-A reductase) but there is a definite risk associated with these drugs.

The most common side effects of Statins are nausea, headache, dizziness, rash, sleep disturbances, tendinitis, polyneuropathy and irritability^{7,8}. Statins can cause elevations in liver enzymes in 1 of 100 patients⁹. Myalgia, asymptomatic increase in creatine kinase (CK), myositis and rhabdomyolysis are also included in the reported side effects of Statins^{10,11}. There is growing interest in using herbal remedies for the common ailments due to side effects of conventional allopathic drugs. Regular intake of GT has been found effective in controlling blood glucose level, serum cholesterol level, reactive oxygen species and many more¹².

There are three main varieties of tea; green, black and oolong which originate from the same plant *Camellia sinensis*. The difference between the teas is in their processing. Green tea is prepared in such a way as to preclude the oxidation of green leaf polyphenols. The unfermented GT leaves contain the highest concentration of powerful antioxidants called

Polyphenols and the healthful properties of GT are largely attributed to these compounds¹³. It contains a variety of polyphenols, including flavanols, flavandiol, flavanoids and phenolic acids. Polyphenols may account for up to 30% of the dry weight and they give GT a somewhat bitter flavour. Most of the GT polyphenols are flavanols, commonly known as catechins. It is commonly sold as dried leaves tea which is taken as brewed in hot water. Some major GT catechins are,¹⁴ Epigallocatechin Gallate (EGCG) 60%, Epigallocatechin (EGC) 20%, Epicatechin Gallate (ECG) 13%, Epicatechin (EC) 6% and Gallocatechin (GC) 2%.

OBJECTIVE

Numerous research studies in different parts of the world, particularly in China, Japan, Taiwan, UK and US have been conducted on animals and humans and their findings have confirmed the hypocholesterolemic effect of green tea in people having high serum cholesterol and atherosclerotic CAD¹⁵⁻¹⁸. The present study was first of its kind in Pakistan and was aimed to evaluate the hypocholesterolemic effect of GT under the local dietary and climatic conditions prevailing in Pakistan. Through this study, GT can provide a safer and cheaper alternative to lower serum cholesterol levels in Pakistani population.

METHODOLOGY

The present study was conducted primarily at the University of Lahore (TUOL). An institutional ethical review board of TUOL approved the study. All participants signed a written consent and agreed for a two months follow up. Participants were explained the purpose of the study and a clinical questionnaire was filled by each participant to get a full account of subject's past and present history of illness, family and drug history (if any), dietary and social habits and the extent of physical activity per day. Sixty male and female individuals participated in the study and they were placed in two groups, A and B, each containing 30 subjects;

- Group-A. Subject with normal serum cholesterol (aged 45-55 years)
- Group-B. Hypercholesterolemic subjects aged 50-60 years who were not taking any cholesterol lowering drugs.

Exclusion Criteria

Women with history of menorrhagia and individuals on anti-coagulants other than low dose Aspirin were not enrolled in the study.

The reason for this exclusion was the effect of GT on platelets aggregation which has earlier been reported¹⁹.

DOSAGE PLAN

All members of these groups were given the same brand and same dose of green tea which was purchased from local market. Two tea bags of G.T, each weighing 15 gm were advised twice a day for sixty days. All the participants were advised to follow a low fat diet (containing 20 % fat, mainly derived from unsaturated fatty acids and less from saturated fatty acids) and to perform moderate exercise (30 minutes brisk walk 5 days a week).

SERUM CHOLESTEROL ESTIMATION

12-hour fasting blood samples were collected from every subject on day 1 and then at two weeks interval till last day (60th day). Serum cholesterol estimation was carried out by standard enzymatic Colorimetric method (CHOD-PAP METHOD) All spectrophotometric measurements were carried out using Apel PD-303 (Japan) UV-visible spectrophotometer. The data thus collected was subjected to T-test and the null hypothesis was rejected if $P > 0.001$ ²⁰.

RESULTS

Group B showed significant lowering of serum cholesterol after taking 15gm of GT twice daily ($p < 0.001$). Results were better for those subjects who observed dietary restrictions and exercise routines. Individuals in group A with normal serum cholesterol levels did not show any significant lowering in serum cholesterol level ($p < 0.001$).

DISCUSSION

Serum cholesterol level is a major modifiable risk factors for Atherosclerosis and CAD²¹. Numerous research studies conducted world wide, demonstrate that the risk of coronary heart disease and other forms of atherosclerotic vascular disease rises with serum

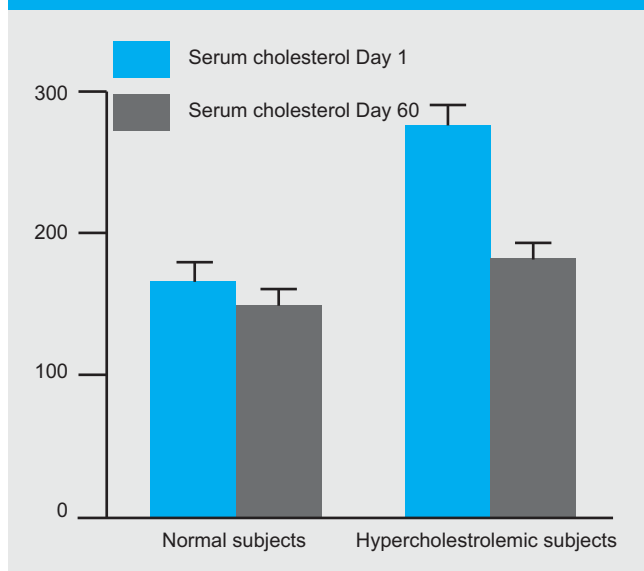
Table-I. Basic characteristics of study population

Groups / Basic Characteristics	A	B
No. of Subjects	30	30
Gender		
Male	17	19
Female	13	11
Hypertension	01	07
Family history of hypercholesterolemia	03	11
Family history of ischemic heart disease	05	09
Age (in years)	50±5	55±5

Table-II. Serum cholesterol levels before and after the treatment (green tea) in both groups

Groups	Serum cholesterol mg/dl on day 1	Serum cholesterol mg/dl day 60	P-value
A (n=30)	176±14	172±10	0.330
B (n=30)	278±24	192±12	0.001

Fig-1. Serum cholesterol levels before and after the treatment (green tea) in both groups



cholesterol concentration and in particular the ratio of total cholesterol to HDL-cholesterol. Lowering the level of LDL-C and total cholesterol reduces the risk of cardiovascular events including death, myocardial

infarction and stroke²².

Patients with high serum cholesterol are often prescribed one or more of the cholesterol lowering drugs from Statin group (competitive inhibitor of HMG Co-A Reductase). Due to the large number of side effects, many patients cannot take these drugs on a long term basis²³. Hence, there is a strong need for an alternative cholesterol lowering therapy with better compliance.

Sixty individuals were included in this study which was conducted primarily at TUOL. Participants were placed in two groups and GT in a dose of 3 grams twice daily for sixty days was prescribed to individuals included in normal and hypercholesterolemic groups. In this study, there was a significant lowering of serum cholesterol levels ($p < 0.001$) in group B. These findings are in conformity with the studies conducted in Japan by Imai and Nagao²⁴ where the effect of drinking green tea on lowering serum cholesterol levels was found to be significant ($p < 0.001$).

In the light of previous studies carried out elsewhere in the world, the observed mechanism of action of green tea catechins in lowering serum cholesterol is following:

1. GT catechins decrease micellar solubility and intestinal absorption as well as increase fecal excretion of dietary cholesterol. The proposed mechanism of action is inhibition of both gastric and pancreatic lipases. This cholesterol lowering effect of GT has been confirmed by both animal and human based studies²⁵⁻²⁹.
2. It has been reported that GT lowers body weight through inhibition of catechol-o methyltransferase (COMT) that inhibits nor-epinephrine breakdown (carried out by COMT)³⁰. This effect of GT can be helpful in treating hypercholesterolemia in obese patients.

CONCLUSIONS

Based on these findings, it was concluded that GT intake can significantly lower raised serum cholesterol level in hypercholesterolemic individuals in Pakistan ($p < 0.001$, True hypothesis).

Copyright© 01 Feb, 2012.

REFERENCES

1. Sania Nishtar. **Prevention of coronary heart disease in south Asia**: The Lancet 2002; 360:1015-1018.
2. Aziz K, Aziz S, Patel N, Faruqi AM, and Chagani H. **Coronary heart disease risk-factor profile in a lower middle class urban community in Pakistan** East Mediterr Health J 2006 ;12(1-2):80.
3. Jung San Huang. **Link between cholesterol and Heart Disease**. 2007; Saint Louis University Science Daily.
4. Basu A, Lucas EA. **Mechanism and effects of Green Tea on Cardiovascular heart Diseases**. Nutr. Rev. 2007; 65(8 Pt 1): 361-75.
5. Babu PV Sabitha KE, Shyam Aladevi CS. **Theurapeutic effects of Green Tea extract on oxidative stress in aorta and heart of Streptozotocin diabetic rats**. Chem Biol Interact. 2006; 162 (2): 114-20.
6. Shashkin P, B Dragulev and K ley. **Macrophages differentiation to form foam cells and development of atherosclerotic plaques**. Curr Pharm Des 2005; 11:3061-3072.
7. Backes JM and PA Howard. **Association of HMG-CoA Reductase Inhibitors with Neuropathy** Ann. Pharmacother 2003; 37(2): 274 – 278.
8. Marie I, H Delafentre and N Massy. **Tendinous disorders attributed to statins: A study on ninety-six spontaneous reports in the period 1990-2005 and review of the literature**. Arthritis Care Res 2008; 59:367-372.
9. Gaist D, U Jeppesen and M Andersen. **Statins and risk of polyneuropathy: A case-control study**. Neurology 2002; 58: 1333–1337.
10. Omar MA, JP Willson and TS Cox. **Rhabdomyolysis and HMG-COA reductase inhibitors**. Ann Pharmacother 2001; 35:1096-1107.
11. Thompson PD, P Clarkson and RH Karas. **Statin-associated myopathy**. JAMA 2002; 289:1681-1690.
12. **Green Tea Supplementation Affects Body Weight, Lipids, and Lipid Peroxidation in Obese Subjects with Metabolic Syndrome** J. Am. Coll. Nutr. 2010 29: 1 31-40
13. **Green tea intake lowers fasting serum total and LDL cholesterol in adults: a meta-analysis of 14 randomized controlled trials** Am J Clin Nutr 2011 94: 2 601-610
14. K. C. Maki, M. S. Reeves, M. Farmer, D. Wilder, **Green Tea Catechin Consumption Enhances Exercise-Induced Abdominal Fat Loss in Overweight and Obese in Adults** J. Nutr. February 2009 vol. 139 no. 2 264-270
15. Tea's effect on Atherosclerosis. Pilot Study (TEA Study); July 2005. **Beth Israel Deaconess Medical Center** .www.Clinical Trial.gov.
16. Berube-Parent S, et al. **Effects of encapsulated Green Tea and Guarana extracts containing a mixture of EGCT and caffeine on 24-hour energy expenditure and fat oxidation in men**. Br J Nutr; 2005. 94(3): 432-6.
17. Kei Nakachi Satoru Matsuyama Saloshi Miyake et al. **Biofactors**; 2000; 13 (14): 49-54.
18. RA Riemersma, CA Rice-Evans, RM Tyrell. **Tea Flavonoids and cardiovascular health**. (Mixed Effects) QJM: An International Journal Medicine. 2001; 94 (5): 277-282.
19. Kang WS, KH Chung YH Zhang and YP Yun. **Antiplatelet activity of Green tea catechins is mediated by inhibition of cytoplasmic calcium increase**. J CardiovascPharmacol 2001; 38(6)875-884.
20. Trinder P. **Ann Clin Biochem** 1969; 6:24. Gosset W. **Introduction to Statistics**, 3rd ed. Ronald E Walpole, Collier Mcmillan Publishers 1908:219-21.
21. Torzewski M and KJ Lackner. **Initiation and progression of atherosclerosis: oxidative modification on LDL**. Clin Chem Lab Med 2006; 44:1389-1394.
22. Anonymous. **Expert panel on detection, evaluation and treatment of high blood cholesterol in adults**. JAMA 2001; 285: 2486-2497.
23. Holman JR. **Some Docs in Denial about Statin Side Effects** DOC News 2007; 4(12): 1 – 12.
24. Nagao T, Kokimitsu I. **A green Tea extract high in catechins reduces body fat and cardiovascular fat and cardiovascular risks in humans**. Obesity (Silver Spring). 2007; 15: 1473-1483.
25. Unno T, M Tago and Y Suzuki. **Effect of tea catechins in postprandial plasma Lipid responses in human subjects**. Br. J Nutr 2005; 93:543-7.

26. Vinson JA, K Teufel and N Wu. **Green and black teas inhibit atherosclerosis by lipid antioxidant and fibrinolytic mechanism.** Jour Agri food chem 2004;52: 3661-5.
27. Raederstroff DG and V Elste. **Effects of EGCG on lipid absorption and plasma lipids in rats.** J Nut Biochem 2003; 14:326-32.
28. Maron DJ, GP Lu and ZG Wou. **Cholesterol lowering effects of theaflavin enriched green tea extract.** Arch intern Med 2003; 163:1448-53.
29. Sano J. **Effects of green tea intake on the development of coronary artery disease.** 2004; 68:665-70.
30. Shixian Q, Vancrey B, Shi J. **Green tea extract thermogenesis-induced weight loss by epigallocatechin gallate inhibition of catechol-O-methyltransferase.** J Med Food. 2006 ;9(4): 451-8.

Article received on: 12/12/2011

Accepted for Publication: 01/02/2012

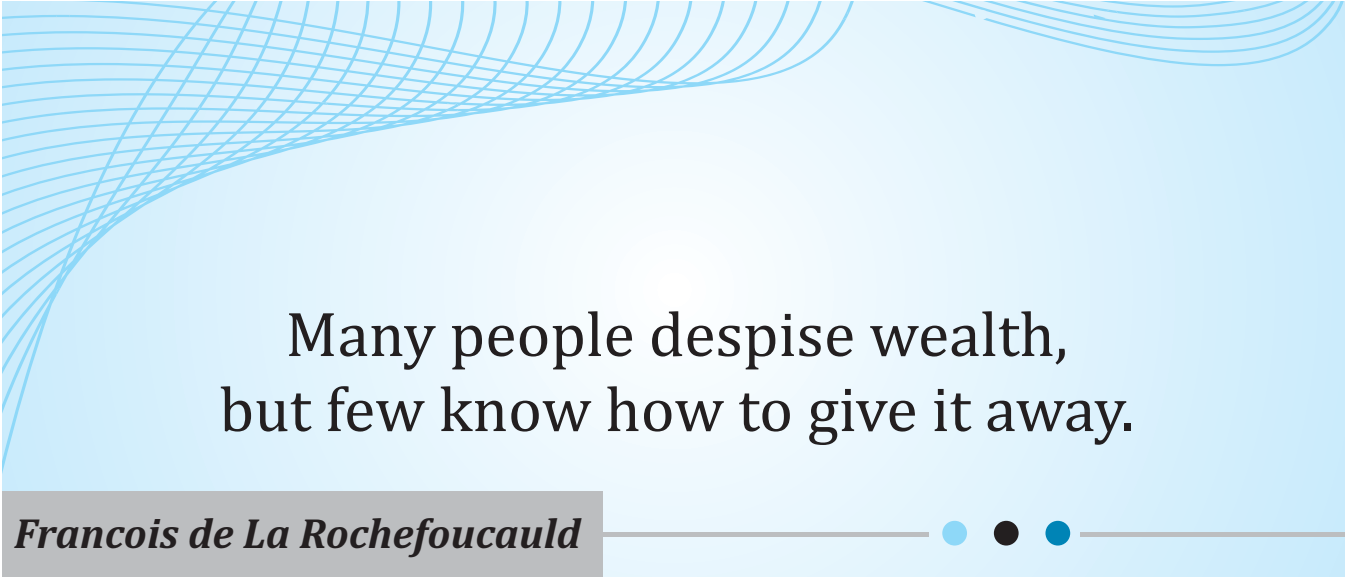
Received after proof reading: 10/05/2012

Correspondence Address:

Dr. Farah Deeba
Biochemistry Department
UCMD, University of Lahore
maddarch@yahoo.com

Article Citation:

Ahmad S, Deeba F, Mushtaq M, Irshad G, Hafiz S. Raised serum cholesterol; evaluation of hypocholesterolemic effect of green tea (Camillia Sinensis). Professional Med J Jun 2012;19(3): 346-350.



Many people despise wealth,
but few know how to give it away.

Francois de La Rochefoucauld