

Shogaols exhibit cardiodepressant activity at low doses and cardiostimulant properties at higher doses

Abstract

Herbal medicine ginger has proved itself as one of the potent antihyperlipidemic and antiobesity herb with least adverse effects. We did try to compare its hypolipidemic effects with placebo effects when used in mild to moderate hyperlipidemic patients. It was placebo-controlled single blind research study. Research was conducted at National hospital, Lahore, from July to November 2016. Consent was taken from sixty hyperlipidemic patients age range from 25 to 60 years. Both gender male and female patients were enrolled. Patients were randomly divided in two groups, 30 patients were on drug ginger pasted-powder advised to take 5 grams in divided doses with their normal diet for the period of three months. Thirty patients were on placebo pasted-wheat powder, with same color as of ginger powder, advised to take 5 grams in divided doses with their normal diet for the period of three 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. Three 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 body weight decrease was non-significant when analyzed biostatistically.

Volume 12 Issue 3 - 2019

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Received: May 28, 2019 | **Published:** June 21, 2019

Introduction

There is proved link between serum lipids with coronary heart disease. In specific ethnic population, 1% percent increased lipids especially LDL-cholesterol in plasma increases 2% risk for development of CAD.¹⁻⁴ Other risk factors for CAD include diabetes mellitus, cigarette smoking, hypertension and hyperthyroidism.⁵ Allopathic regimen for treating hyperlipidemia include use of statins, fibrates, niacin and resins.⁶⁻⁸ But all these medicines have low patient compliance due to their adverse effects. Medicinal herbs like ginger has been shown to exhibit antioxidant effects.^{9,10} Many research studies indicate that gingerols and the related shogaols exhibit cardiodepressant activity at low doses and cardiostimulant properties at higher doses. Ginger is obtained from rhizomes of *Zingiber officinale*. The plant belongs to Zingiberaceae family. Since ancient times, it has been widely used as a medicinal herb and spice. Gingerol is the active constituent of fresh ginger. Chemically, gingerol is a relative of capsaicin and piperine, the compounds which give chilli peppers and black pepper their respective spiciness. It is normally found as pungent yellow oil, but also can form a low-melting crystalline solid. Because of containing phytochemical ingredients and as a beneficial therapeutic agent, *Zingiber officinale* has been contributing pivotal roles against a broad range of diseases like dyslipidemia, asthma, diabetes, stroke, and constipation etc, etc.etc. It is reported that 100,000 tons of gingers are annually produced, and 80% of this is produced in China. Both (6)-shogaol and (6)-gingerol, and the gingerdiones, are found in Zingiberaceae and are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis.¹¹⁻¹⁴ 6-gingerol appears to be the antioxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress.¹⁵⁻¹⁷ Ginger oil has dominative protective effects on DNA damage induced by free radicals ie, H₂O₂. Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant.¹⁸ It is well understood in various studies that there are limitations to use phytochemicals due to their broad canvas of pharmacological actions

in human population.¹⁹ Many studies are going to warn therapists about good compliance of medicinal herbs but with keeping in mind, these herb's potent human body's vital organs humulatory effects.²⁰

Material/patients and methods

Sixty patients with high lipid profile were included in the research work conducted at National hospital Lahore from July to November 2016. The study was single blind placebo controlled. Duration of study was four weeks. Already explained and written consent was taken from all participants. Research work on human beings and its objectives were approved from Ethical Committee of the Hospital. Exclusion criteria was alcoholics, chain smokers, patients suffering from any liver disease, renal disease, peptic ulcer, already on vital medicines for treating vital organs of the body. Gender of participants was both male and female patients, age range from 25 to 60 years. Patients were divided in two groups, i.e.; group-I was advised to take 5 grams of ginger in divided doses as covenant everyday for the period of 12 weeks. Group-2 was on placebo therapy. 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. Data were expressed as the mean±SD and paired "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was considered as non-significance and P<0.001 was considered as highly significant change in the results.

Results

In three 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-90	Change in mg/dl	SS/p-value
LDL-c	202.21±1.88	187.72± 1.98	14.49	<0.01
T-C	233.11±1.53	198.44±1.23	34.67	<0.001
Body weight	76.01±2.66	72.80±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-90	Change in mg/dl	SS/p-value
LDL-c	143.25±1.99	142.98±1.98	0.18	>0.05
TC	190.47±2.71	188.99±1.76	0.77	>0.05
Body weight	76.73±2.19	76.56±1.91	0.22	>0.05

KEY: ± 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

Various epidemiological studies have shown the prevalence of the co-existence of hypertension and dyslipidemia, in the range of 15 to 31%. The co-existence of the two risk factors has more than an additive adverse impact on the vascular endothelium, which results in enhanced atherosclerosis, leading to CVD. 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 al.,²¹ 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 al.,²² 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 ZO (zingiber officinale) for 8 weeks. These results augment our research study results. Johsin PT et al.,²³ have mentioned mechanism of action of ginger that it scavenges free radicals in various tissues leading to decreased damage to vascular endothelium. Fajar LM et al.,²⁴ 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 al.,²⁵ proved that in herbal medications, ZO is one of the potent hypolipidemic herb. Solarka YT et al.,²⁶ 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 al.,²⁷ 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 al.,²⁸ 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 al.,²⁹ 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 al.,³⁰ 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.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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