Protective effect of ginger, *Zingiber officinale* Rosc on experimental atherosclerosis in rabbits

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The effects of air dried ginger powder (0.1 g/kg body weight, po, for 75 days) were studied on experimentally induced atherosclerosis in rabbits by cholesterol feeding (0.3 g/kg body weight, po). Cholesterol feeding for 75 days lead to distinct development of atheroma in the aorta and coronary arteries of the rabbits and this was significantly inhibited by about 50% following ginger administration. There was distinct decrease in lipid peroxidation and enhancement of fibrinolytic activity in ginger treated animals. However, ginger did not lower blood lipids to any significant extent. This distinct protection from the development of atherosclerosis by ginger is probably because of its free radical scavenging, prostaglandin inhibitory and fibrinolysis enhancing properties.

Keywords: Atherosclerosis, Antioxidant, Serum Lipids, Fibrinolysis, Prostaglandins

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Ginger (*Zingiber officinale* Rosc) is a popular food spice and occupies an important place in Ayurvedic and Graeco-Arabic system of medicine, where it is commonly used as carminative, digestive and to treat chronic rheumatism and gout[1][2]. Ginger is a dual inhibitor of prostaglandins[3] and possesses antihistaminic and antioxidant factors[4].

Ginger has been evaluated for its effects on blood lipids[5], platelet aggregation[6] and fibrinolysis[7]. However, its effect on experimental atherosclerosis has not been reported so far. Hence, the present study has been undertaken to investigate the effect of air dried whole ginger powder on cholesterol induced experimental atherosclerosis in rabbits.

After approval from Institutional Animal Ethics Committee, 30 Indian albino rabbits weighing between 1 - 1.5 kg body weight obtained from National Institute of Nutrition, Hyderabad were divided in to three groups of 10 each, and fed a common stock diet (bran and fresh vegetables). Except for the control (Group I), all other groups received cholesterol (Merck) 0.3 g/kg body weight daily suspended in 5 ml of milk for 75 days. While group II served as the atheroma control, animals in group III were fed ginger (0.1 g/kg body weight/day) in the form of air dried ginger powder together with cholesterol mixed with 5 ml milk.

The blood samples were collected carefully by puncturing the right ventricle in unanaesthetised animals with a 20 gauge needle after 75 days i.e. at the end of the study. Blood samples were analyzed for serum cholesterol[9], triglycerides[10] and high density lipoprotein cholesterol (HDL-C)[11] by enzymatic method using standard diagnostic kits. (Reckon Diagnostics Ltd.-Baroda). Fibrinolytic activity was determined as per Buckell and Elliot[12], it is based on the principle that the euglobin fraction of the plasma is clotted with thrombin and the time taken for clot lysis is estimated and expressed in units by multiplying the reciprocal of the lysis time in min by 10,000. Lipid peroxidation was assessed by employing lipoprotein oxidation susceptibility (LOS) test[13]. The animals were killed at the end of 75 days and autopsy samples of aorta and coronary arteries were examined for atherosclerosis. The sections were examined by two pathologists who were unaware of experimental protocol. Atheroma was graded macroscopically by mean grateful count percent[14] and microscopically on a 0 – 4 scale[15].

Results are given in Table 1. Feeding cholesterol (0.3 g/kg body weight) daily to rabbits raised their serum cholesterol levels by 10 folds over a period of 75 days. Simultaneous administration of the dried ginger powder together with cholesterol retarded this increase only non-significantly. Serum triglycerides and HDL-C levels were not at all influenced by ginger administration. Fibrinolytic activity decreased by 36% in the group II (P < 0.001). Administration of ginger not only prevented this cholesterol induced fall but actually increased the fibrinolytic activity by 13%
over the control and 76% over the group II ($P < 0.001$). Interestingly, the rise in LOS by cholesterol administration was significantly decreased ($P < 0.001$) by ginger administration.

The macroscopic grading (% mean graticule count) of atherosclerotic changes in the aortas of group II rabbits was about 60.9%. On the other hand, in group III it was only 32%. Microscopically the mean grading in aorta and coronary arteries were $2.3 \pm 0.31$ and $2.6 \pm 0.3$ respectively in the group II, while in the group III it was only $1.4 \pm 0.2$ and $1.4 \pm 0.97$ in the aorta and coronary arteries respectively. Thus ginger appeared to cause a significant ($P < 0.001$) reduction in atheroma, induced by cholesterol both in aorta and coronary arteries.

As expected, there was a marked rise in serum cholesterol in the group II rabbits. Although the ginger treated group had lower values; these were still high enough to be atherogenic, being approximately seven and half times higher than in the normal control. Inspite of this, there was a significant decrease in the extent of atherosclerosis observed in the aorta and the coronary arteries of group III rabbits. The specimens of aorta in the animals of group II were practically laden with raised atheromatous plaques with hemorrhage, thrombus formation and areas of infarction in the myocardium, while the vessel walls of normal group was almost smooth and healthy. The group III rabbits showed marked decrease in the area of involvement in the aorta. Mean graticule count was only half of that observed in cholesterol fed animals. Microscopically also there was significant ($P < 0.01$) decrease in the development of atheroma in aorta and coronary arteries of ginger treated group as compared to the cholesterol fed control. Obviously, ginger did not prevent hypercholesterolemia to an extent that is required to stop the development of atherosclerosis. It probably protected the vessel wall against injury and lipid invasion by some processes other than simply lowering the blood cholesterol.

Formation of oxidized LDL is an important step in the development of atherosclerosis and supplementation of diet with various compounds that have antioxidant properties before the development of vascular disease inhibited atherogenic process. Ginger is also known to have antioxidant effect and this property has been observed in an alcoholic – extract containing shogaol and zingerone. Interestingly in the present study, ginger also demonstrated significant antioxidant property in terms of inhibiting lipid peroxidation. It not only checked the lipoprotein oxidation susceptibility (LOS) significantly ($P < 0.001$) when administered along with cholesterol but also kept it low below the baseline.

Ginger is a dual inhibitor—inhbiting cyclooxygenase and lipoxygenase activities. It strongly inhibits prostaglandin synthesis and some components isolated from ginger were found to be even stronger inhibitors of prostaglandin synthesis than indomethacin. Moreover, it not only inhibits thromboxane synthetase but also raises levels of prostacyclin without a concomitant rise in PGE 2 or PGF 2 alpha. Its platelet aggregation inhibitory property has been observed in healthy individuals and patients with coronary artery disease. Recently, it has also been reported to enhance fibrinolysis.

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<th>Table 1—Effect of ginger (0.1g/kg body weight, po for 75 days) on blood lipids, fibrinolysis and lipoprotein oxidation susceptibility (LOS) in cholesterol-fed rabbits</th>
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<td>Stock diet (Group I)</td>
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<tr>
<td>Serum Cholesterol</td>
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<td>(mg/dl)</td>
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<td>Triglyceride</td>
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<td>HDL - Cholesterol</td>
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<td>Fibrinolytic activity</td>
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<td>(in units)</td>
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<td>LOS (nmol malondialdehyde/mg HDL-C)</td>
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*P values : \< 0.001 : *gr II vs gr I ; ** gr III vs gr II \ns.e. *gr II vs gr I ; ** gr III vs gr II ; * gr III vs gr I \
\< 0.01 : *gr III vs gr I
Ginger contains several classes of compounds. The chemical composition (% of dried ginger is as follows\(^7\): starch 40-60, proteins 10, fats 10, fibres 5, inorganic material 6, residual moisture 10 and essential oil (oleoresin) 1-4. The essential oil of ginger contains various terpins and sesquiterpenes. The predominant sesquiterpenes is zingiberene. The characteristic pungent odour is due to its oleoresin content which is an oily liquid containing oxymethyl phenols like shogaol, zingerone and gingerol etc\(^7\). It therefore has high phenolic content (505 ± 44 mg/100 g). The total flavonoids content (such as quercetin, Kaemferol, luteolin and pelargonidim) is however low (38 ± 3 mg/100 g)\(^6\). Phenolic compounds and flavonoids are antioxidants and have been shown to be potent inhibitor of LDL oxidation \textit{in vitro} and thereby protect against the development of atherosclerosis\(^27\).

In conclusion, ginger has significant protective effect against experimentally induced atherosclerosis in rabbits inspite of high serum cholesterol. This is probably because of its potent antioxidant and fibrinolytic enhancing properties and strong prostaglandin inhibitory and prostacycline enhancing effects. The clinical potential of such a safe and widely used dietary condiment against atherosclerosis warrants further study.

References