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# Dose-dependent effect of ginseng on high-fat diet induced hyperlipidemia in rats: A preventive clue for coronary artery diseases in experimental rats.

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## Abstract

**Background:** Coronary artery diseases (CAD) are among the most challenging diseases in this era; improper dietary habits and sedentary lifestyles are considered as foundation stones for metabolic disorders, including hyperlipidemia, the leading cause of CAD and hypertension. This study was designed to study the dose-dependent effect of ginseng on high-fat diet induced hyperlipidemia in animal models.

**Methodology:** This experimental study was conducted at Dow University of Health Sciences, including 50 male Albino Wistar rats. The rats were randomly divided into 5 groups of 10 animals each. Group 1 was on a normal balanced diet; group 2 was on a high fat diet (HFD), group 3 was on HFD plus ginsenoside 100 mg/kg body wt, group 4 was on HFD plus ginsenoside 200 mg/kg body wt, group 5 was on HFD plus ginsenoside 400 mg/kg body wt. Animals were sacrificed after 12 weeks; blood was drawn then sent to DDRRL for lipid profile.

**Results:** The results revealed that HFD increases body fats, weight increases from initial weight to 27.53% in obese control group 2 while after treating with ginsenoside weight reduced to 11.6%. Lipids levels in the blood; in the obese control group, mean triglyceride level increases from 45 mg/dl to 128.50 mg/dl, mean cholesterol level from 56.3 mg/dl to 106.2 mg/dl, and low-density lipoprotein (LDL) is increased from 6 to 11.9 mg/dl. While concurrent administration of ginseng root extract (ginsenoside) reduces the Lipid levels in blood according to the dosage of ginseng root extract, the mean triglyceride level in group 4 is reduced to 46.10 mg/dl from 128.50 mg/dl. The mean cholesterol level in group 4 is reduced to 400 mg/dl from 106.2 mg/dl. LDL is reduced in group 4 to 7.5 mg/dl from 11.9 mg/dl.

**Conclusion:** This study provides evidence that ginsenoside has an anti-hyperlipidemic effect, so it might help prevent CAD.

## Keywords

Hyperlipidemia, Hypertension, Coronary Artery Disease, Ginsenoside.

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## Introduction

This is the era of a sedentary lifestyle; people depend on junk food that is deep-fried and processed, have no time for exercise, and mostly use vehicles for traveling instead of walking or cycling. These are related to the fatty deposition in the body around the waist, arteries, liver, abdominal viscera, and muscles, defined as obesity[1]. Obesity is the major cause of metabolic syndromes like Diabetes mellitus, hypertension, and coronary artery disease[2]. Obesity is also a root cause of multiple risk factors like hyperglycemia, hyperlipidemia, reactive oxygen species (ROS), and exosome[3].

Hyperlipidemia or abnormal fat depositions are the recognized cause of coronary artery disease leading to myocardial infarction[4]. It is also a risk factor for hypertension leading to heart failure and cerebral artery disease leading to stroke[5]. There is a correlation of obesity with decrease adiponectin leading to fatty accumulation and plaque formation in blood vessels[6].

Obesity often increases insulin resistance[7], which impairs glucose transport from blood to the cells. Increased glucose levels in the blood but decrease at cellular levels causes peripheral lipolysis, triglyceride synthesis, and hepatic uptake of fatty acids resulting in non-alcoholic fatty liver disease[8]. Abnormal intrahepatic fat deposition disturbs its metabolism and causes dyslipidemia due to an imbalance between uptake and storage of very low-density lipoproteins (VLDL)[9]. An increase in triglyceride and VLDL makes plaque with calcium inside the arterial lumen, narrowing the diameter of vessels[10]. In the case of coronary arteries, lack of oxygenated blood to cardiac muscles (ischemia) resulting in necrosis (Myocardial infarction)[11].

The present study was designed to provide prevention against coronary artery disease occurred by fatty deposition in coronary arteries by reducing fat contents in blood including (TG), cholesterol, Low-density lipoprotein (LDL), Very low-density lipoproteins (VLDL) by a herb named Ginseng, which is easily found in Asia[12]. A glycosylated saponin acts through AMPK (Adenosine monophosphate kinase) on pancreases to increase insulin sensitivity[13]. It directly decreases leptin level and body fats[14]. Ginseng-induced appetite suppression has been reported when it acts on the hypothalamus [15]; it also improves insulin-receptor sensitivity by improving mitochondrial functions in skeletal muscles[16].

## Methodology

This experimental study included 50 male albino Wistar rats weighing 100-150 gm were purchased from the Animal House of Dow University of Health Sciences, Ojha Campus, Karachi. Rats were randomly divided into five groups of 10 animals each. Group 1 was on a balanced diet; Group 2 was on a high fat diet (HFD), Group 3 was on HFD with ginseng root extract 100 mg/Kg body wt, Group 4 was on HFD with ginseng root extract 300 mg/Kg body weight and group 5 was on HFD with ginseng root extract 400 mg/Kg body weight. The dose of the drug was calculated as mg/Kg/ml of their body weight. A protocol of a total of 12 weeks was followed. During this period, weekly weight was noted, and after 12 weeks, final weight was noted, blood was collected through the cardiac puncture, and lipid profiles were estimated in DDRRL (Dow diagnostic research and reference laboratory).

### Preparation of high-fat diet & ginseng root extract

A fatty diet was prepared in its kitchen by mixing beef tallow, cheese, and butter with a normal standard rodent diet. Ginseng root extract was prepared in the laboratory of IBBPS (institute of biological, biochemical, and pharmaceutical sciences) DUHS.

The data was analyzed on SPSS version 20.0. ANOVA test was applied to evaluate the significance of the groups. Post Hoc Dunnette t-test was applied for comparing the groups. A p-value $< 0.05$ was considered significant.

## Results

This experimental research work comprises 5 groups. Each has 10 animals; initial weights were measured before starting their experimental diet,

then weekly, and finally, after the 12th week of study, i.e., the final weight.

Mean Initial weight was measured as 123 mg, then high fat diet was started in all 4 groups except the 1st one (control), weight increased to 236 mg from 123 mg. Then treatment with ginseng root extract was provided in different doses, and final weight was measured; in group 3, it was 211 mg, 192 mg in group 4, and 171 mg in group 5.

The difference between their initial and final weight was obtained as the weight changed in groups. There was a significant increase in weight in the obese group, while with the use of ginseng root extract, weight and fat contents were reduced in a dose-dependent manner. Group 5 was given ginseng root extract in the potency of 400 mg/dl; the weight was reduced to nearly normal (171 mg).

Fatty meal digestion, absorption, and accumulation result in weight gain. Fats are deposited in the liver as fat droplets altering its metabolic functions, acting on insulin receptors causing insulin resistance, storing fats in muscles and the abdomen (Visceral fats). Free fatty acids, chylomicrons, TG and cholesterol, are also floating in blood. This experiment demonstrated the preventive effect of ginsenoside in animals taking a high-fat diet. The tables and graph revealed the fact that it reduces body weight by decreasing absorption of fats, increasing insulin sensitivity, and increasing mitochondrial biogenesis.

**Table 1: Difference between the measured parameters in the studied groups after administration of ginseng root extract (ginsenoside).**

| Groups | Mean Weight | Triglyceride | Cholesterol | LDL |
|---|---|---|---|---|
| | Mean±SD | | | |
| **Group 1** | 23.20±7.11 | 45.60±3.06 | 56.30±4.71 | 6.80±1.22 |
| **Group 2** | 118.30±6.46 | 128.50±36.02[b] | 106.20±6.97[b] | 11.90±1.66[b] |
| **Group 3** | 79.00±21.48 | 184.30±50.70[ab] | 81.10±10.26[ab] | 9.60±1.17[ab] |
| **Group 4** | 58.00±18.89 | 179.40±40.06[ab] | 76.90±10.60[ab] | 8.30±1.15[a] |
| **Group 5** | 36.70±12.48 | 46.10±4.22[a] | 62.60±6.23[ab] | 7.50±1.35[a] |

[a]Mean values were significantly different from group 2.
[b]Mean values were significantly different from group 1.

**Plasma Triglyceride (TG) levels**

The mean TG level in group 1 was found to be 45.6 mg/dl while in the obese group is found to be 128.50 mg/dl, then treated with ginseng root extract in doses of 100 mg/kg of body weight, 200 mg/kg of body weight and 400 mg/kg of body weight. After 6 weeks, these groups were sacrificed, and blood was sent for TG levels. Mean TG level was measured in group 3 as 184.30 mg/dl, group 4 was 179.40 mg/dl, and group 5 was 46.0 mg/dl. TG is found to be elevated in animals on a fatty diet, but ginseng reduces its levels by acting through AMPK activity. TG level of group 5 (HFD+ ginsenoside 400 mg/kg) reaches the TG levels of the control group.

**Plasma cholesterol levels**

The cholesterol level in the control group, which is on a balanced diet, was found to be 56.3 mg/dl. HFD was given to groups 2, 3, 4, and 5 for 6 weeks; group 2, which was obese control, had a cholesterol level of 106.2 mg/dl (p=0.0001). Then in groups 3, 4, and 5, ginseng root extract was giving in different doses for 6 weeks and finally sacrificed, and the mean cholesterol level was measured as 81 mg/dl, 76.0 mg/dl, and 62.60 mg/dl. By taking a high-fat diet, cholesterol level was found to be increased in the obese model, while ginsenoside reduces its levels in treated groups depending upon the dose of ginsenoside.

**Plasma low-density lipoprotein (LDL) levels**

LDL was measured in the control group after 6 weeks of a normal balanced diet, then HFD was giving for further 6 weeks, and LDL was measured, which was increased from 6 to 11.90 mg/dl. Ginseng root extract was administered orally for 6 weeks in doses of 100 mg/kg body weight, 200 mg/kg body weight, 400 mg/kg body weight. LDL levels were reduced to 81 mg/dl in group 3, 76 mg/dl in group 4, and 62 mg/dl in group 5. Then post HOC Dunnette t-test was applied; it showed a significant increase in LDL level from group 1 to group 2, a significant reduction between group 2 and group 5.

## Discussion

This preclinical study demonstrates that high-fat diet induced obesity and hyperlipidemia are the major biomarkers for predicting coronary artery diseases. Coronary artery disease is a challenge for this era; not only old persons but youngsters and adults also become victims of it[17]. Many researchers demonstrated that a high carbohydrate diet causes obesity and its outcomes, but this study focused on junk food or deep-fried food as the cause of increased lipids and weight gain.

Ginseng was used in herbal medicine and Chinese traditional medicine for centuries. In allopathic, it should be introduced. It can be used as a vegetable in a routine diet as it is safe for humans[18].

The blockage of the coronary artery is usually by plaque which is formed by free-floating lipids, triglycerides, and low-density lipoproteins with calcium and other minerals[19]. Due to the narrowing of the artery lumen, blood cannot reach the distal area resulting in a lack of oxygen and nutrient supply to that area, causing ischemia, then fibrosis, and lastly, infarction[20].

Scientists found a negative correlation between LDL and cholesterol with coronary artery disease[21]. Our results were in contradiction as we found a significant rise in LDL levels with cholesterol levels. This experiment was performed on male rats of weight 100 -150 were chosen due to their similarities with humans also used by other researchers[22].

Results of the present study revealed that a high-fat diet increases excessive fat deposition in the body, resulting in weight gain or obesity, which was reported earlier[23]. Similarly, this was observed in animals taking a high-fat diet[24]. According to many researchers, obesity itself is the predictor of CAD[25]. Ginsenoside is a glycosylated saponin found in the roots of a ginseng plant. Although leaves, fruits, and flowers also have saponins but roots are more potent[26].

Ginseng reduces serum lipid in this study in favor of study with the difference is that they reduce atherosclerosis using ginseng and exercise[27]. Limitations of this study included constraint of time and funding as it's research related to degree requirements. While the strength includes the use of Ginseng as a preventive measure for cardiovascular disorders. Ginseng is low-cost and easily available.

## Conclusion

The study concludes that the use of Ginseng might prevent coronary heart diseases. The contribution of a high-fat diet in developing obesity and enhancing lipid levels, resulting in coronary artery diseases. Ginseng, in our study, reduces the LDL, TG, and cholesterol levels and also prevents the initiation of fat deposition in coronary arteries.

## Conflicts of Interest

The authors have declared that no competing interests exist.

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## References


1. Shalaby MA, Hammouda AA-E. Antiobesity, antioxidant and antidiabetic activities of red Ginseng plant extract in obese diabetic rats. J. Intercult. Ethnopharmacol. 2013;2(3):165-172.
2. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, Nakayama O, Makishima M, Matsuda M, Shimomura I. Increased oxidative stress in obesity and its impact on metabolic syndrome. J. Clin. Investig. 2017;114(12):1752-1761.
3. Hwang L-C, Bai C-H, Chen C-J. Prevalence of obesity and metabolic syndrome in Taiwan. JFMA. 2006;105(8):626-635.
4. Nordestgaard BG, Benn M, Schnohr P, Tybjærg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA. 2007;298(3):299-308.
5. Jimenez-Conde J, Biffi A, Rahman R, Kanakis A, Butler C, Sonni S, Massasa E, Cloonan L, Gilson A, Capozzo K, Cortellini L. Hyperlipidemia and reduced white matter hyperintensity volume in patients with ischemic stroke. Stroke. 2010;41(3):437-442.
6. Kanaya AM, Wassel Fyr C, Vittinghoff E, Havel PJ, Cesari M, Nicklas B, Harris T, Newman AB, Satterfield S, Cummings SR, Health ABC Study. Serum adiponectin and coronary heart disease risk in older Black and White Americans. J. Clin. Endocrinol. Metab. 2006;91(12):5044-5050.
7. Kahn BB, Flier JS. Obesity and insulin resistance. J. Clin. Investig. 2000;106(4):473-481.
8. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Menys V, Fuller JH, Cards Investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. The Lancet. 2004;364(9435):685-696.
9. Adiels M, Taskinen M-R, Borén J. Fatty liver, insulin resistance, and dyslipidemia. Curr. Diabetes Rep. 2008;8(1):60.
10. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. Ann. Intern. Med. 2000;132(4):270-278.
11. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. NEJM. 2007;356(24):2457-2471.
12. Li Z, Ji GE. Ginseng and obesity. J. Ginseng Res. 2018;42(1):1-8.
13. Lee SH, Lee HJ, Lee YH, Lee BW, Cha BS, Kang ES, Ahn CW, Park JS, Kim HJ, Lee EY, Lee HC. Korean red ginseng (Panax ginseng) improves insulin sensitivity in high fat fed Sprague-Dawley rats. Phytother Res. 2012;26(1):142-147.
14. Wu Y, Huang XF, Bell C, Yu Y. Ginsenoside Rb1 improves leptin sensitivity in the prefrontal cortex in obese mice. CNS Neurosci. Ther. 2018;24(2):98-107.
15. Lee S, Rhee D-K. Effects of ginseng on stress-related depression, anxiety, and the hypothalamic–pituitary–adrenal axis. J. Ginseng Res. 2017;41(4):589-594.
16. Lee HJ, Lee YH, Park SK, Kang ES, Kim HJ, Lee YC, Choi CS, Park SE, Ahn CW, Cha BS, Lee KW. Korean red ginseng (Panax ginseng) improves insulin sensitivity and attenuates the development of diabetes in Otsuka Long-Evans Tokushima fatty rats. Metabolism. 2009;58(8):1170-1177.
17. Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, Williams GR. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. Circulation. 2004;110(10):1245-1250.
18. Shin B-K, Kwon SW, Park JH. Chemical diversity of ginseng saponins from Panax ginseng. J. Ginseng Res. 2015;39(4):287-298.
19. Wykrzykowska J, Lehman S, Williams G, Parker JA, Palmer MR, Varkey S, Kolodny G, Laham R. Imaging of inflamed and vulnerable plaque in coronary arteries with 18F-FDG PET/CT in patients with suppression of myocardial uptake using a low-carbohydrate, high-fat preparation. J. Nucl. Med. 2009;50(4):563-568.
20. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio AL, Crea F, Goudevenos JA, Halvorsen S, Hindricks G. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). EHJ. 2018;39(2):119-177.
21. Al-Kafaji G, Al-Mahroos G, Abdulla Al-Muhtaresh H, Sabry MA, Abdul Razzak R, Salem AH. Circulating endothelium-enriched microRNA-126 as a potential biomarker for coronary artery disease in type 2 diabetes mellitus patients. Biomarkers. 2017;22(3-4):268-278.
22. Hajnal A, Smith GP, Norgren R. Oral sucrose stimulation increases accumbens dopamine in the rat. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2004;286(1):R31-R7.

23. Cantó C, Houtkooper RH, Pirinen E, Youn DY, Oosterveer MH, Cen Y, Fernandez-Marcos PJ, Yamamoto H, Andreux PA, Cettour-Rose P, Gademann K. The NAD+ precursor nicotinamide riboside enhances oxidative metabolism and protects against high-fat diet-induced obesity. Cell Metab. 2012;15(6):838-847.
24. Buettner R, Schölmerich J, Bollheimer LC. High-fat diets: modeling the metabolic disorders of human obesity in rodents. Obesity. 2007;15(4):798-808.
25. Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsuzawa Y, Chao CL, Chen CL, Tai TY, Chuang LM. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. J. Clin. Endocrinol. Metab. 2001;86(8):3815-3819.
26. Jiao L, Li B, Wang M, Liu Z, Zhang X, Liu S. Antioxidant activities of the oligosaccharides from the roots, flowers and leaves of Panax ginseng CA Meyer. Carbohydr. Polym. 2014;106:293-298.
27. Lee J, Cho J-Y, Kim W-K. Anti-inflammation effect of Exercise and Korean red ginseng in aging model rats with diet-induced atherosclerosis. NRP. 2014;8(3):284-291.