INT. J. BIOL. BIOTECH., 5 (1-2): 87-91, 2008.

ANTIATHEROGENIC EFFECT OF FRESH GINGER (*ZINGIBER OFFICINALE*) IN HYPERLIPIDEMIC RABBITS

Ghazala Yasmeen and Nazish Iqbal Khan

Department of Physiology, University of Karachi, Karachi 75270, Pakistan.

ABSTRACT

Hyperlipidemia is one of the major contributors to atherosclerosis and coronary heart disease. Non-pharmacological dietary therapy and exercise are the first line of treatment in Hyperlipidemia and several dietary components with such effects have been known. The present study has been undertaken to investigate the antiatherogenic effect of fresh grated ginger (*Zingiber Officinale*) in cholesterol fed rabbits with relation to its antihyperlipidemic activity. The mark rise in serum cholesterol, triglyceride and LDL-C in cholesterol fed rabbits was significantly reduced by the administration of fresh ginger ($p<0.05$) while a rise in plasma HDL-C was observed. These findings suggest that ginger has strong antihyperlipidemic effects and its dietary supplementation may be used effectively for the primary prevention trials against atherosclerosis and coronary heart disease.

Key words: Atherosclerosis, Cholesterol, HDL-C, Hyperlipidemia, LDL-C

INTRODUCTION

Cardiovascular Disease (CVD) is the leading cause of mortality in the developed world (Anonymous, 1993) and atherosclerosis, the principal cause of myocardial and cerebral infarctions. The most common and important cause of premature coronary artery disease is known to be lipid disorders. The role played by dyslipidemia in the genesis of coronary atherosclerosis is well established. More specifically, high levels of total cholesterol and low density lipoprotein (LDL) cholesterol, reduction in high density lipoprotein (HDL) cholesterol and increase in triglyceride (TG) levels predispose to coronary disease (Castelli, 1998). Substantial evidence from basic and clinical research suggests that atherosclerosis can be prevented and that its progression can be retarded. Reduction in the concentration of serum lipids, especially cholesterol, is a major goal in several primary and secondary prevention initiatives. Generally two options are available for the treatment of coronary artery disease (CAD) i.e. pharmacological and non pharmacological therapies. Non pharmacological approaches include phytotherapies. Plant derived products have been used for medicinal purposes for centuries. At present, it is estimated that about 80% of the world population relies on botanical preparations as medicines to meet their health needs (Stanely, 2001). Herbs and spices are generally considered safe and proved to be effective against certain ailments (Polasa and Nirmala, 2003).

Ginger (Urdu: Adrak) is an un-dried rhizome of the plant, *Zingiber Officinale* Roxoe (Zingiber Aceae), rhizomes have been described as aromatic, thick lobed and pale yellowish (Anonymous, 1976). It is one of the best known spices and frequently added in most of the dishes used as every day food in the East. It is a sweet, pungent, heating appetizer, an aphrodisiac and carminative (Fuhrman *et al*., 2000). It is extensively used in herbal medicine because of its action as rubifacient, anti-asthmatic and stimulant to the gastrointestinal tract (Kirtikar & Basu, 1975; Sharma *et al*., 1990). Fresh ginger contains 80.9% moisture, 2.3% protein, 0.9% fat, 1.2% minerals, 2.4% fiber and 12.3% carbohydrates (Govindarajan, 1982).. The minerals present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacin and vitamin C. The composition varies with the type, variety, agronomic conditions, curing methods, drying and storage conditions (Govindarajan, 1982). Gingerols were identified as the major active components in fresh ginger rhizome and gingerol [5-hydroxy-1-(4-hydroxy-3-methoxy phenyl) decan-3-one is the most abundant constituent in the gingerol series.

In traditional Chinese medicine, ginger is used to improve the flow of body fluids. It stimulates blood circulation throughout the body by powerful stimulatory effect on the heart muscle and by diluting blood (Shoji *et al.*, 1982). The improved circulation is believed to increase the cellular metabolic activity, thus contributing to the relief of cramps and tension. Tanabe *et al.* (1993) have showed that the active constituents in ginger reduced the blood pressure and decreased cardiac workload. Ginger reduced the formation of proinflammatory prostaglandins and thromboxane thus lowering the clotting ability of the blood (Bordia *et al*., 1997). Ginger is also known to possess antioxidant properties (Kikuzaki and Nakatani, 1993; Jayakumar *et al*., 1999). The objective of present study is to investigate the effect of fresh grated ginger (*Zingiber Officinale*) consumption on dietary hypercholesterolemia in experimental rabbits.

MATERIALS AND METHODS

Preparation of ginger: Fresh ginger was purchased on daily basis from the local market in Karachi, Pakistan and was finely chopped before mixing in the normal diet of rabbits.

Animals: Total 16 healthy female white rabbits were used in the study. The animals were two months old at the start of experiment and had a body weight 1.75 ± 0.5 Kg.

Study Design: The study was prospective analytical, done on experimental animals chosen randomly for different treatments.

Experimental Protocol: Initially all experimental animals were acclimatized in a well ventilated room for about seven days provided with free access to food and water. The body weights and other physical conditions were closely monitored throughout the study. After an over night fast, blood was drawn from the marginal ear vein and base line values for all parameters were checked. Rabbits were then divided into two groups of equal sizes.

Group I (n=8): Fed normal rabbit chow and served as a control.

Group II (n=8): Fed hypercholesterolemic diet (HCD) i.e. 1g butter fat / 100g of daily diet (modified from Moghadasian *et al*., 1999).

The above prescribed diet in both groups was continued for four weeks. Food intake was recorded periodically to avoid differences between groups in the amount of feed consumed. After four weeks: group II animals were maintained on HCD and in addition received fresh grated ginger 200mg/kg of body weight orally for four weeks (modified from Bhandari et al., 1998).

Blood collection: Blood samples were collected after every dietary modification using sterile disposable syringe and needle. The blood was transferred into glass tubes and centrifuged at 3000 rpm. Plasma was collected in appendorffs and was kept refrigerated until used. Body weights were measured simultaneously.

Biochemical Analysis: Plasma cholesterol and triglyceride levels were measured using kit (Clonital Italy), HDL-C levels were measured by dextran sulphate Mg (II) method, using kit (QCA, France). LDL-C concentration was determined by polyvinyl sulphate method using kit (QCA, France).

Statistical analysis: The data expressed as mean ± S.E.M (standard error of mean). and were analyzed by analysis of variance (ANOVA) followed by Student's *t*-test. A value of $P<0.05$ was chosen as the criteria of statistical significance.

RESULTS

Pathogenesis Of Hypercholesterolemia In Cholesterol Fed Rabbits: The plasma total cholesterol, triglycerides, LDL-C and HDL-C levels in rabbits fed on normal diet (group I) alone remained stable throughout the experimental period and no significant variations in their values were found (Table I).

Conversely in the HCD treated animals (group II); a rise in the total body weight (16%) and 5-fold increase in total plasma cholesterol was observed. A highly significant increase in serum triglyceride levels (4-fold) and lipoproteins both LDL-C and HDL-C (2 folds) was observed (Figure I & II).

Table I: The effect of ginger (*Zinigiber Officinale)* on lipid profile of hyper-lipidemic rabbits

PARAMETERS	CONTROL	HCD FED[1]	GINGER TREATED[2]
BW (gm)	1313 ± 65.5	1526.3 ± 52*	1432.5 ± 38.7^{NS}
TC (mg/dl)	22.68 ± 1.26	124.56 ± 3.61***	109.52 ± 1.10**
HDL-C (mg/dl)	22.28 ± 2.57	44.81 ± 3.42***	48.18 ± 1.41^{NS}
LDL-C (mg/dl)	15.58 ± 2.9	35.74 ± 2.07***	25.73 ± 1.02***
TG (mg/dl)	35.01 ± 1.14	152.23 ± 0.91***	130.55 ± 3.43**

Mean ± S.E.M. (n = 8); NS: Non-Significant, *** p < 0.005, ** p < 0.01, * p < 0.05; [1]As Compared with Control, [2]As Compared with HCD Fed

Effect of Fresh Ginger on Hypercholesterolemic Rabbits: Fresh ginger showed significant antihyperlipidemic action. It significantly (P<0.01) reduced the levels of plasma cholesterol, triglycerides ($p < 0.01$) and LDL – C ($p < 0.005$) as compared to hyperlipidemic rabbits. HDL-C levels were increased with ginger administration but the change was statistically non-significant. The reduction in total body weights of animals were also non-significant (Table I).

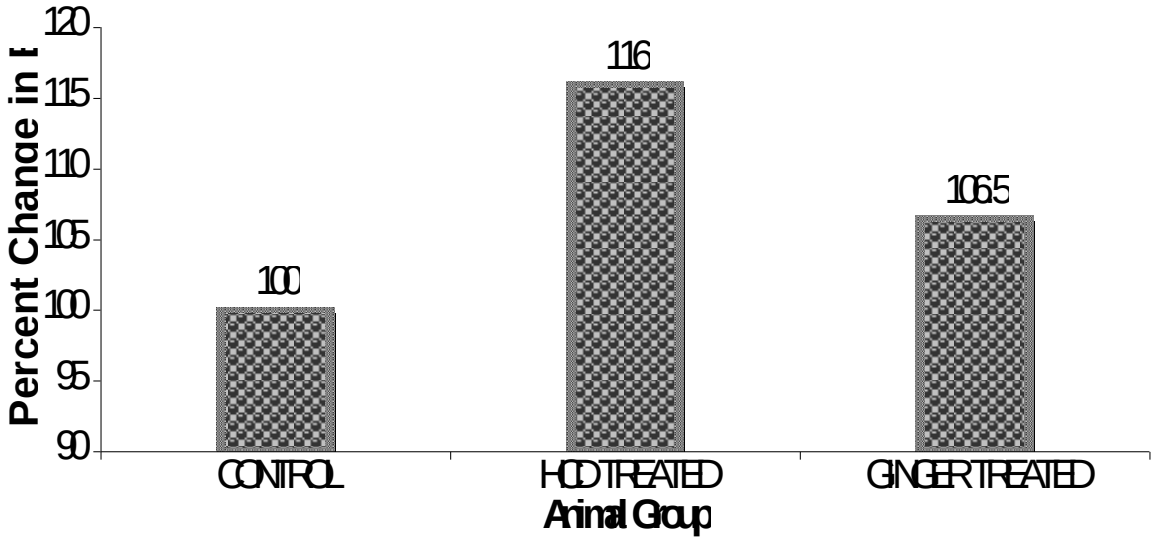

Fig. 1. Percent effect of ginger (*Zinigiber Officinale)* on body weights of experimental animals.

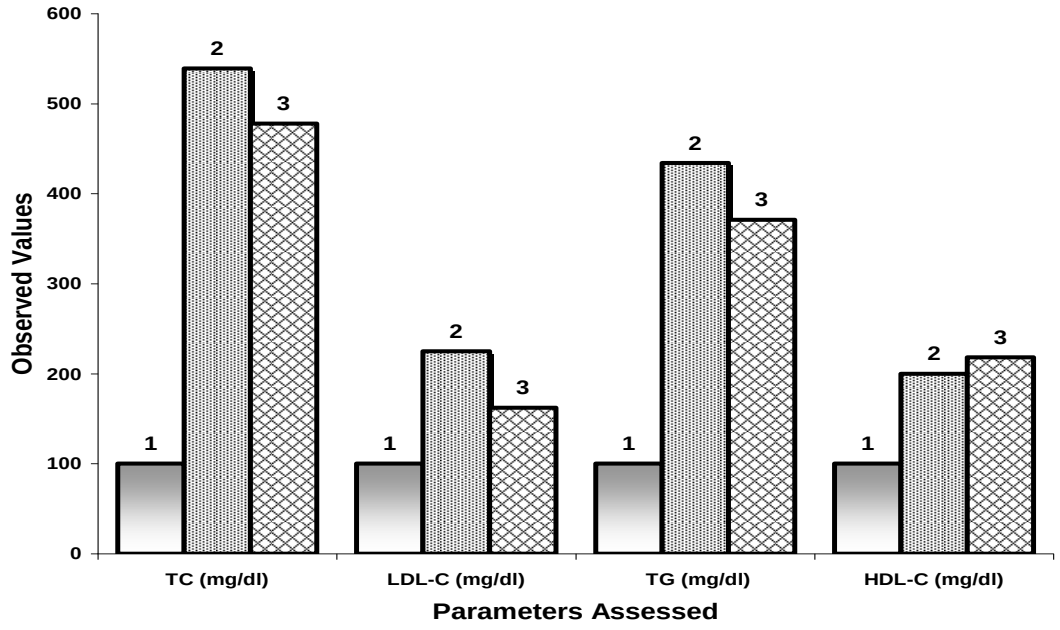

Fig. 2: Percent variations in lipid profile of experimental animals 1: Control, 2: HCD-Fed, 3: Ginger Treated

DISCUSSION

Atherosclerosis is a multi-factorial disease associated with different risk factors. Hypercholesterolemia is a major risk factor for atherosclerosis (Dominiczak, 1998; Sniderman *et al*., 1980), and reduction in plasma

cholesterol concentration by drug therapy has reduced cardiovascular incidence (Gotto and Grundy, 1999; Katerndahl and Lawler, 1999). In addition to diet, use of medicinal plants as a non-pharmacologic modality in preventing alteration in lipid metabolism has received wide attention world wide (Bhandari *et al.,* 1998).

Our study demonstrated that dietary consumption of raw ginger by rabbits significantly reduced the development of atherosclerosis along with an impressive reduction in the levels of plasma total cholesterol and LDL cholesterol in full agreements with Bhandari *et al*. (1998) and Sharma *et al*. (1996) who used ginger extracts. The hypolipidemic effect of ginger could have possibly resulted, at least in part, from the inhibition of cellular cholesterol biosynthesis observed after consumption of ginger extract (Fuhrman *et al.,* 2000). Reduced plasma cholesterol concentration is also associated with increased activity of the LDL receptor, which in turn leads to enhanced removal of LDL from plasma (Ness *et al*., 1996). These results are in agreement with previously reported data, showing that plant foods possess cholesterol-suppressive capacity (O'Brien and Reiser 1979).

There are several mechanisms by which plant products may lower cholesterol and triglyceride levels including increased removal of very low density lipoprotein (vLDL) by peripheral tissues as reported by Harris *et al*., (1984) Srinivasan and Sambaiah, (1991). This protective hypolipidemic effect of ginger may be due to enhanced activity of hepatic cholesterol-7 alpha hydroxylase enzyme (Giri *et al.,)*, which is a rate limiting enzyme in the bile acid biosynthesis. Increase activity of this enzyme stimulates the conversion of cholesterol to bile acid. Faecal excretion of cholesterol is significantly enhanced after *Zingiber* extract feeding (Sharma *et al*., 1996) and is suggestive of the fact that modulation of absorption was affected.

The positive effect of ginger on HDL-C also confirms its role in the protection against atherosclerosis. There are epidemiological studies that have demonstrated an inverse relationship of high density lipoprotein cholesterol to the incidence of coronary heart disease, the ultimate outcome of atherosclerosis (Castelli *et al*., 1986; Gordon *et al*., 1977; Gordon, 1985; Miller and Miller, 1975). The protective role of HDL-cholesterol in atherogenesis was shown in the Helsinki Heart Study (Frick *et al*., 1987). HDL is believed to mobilize cholesterol from developing an existing atheroma and transport it to the liver for excretion in the bile, thereby earning its designation as the good cholesterol (Ridker *et al*., 2001).

CONCLUSION

We concluded that consumption of fresh ginger may be prove to be beneficial against atherogenesis hence protective against CAD. It also may play role in lowering the levels of plasma cholesterol, triglycerides, LDL-C and improve the levels of HDL-C.

ACKNOWLEDGEMENT

The authors are extremely obliged to Prof. Mrs. Ruquiya Arshad, ex-Chairperson, Department of Physiology, University of Karachi for her generous cooperation in this study.

REFERENCES

Anonymous (1976). *Wealth of India*, Vol. 1, Council of Scientific and Industrial Research,New Dehli. Pp. 35 – 38.

Anonymous (1993). National centre for Health Statistics, Vital statistics of the United states. Washington, DC. US. Government Printing office. Public Health Service II.

Bordia, A., Verma, S.K. and Srivastava, K.C. (1997). Effect of ginger (*Zingiber officinale* Roscoe) and fenugreek on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. *Prostaglandins. Leukot Essent Fatty Acids*, 56: 379.

Bhandari U., J.N. Sharma and R. Zafar (1998). The protective action of ethanolic ginger (*Zingiber Oficinale*) extract in cholesterol-fed rabbits. *J. Ethnopharmacol*., 61:167-171.

Castelli, W.P. (1998). The new pathophysiology of coronary artery disease. *Am. J. Cardiol*., 82: 60 – 65.

Castelli, W.P., R.J. Garrison, P.W. Wilson, R.D. Abbott, S. Kalousdian and W.B. Kannel (1986). Incidence of Coronary Heart Disease and lipoprotein cholesterol levels. *J. Am. Med. Assoc*., 256: 2835 – 2838.

Dominiczak M. H. (1998). Hyperlipidemia and cardiovascular disease. *Curr. Opin. Lipidol*., 9: 609-611

Frick, M.E., O. Elo, K. Happa *et al*. (1987). Helsinki Heart Study: Primary prevention rial with gemfibrozil in middle aged men with dyslipidaemia. Safety of treatment changes in risk factors and Incidence of Coronary Heart Disease. *N. Engl. J. Md*., 317: 1237 – 1245

Fuhrman B., M. Rosenblat, T. Hayek, R. Coleman and M. Aviram (2000). Ginger Etract Consumption Reduces Plasma Cholesterol, Inhibits LDL Oxidation and Attenuates Development of Atherosclerosis in Atherosclerotic, Apolipoprotein E-Deficient Mice. *J. of Nutrition*, 130: 1124-1131.

Giri, J., T.K.S. Devi and S. Meerarani (1984). Effect of ginger on serum cholesterol levels. *Indian J. Nutrition and Dietetics*, 21: 433 – 437.

Gordon, D.J. (1985). (For the lipid research clinics coronary primary prevention trials investigations) Plasma High Density Lipoprotein Cholesterol and Coronary Heart Disease in Hypercholesterolemic man. *Circulation*, 72: 111 – 185.

Gordon, T., W.P. Castelli, M.C. Hjortland, W.B. Kannel, and T.R. Dawber (1977). High Density Lipoprotein as a Protective factor against Coronary Heart Disease. The Framingham study. *Am. J. Med*., 62: 707 – 714

Gotto A. M., Jr and S. Grundy (1999). M. Lowering LDL cholesterol: questions from recent meta-analyses and subset analyses of clinical trial Data Issues from the interdisciplinary council on reducing the risk for coronary heart disease, ninth council meeting. *Circulation*, 99: E1-E7

Govindarajan, V.S. (1982), Ginger: Chemistry, technology and quality evaluation (Part I). *Crit Rev Food Sci Nutr*., 17: 1.

Gujaral, S., H. Bhumra and M. Swaroop (1978). Effect of ginger oleoresin on serum and hepatic cholesterol levels in cholesterol fed rats. *Nutrition Reports Internationale*, 17: 183–187.

Harris, W.S., W.E. Conner, D.R. Illingworth and D.M. Foster (1984). The mechanism of the hypotriglyceridaemic effect of dietary omega – 3 fatty acids in man. *Clin. Res*., 32: 560.

Jayakumar, S.M. Nalini *et al*. (1999). Antioxidant activity of ginger (Zingiber officinale Roscoe.) in rats fed a high fat diet. *Med Sci Res*., 27: 341.

Katerndahl D. A., and W.R. Lawler (1999). Variability in meta-analytic results concerning the value of cholesterol reduction in coronary heart disease: a mata-meta-analysis. *Am.J. Epidemiol*., 149: 29-441

Kikuzaki, H. and N. Nakatani (1993) Antioxidant effect of some ginger constituents. *J Food Sci*., 58: 1407.

Kirtikar, K.R. and B.D. Basu (1975). *Indian Medicinal Plants*, Vol 9, 2nd Ed. In: Singh B., Singh, M.P., (Eds.), Dehradun, India, pp. 2435 – 2439.

Miller, G., and N.E. Miller (1975), Plasma High Density Lipoprotein Concentration and Development of Ischemic *Heart disease. Lancet*, 1: 16 – 19

Moghadasian, M.H., B.M. Manus, D.V. Godin, B. Rodrigues and J.J. Frohlich (1999). Proatherogenic and Antiatherogenic effects of probucol and phytosterols in polipoprotein E-deficient mice: possible mechanism of action. *Circulation*, 99: 1733 – 1739.

Ness G. C., Zhao Z., and D. Lopez (1996). Inhibitor of cholesterol biosynthesis increase hepatic low density lipoprotein receptor protein degradation. *Arch. Biochem Biophys*. 325: 242-248.

O'Brien B.C. and R. Reiser (1979). Comparative effects of purified and human-type diets on cholesterol metabolism in the rat. *J. Nutr*., 109: 98-104

Polasa, K. and K. Nirmala (2003). Ginger its role in Xenobiotic metabolism. *ICMR Bulletin*, 33 (6).

Ridker P.M., J. Genest and P. Libby (2001). *Risk factors for atherosclerosis disease. Heart Disease* ed.,6. Philadelphia, WB Saunders, P. 1010.

Sharma I., D. Gusain and V.P. Dixit (1996). Hypolipidaemic and antiatherosclerotic effects of Zingiber Officinale in cholesterol fed rabbits. *Phyto. Res*., 10: 517-518

Sharma, I., M. Varma and V.P. Dixit (1990). Hypolipidaemic effect of Panchcole, an ayurvedic remedy in rabbits. *Int. J. Crude Drug. Res*., 2: 33–38.

Shoji, N.,. A. Iwasa, T. Jakemoto, Y. Ishida and Y. Ohizuma (1982). Cardiotonic principle of ginger (*Zinigiber officinale* Roscoe). *J Pharm Sci*., 7: 1174.

Sniderman A., S. Shapiro D. Marpole D. Skinner B. Teng and P. Kwiterovick (1980). Association of coronary atherosclerosis with hyperapobetalipoproteinemia: increased protein but normal cholesterol levels in human plasma low density beta lipoproteins. *Proc. Natl. Acad. Sci*., USA. 77: 604-608

Srinivasan K., and K. Sambaiah (1991). The effect of spices on cholesterol 7 alpha-hydroxylase activity and on serum and hepatic cholesterol levels in the rat. *Int. J. Vitam. Nutr. Res*., 61: 363-369

Stanely J. and Swierzewski (2001). A review on naturopathic medicine, Botanic/herbal medicine. Online: http://www.alternativemedicinechannel.com/naturopathic/botanical.shtml

Tanabe, M., Y.D. Chen, K. Saits and Y. Kano (1993). Cholesterol biosynthesis inhibitory component from *Zingiber officinale* Roscoe. *Chem Pharm Bull.,* 41: 710.

(*Accepted for publication April 2008*)