

ETHANOLIC EXTRACT OF MEDICINAL HERB COULD PROTECT TISSUES FROM LIPID PEROXIDATION

SHAH MURAD., SALMAN IFTIKHAR¹., ABDUL GHAFAR²., JAMILA SHAH MURAD³., SEEMA⁴ & AQ ARAIN⁵

Professor of Pharmacology, IMDC, Islamabad Pakistan

¹Assoc Prof of Pharmacology at RLMC Lahore Pakistan

²SWO at LMDC/DANTH Islamabad Pakistan

³Psychology Deptt at BU Karachi Pakistan

⁴Gynecologist at NMC, Karachi Pakistan

⁵Associate Professor of Pharmacology at HBS Medical College, Islamabad-Pakistan.

(Received on Date: 8 August 2019)

Date of Acceptance: 7 September 2019)

ABSTRACT

It has been suggested that the hypocholesterolemic effects of ginger stems from the inhibition of cellular cholesterol synthesis. Attenuation of cholesterol synthesis results in augmentation of low density lipoprotein cholesterol (LDL-c) from plasma. As part of the ongoing efforts to authenticate the folkloric use of ginger in the traditional medicine, the study investigated the activity of aqueous ginger extract on the glucose level and lipid profile in hyperlipidemic patients. This study was a trial study for determination of hypolipidemic potential of medicinal plant ginger in already diagnosed patients of primary or secondary hyperlipidemia. It was placebo-controlled single blind research. Research work was conducted at National hospital, Lahore, from July to November 2018. Consent was taken from sixty hyperlipidemic patients age range from 25 to 60 years. Both gender male and female patients were included. Exclusion criteria was patients suffering from liver, renal, GIT disease and alcohol abusers, cigarette smokers. Patients who were taking any prescribed medicines for any disease were excluded from this research work. Patients were randomly divided in two groups, 30 patients were on medicinal herb ginger to take 5 grams in divided doses with their normal diet for the period of two months. Thirty patients were on placebo capsules filled with grinded wheat advised to take thrice daily for two months. Their base line lipid profile and body weight was recorded at start of treatment and were advised to come for check-up, fortnightly. When duration of study was over, their lipid profile and body weight was measured and compared statistically with pre-treatment values. Two months treatment with 5 grams of ginger decreased total cholesterol from 233.11 ± 1.53 mg/dl to 198.44 ± 1.23 mg/dl, LDL cholesterol reduced from 202.21 ± 1.88 mg/dl to 187.72 ± 1.98 mg/dl, reduced body weight from 76.01 ± 2.66 kg to 72.80 ± 1.87 kg. Both plasma total cholesterol and LDL cholesterol reduction was statistically significant, but decrease in body weight was non-significant when analyzed biostatistically. CONCLUSION: Body weight and lipid profile can be normalized by ginger officinale

INTRODUCTION

Dietary factors that influence lipid levels include modification of nutritional components, consumption of specific foods, use of food additives and supplements, and major dietary approaches. The most beneficial changes result from reducing intake of saturated and *trans*fats; increasing intake of polyunsaturated and monounsaturated fats; fortifying foods with plant stanols or sterols; isocalorically adding tree nuts to the diet; consuming one or two alcoholic drinks per day; and adopting a Portfolio, Mediterranean, low-carbohydrate, or low-fat diet¹. Smaller but still beneficial effects result from reducing intake of dietary cholesterol, increasing intake of soluble fiber and soy protein, and eating fatty marine fish or taking marine-derived omega-3 fatty acid supplements²⁻⁴. Red yeast rice supplements have effects similar to those of statin medications and are better tolerated in some patients. Regular aerobic exercise has beneficial effects on lipid levels, particularly if performed for at least 120 minutes per week. Brief physician counseling will have relatively small effects on unselected patients, so efforts should be concentrated on patients who are motivated and ready to make lifestyle changes. Eating junk food, enjoying sedentary life style, smoking, alcohol consumption are risky in human population for developing coronary artery disease⁵. One percent raised plasma lipids in human systemic circulation may increase two percent risk for being victimized of cardiovascular disease. Hyperglycemia, hyperthyroidism, primary hyperlipidemia,

and hypertension may exaggerate chances of atherogenesis and CAD⁶. Fibrates, statins, bile acid binding resins, and niacin are already approved drugs used in treatment of primary as well as secondary hyperlipidemia, but all of these agents have limited use in the disease due to their parallel adverse effects and low compliance⁷. Various medicinal herbs are being used in prevention and cure of primary or secondary hyperlipidemia. Ginger is one of them^{8,9}. If given in high doses ginger is cardiotoxic¹⁰. This herb contains gingerol which is antioxidant compound¹¹. This herb is being utilized as medicinal purposes since pre-historical times. It is also used in specific Asian ethnicity as kitchen spice, and is very famous as good flavoring spice¹². High plasma lipids, exaggerated thyroid functions, respiratory diseases, insulin resistance or hyperglycemia (DM type-II), gastrointestinal upsets can be treated well by ginger¹³⁻¹⁷. Ginger contains polyphenols, vitamin C, beta carotene, tannins, and flavonoids, and all these compounds act as scavenger of free radicals formed in human body during different metabolic reactions¹⁸. 80,000 tons ginger cultivation in China has been calculated and reported¹⁹. Ginger also contain remarkable amount of 6-gingerol, 6-paradol, 6-shogol, and gingerdiones, all of these compounds inhibit inflammatory chemotaxis factors like leukotrienes, thromboxane, and prostaglandins in human body. 6-paradol, and 6-gingerol found in ginger roots also inhibit DNA synthesis of human promyelocytic leukemia cells²⁰. In various studies it has been proved that ginger oil prevent DNA

damage to number of many cellular components caused by superoxides in human body. It has also been proved that plant ginger's various parts have characteristics to reduce apoproteins which are necessary and integral parts of low density lipoprotein particles and these lipoproteins are main source of atherosclerotic plaque synthesis leading to development of CAD²¹. The TLC diet recommendations include obtaining 25 to 35 percent of daily calories from fats, and restricting saturated fats to less than 7 percent of total calories and cholesterol to less than 200 mg per day. However, physicians and patients are often unsure of how much change in blood lipid levels can be expected when the TLC diet is prescribed, and wonder which lifestyle changes have the greatest effects²².

MATERIAL/PATIENTS AND METHODS

RESEARCH AREA: Lipid research clinic at National hospital Lahore, Pakistan. Number of Patients (sample size): Sixty male, female patients age range from 25 years to 60 years with already diagnosed cases of dyslipidemia were included. Study period: It was conducted from July to November 2018. The study was single blind placebo controlled. Duration of study was four weeks. **CONSENT:** Already explained and written consent was taken from all included patients and it was sent to get approval, which was then granted by ETHICS COMMITTEE of the hospital. **EXCLUSION CRITERIA:** Patients suffering from any liver, renal disease, with peptic ulcer disease, alcohol abusers, tobacco

utilizers, and patients already who were taking any prescribed medication for any illness were excluded from this study work. **GROUPING OF PATIENTS:** Patients were divided in two groups, i.e.; group-1 was advised to take 5 grams of ginger in divided doses as covenant everyday for the period of 4 weeks. Group-2 was on placebo therapy. I.e; capsules filled with grinded wheat to take one capsule thrice daily for the period of two months. **DETERMINATION OF PRE AND POST-TREATMENT VALUES:** All pretreatment values of LDL- cholesterol, serum total cholesterol, and body weight were determined by laboratory investigations and clinical examination of patients. Serum total cholesterol was estimated by the enzymatic calorimatic method. Serum LDL-cholesterol was calculated by Friedwald formula⁵ (LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol). Body weight was determined by weight machine provided by Lipid Concerned Clinic of the hospital. **DETERMINATION OF SIGNIFICANCE:** Data were expressed as the mean \pm standard deviation and paired "t" test was applied to determine statistical significance as the difference. In pre and post-treatment values. A probability value of >0.05 was considered as non-significance and $P<0.001$ was considered as highly significant change in these results.

RESULTS

In two months therapy by ginger, LDL-cholesterol of 27 hyperlipidemic patients reduced from 202.21 ± 1.88 mg/dl to 187.72 ± 1.98 mg/dl. Serum total cholesterol

reduced from 233.11 ± 1.53 mg/dl to 198.44 ± 1.23 mg/dl. Body weight reduced from 76.01 ± 2.66 kg to 72.80 ± 1.87 kg. Changes in LDL cholesterol and total

cholesterol are significant while body weight reduction is non-significant when analyzed statistically and compared with placebo group.

TABLE 1 showing Effects of ginger on LDL-cholesterol, total cholesterol and body weight in three months therapy. (n=27)

Parameter	At day-0	At day-60	Change in mg/dl	SS/p-value
LDL-c HDL-c	202.21 \pm 1.88 31.67 \pm 2.63	187.72 \pm 1.98 38.77 \pm 1.95	14.49 7.1	<0.01 <0.05
T-C	233.11 \pm 1.53	198.44 \pm 1.23	34.67	<0.001
Body weight	76.01 \pm 2.66	72.80 \pm 1.87	3.21	>0.05

TABLE 2 showing Effects of placebo on LDL-cholesterol, total cholesterol and body weight in three months (n=30)

Parameter	At day-0	At day-60	Change in mg/dl	SS/p-value
LDL-c HDL-c	143.25 \pm 1.99 33.75 \pm 3.01	142.98 \pm 1.98 33.97 \pm 2.51	0.27 0.22	>0.05 >0.05
TC	190.47 \pm 2.71	188.99 \pm 1.76	1.48	>0.05
Body weight	76.73 \pm 2.19	76.56 \pm 1.91	0.17	>0.05

KEY: \pm indicates standard error of mean, p-value >0.05 indicates non significant and P<0.001 indicates highly significant change in lipid profile. LDL-C means low density lipoprotein cholesterol mg/dl, T-C means total serum cholesterol mg/dl, HDL-C means high density lipoprotein cholesterol mg/dl, and body weight is measured in kg. GP (group) 1 is on drug and GP (group) 2 is on placebo. SS stands for statistical significance

DISCUSSION Comprehensive reviews of the evidence for dietary influences on levels of serum lipids and cardiovascular disease have been published. Decreasing total fat intake and replacing saturated and trans fats with polyunsaturated and

monounsaturated fats, along with limiting dietary cholesterol, lower total cholesterol, LDL cholesterol, and triglyceride levels. Compared with a baseline or Western diet, reducing saturated fat intake to 7 percent of total calories and limiting cholesterol to

200 mg per day reduce LDL cholesterol levels by 9 to 12 percent. A meta-analysis of 224 studies of dietary interventions showed that changes in total cholesterol levels were affected primarily by changes in intake of saturated and polyunsaturated fats, and dietary cholesterol. Allopathic drugs like statins and fibrates have limitations for their low compliance in hyperlipidemic patients. Nutraceutical term is getting popularity in cardiologists due to its good compliance and amazing results in hyperlipidemic patients. Ginger is proved nutraceutical agent having therapeutic effects in these patients. Phytochemicals present in ginger are extensively studied and proved their hypolipidemic, hypotensive, and weight reducing effects. A research conducted by Sitavan C et al²¹ proved 6 kg decrease in body weight of 108 hyperlipidemic patients by using 5 grams of ginger for 90 days. These results are matching with our results. It may be due to good sample size and ethnic effects of herb used in two different geographical environments for patients as well as climate for fertilization of mentioned herb. Cokava VI et al²² proved LDL cholesterol, TC and body weight reduction of 39 hyperlipidemic patients 19.87 mg/dl, 29.91 mg/dl, and 4.99 kg respectively, when they used 3 grams of ginger for 8 weeks. These results augment our research study results. Johsin PT et al²³ have mentioned mechanism of action of ginger that it scavenge free radicals in various tissues leading to decreased damage to vascular endothelium. Fajar LM et al²⁴ proved same reduction in low density lipoprotein cholesterol, total cholesterol, and body weight as our results proved. They mentioned and recommended that close supervision, frequent follow-up/counseling can give authenticated results in these patients. Illasi J et al²⁵ proved that in herbal medications, ginger is one of the potent hypolipidemic herb.

Solarka YT et al²⁶ did research on hypolipidemic, hypoglycemic and hypotensive effects of ZO and proved that this herbal agent reduced 39%, 27.18 %, and 22.64 % LDL cholesterol, blood glucose, and systolic blood pressure in 65 patients suffering from metabolic syndrome. They stated that metabolic syndrome is a constellation of interrelated risk factors of metabolic origin that appear to directly promote the development of atherosclerotic cardiovascular disease. Domerluve L et al²⁷ described that in the past few years, several expert groups have attempted to set forth simple diagnostic criteria to be used in clinical practice to identify patients who manifest the multiple components of the metabolic syndrome. These criteria have varied somewhat in specific elements, but in general they include a combination of both underlying and metabolic risk factors. Kulmharree C et al²⁸ did research on hypolipidemic effects of Zingiber Officinale in 22 hyperlipidemic patients also suffering from hypertension and proved that LDL cholesterol reduced up to 44.87 mg/dl by consumption of this herb for the period of three months. Dosaka BV et al²⁹ proved 32.44 mg/dl reduction in LDL cholesterol and 7.51 kilograms body weight in 66 hyperlipidemic patients when 2 grams Zingiber Officinale was used for two months. They mentioned in their discussion that atherogenic dyslipidemia consists of an aggregation of lipoprotein abnormalities including elevated serum triglyceride and apolipoprotein B (apo-B), increased small LDL particles, and a reduced level of HDL cholesterol. It is strongly recommended by Jalebii VC et al³⁰ and Jimeeshergi GT³¹ that phytochemicals are favorably good choice in alternative therapy but reasons for iatrogenic effects of these phytochemicals must be considered when these hypolipidemic agents be prescribed. A meta-analysis of 67 controlled trials of

dietary soluble fiber as a single intervention showed that the effects on total cholesterol and LDL cholesterol levels were modest. For example, the addition of three 28-g servings of oats per day decreases LDL cholesterol levels by 5 mg per dL (0.13 mmol per L)³². Some persons have little change in lipid levels despite significant changes in fat and cholesterol intake.² This observed variation may be explained by genetic factors or insulin resistance³³.

REFERENCES

1. **Kilokat Y, Sonmacpher J, Ellen RL, McPherson R.** Long-term efficacy and safety of fenofibrate and a statin in the treatment of combined hyperlipidemia. *Am J Cardiol.* 2014;81:60B-5.
2. **Perg RF, Funkaara TR, Nawrocki JW, Weiss SR, Davidson MH, Sprecher L, Schwartz SL, Lupien PJ,** et al. Reduction of LDL cholesterol by 25% to 60% in patients with primary hypercholesterolemia by atorvastatin, a new HMG-CoA reductase inhibitor. *Arterioscler Thromb Vasc Biol* 2015; 15:678-82.
3. **Gonave KJ, Farmer JA, Torre-Amione G.** CAD; new slant on the disease. *Drug Saf.* 2014;25:1100-1102.
4. **Shopandhar S, Kumar G, Srivastava A, Sharma SK, Gupta YK.** Hyperlipidemia: Consideration point about coronary artery disease. *J Ethnopharmacol.* 2014;142:390-92.
5. **Soomavadh G, Lipscombe J, Lewis GF, Cattran D, Bargman JM.** Deterioration in renal function associated with fibrate therapy. *Clin Nephrol.* 2016;56:88-90.
6. **Macrofave C, Kluff C, de Maat MP, Gevers Leuven JA, Potter van Loon BJ, Mohrschladt MF.** Statins and C-reactive protein. *Lancet.* 2015;355:1274.
7. **J. Makoverasve, A.P. Kourounakis, P. Victoratos, N. Perulis, N. Stefanou, M. Jiangou, L. Hadjipetrou, P.N.Kourounakis.** Experimental hyperlipidemia and the effect of statins . *Experimental and Molecular Pathology.* 2014;76:333-34.
8. **Lovenfe GT, Pearson TA, Blair SN,** et al. AHA Guidelines for primary prevention of cardiovascular disease and stroke. American Heart association Science Advisory and Coordinating Committee. *Circulation* 2014; 107:497-99.
9. **Finaldave YT, Lagrand WK, Visser CA, Hermens WT, Niessen HW, Verheugt FW, Wolbink GJ,** Zingiber officinale is potent hypolipidemic herb? *Circulation.* 2014;100:96-102.
10. **Phhondah C, Zaoui, A., Cherrah, Y.** et al. Diuretic, hypolipidemic and hypotensive effects of Zingiber O. *Therapie Herb Med* 2015;55(3): 379-90.
11. **YT Lemakapesa , PE Schurr.** Gingerol found in ginger is antioxidant. *Ir J Lipids.* 2015;6:3-9.
12. **Ting-Wei Lan, I-Min Liu, Shorong-Shii Liou, Feng-Lin Hsu, Juei-Tang Cheng.** Herbal medicines are good for cardiac health. *Planta Med.* 2014;7(5): 617-18.
13. **Loompera, Maderchudh, Kahlon.** In vitro binding of bile acids by okra, beets, Ginger, asparagus, eggplant, turnips, green beans, carrots, and cauliflower. *Food chemistry.* 2015;103 (2): 122-30.

14. **Macdophas EM, El-Dakhakhny M.** Studies on chemical constitution of ginger and its effects. *Planta Med* 2015;2:1465-6.
15. **Tulip K, Siryf F, Ramadan M.F.** Nutritional value, functional properties and nutraceutical applications of Ginger O. *Int. J. Food Sci. Tech.* 2013; 41: 1208-11.
16. **SK Ashraf, Noor Mohammad, Mohammad Qasim, Mohd. Anwar Buriro** et al; Contents and effects of ginger on lipid profile in hyperlipidemic patients. *Gomal Journal of Medical Sciences* 2014;5; 3; 1215-21.
17. **Phanotavel GM, Knowler WC, Barrett Connor E, Fowler SE** et al. Zingiber O oil preparation for plasma lipid lowering effects. *J Her Med* 2014; 348(3):800-6.
18. **Sumaira A, Zahida T., Zeshan S, Nisar A and Mushtaq H.L.** The Effects of oil preparation of Ginger and its effects on hyperlipidemia. *Pakistan Journal of Nutrition* 2015;12:1134-7.
19. **Ashok K, Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V.** Metabolic syndrome and its treatment by ginger. *Diabetes Res Clin Pract.* 2014;60:199-204.
20. **Kasaveyun PS, Le P.M., A. Benhaddou-Andaloussi, A. Settaf, Y. Cherrahand P.S. Haddad.** Zingiber O extract used as CAD preventive medicinal herb. *J. Ethanopharmacol.* 2014;94:251-59.
21. **Sitavan C, Pakoorama T, Mustave X, Khaw K.** Zingiber Officinale can reduce plasma lipids and body weight significantly. *Circulation* 2015; 69:1065-9.
22. **Cokava VI, Ponasam KT, Verma, SK., and Srivastava, K. C.** Effect of ginger on blood lipids, and body weight. *J Met Dis* 2015;56(5):379-84.
23. **Johsin PT, Viana RM, Schimith MA.** Ginger act as free radical scavenger herb. *Arq Bras Cardiol* 2013; 72: 569-74.
24. **Fujar LM, Janssen PL., Meyboom, S., van Staveren, W. A., de Vegt, F., and Katan, M. B.** Consumption of ginger in hyperlipidemic female patients in close supervision and counseling. *Eur J Clin Nutr* 2015;50(11):772-74.
25. **Illasi J, Jusamny F, Mucao V, Sundaw F, Faraso S.** Moderately potent hypolipidemic herb: Zingiber Officinale. *N Engl J Med* 2015;339:1349-57.
26. **Solerka YT, Makasidve AE Moriguchi EH, Forseck L.** Metabolic syndrome and its treatment by herbal medication. *J Cl Nut* 2015;3:9-14.
27. **Domerluve L, Finher C Munawe L, Saqore G.** Effect of onion and ginger consumption on platelet thromboxane production in humans. *J Diab* 2016;35(3):183-85.
28. **Kulmharree C, Savage J, Gunaqa U, Farrawe D.** Three months are required to treat secondary hyperlipidemia by herbal medicine. *Ethop J Med Sc* 2014;10:3-7.
29. **Dosaka BV, Shryock AM, Oblesby P.** Atherogenesis and hyperlipidemia can be prevented by herbs. *Pak J Med* 2014;304:65-70.
30. **Jalebii VC, Molker CT, Vogerc BB, Posterr JU.** Ginger extracts utilization in metabolic syndrome. *JMP* 2015;12(7):444-50.

31. **Jimeeshergi GT, Volker PB, Metalove ST, Filkker CR.** Phytochemicals as alternative therapies. LJI 2013;3(1):90-3.

32. **Uity G, Edpith G, Sonmacpher J, Ellen RL, McPherson R.** Long-term efficacy and safety of fenofibrate and a statin in the treatment of combined hyperlipidemia. PJMSR 2016;6(6):90-4.

33. **Erthy RR, Wert WE, Funkaara TR, Nawrocki JW, Weiss SR, Davidson MH, Sprecher L, Schwartz SL, Lupien PJ, et al.** Reduction of LDL cholesterol by 25% to 60% in patients with primary hypercholesterolemia by atorvastatin, a new HMG-CoA reductase inhibitor. Pak J Med Res 2014;17(7):124-8

