Study of hypolipidaemic and antiatherogenic activity of *Zingiber Officinale Roscoe* (Ginger) in adult albino rats

Nagaraj B Malipatil[1], S Manjunath[2],Shruthi DP[3]

[1]Department of Pharmacology Srinivas Institute of Medical Sciences and Research Centre, Surathkal, Mangalore[1]
[2]Department of Pharmacology S. Nijalingappa Medical College, Bagalkot
[3]Department of Orthodontics and Dentofacial Orthopaedics, Dayanand Sagar College of Dental Sciences, Bangalore

Abstract

Background: Hyperlipidemia is the greatest risk factor of coronary heart disease. Currently available hypolipidemic drugs have been associated with number of side effects. Herbal treatment for hyperlipidemia has no side effects and is relatively cheap and locally available. Literature claims that Gingiber Officinale Roscoe (Ginger) can reduce the blood lipid levels. Aim: Present study evaluated the hypolipidaemic and antiatherogenic activity of Gingiber Officinale Roscoe (Ginger) in adult albino rats. Material and methods: Hypolipidaemic and Antiatherogenic activity of aqueous extract of ginger at the dose of 500 mg/kg given orally (p.o) was compared with Atorvastatin given at the dose of 7 mg/kg orally (p.o) in high fat fed adult albino rats. Results: Aqueous extract of ginger reduced the serum levels of total cholesterol (99.1±1.47 vs 77.5±4.7), LDL (50.13±3.92 vs 29.0±3.92), triglycerides levels (83.6±1.88 vs 57.03±3.26) and increased serum HDL levels (25.7±1.5 vs 37.05±1.4). Conclusion: Ginger also significantly reduced the atherogenic index (2.91±0.23 vs 1.11±0.16).

Key words: Hypolipidaemia, Antiatherosis, Zingiber Officinale Roscoe, Ginger, Atherogenic Index.

Introduction

Hyperlipidaemia is one of the major cause of various cardiovascular and central nervous system disorders. Both genetic disorders and diets rich in saturated fat and cholesterol, contribute to the elevated lipid levels. It is a major cause of atherosclerosis and atherosclerosis associated conditions such as coronary heart disease, ischaemic cerebrovascular diseases and peripheral vascular diseases[1]. Atherosclerosis is an age related disease, widely prevalent in industrialized countries, affecting primarily the intima of large and medium sized arteries and is characterized by fibro-fatty plaques or atheromas[2]. The exact cause of atherosclerosis is not known, although several factors have been blamed in the pathogenesis of atherosclerosis. A lot of experimental and epidemiological evidence suggest, a relationship between atherosclerosis and elevated levels of plasma lipids. Recent work has incriminated, folic acid deficiency leading to elevated plasma levels of homocysteine and chronic infection with Chlamydia pneumonia in the pathogenesis[3]. The importance of traditional system of medicine and of certain traditional medical practices has now been recognized all over the world. It is well known that India, the cradle of ancient civilization had acquired a high degree of knowledge, on the nutritional and medicinal properties of large number of plant products. The common man in India used many common plants or plant products as household remedies. Zingiber officinale Roscoe (Ginger) is widely used spice and functional food. Ginger being aromatic and pleasantly pungent, is commonly

Address for Correspondence

Dr. Nagaraj B Malipatil, Assistant Professor of Pharmacology

Srinivas Institute of Medical Sciences and Research Centre, Surathakal, Mangalore, Karnataka

E-mail:- nagaraj.malipatil@gmail.com

used in the preparation of condiments, curries and ginger bread. Ginger is extremely valuable in dyspepsia, flatulence, colic, spasms and other painful affection of stomach [4]. The pharmacological effects of Zingiber officinale in animal models have been reported to have hypolipidemic[5] and anti-inflammatory effects[6]. Other pharmacological actions of ginger and compounds isolated therefrom include antioxidant[7], hypoglycemic[8], analgesic[8], antiplatlelet[9], antiemetic[10], antithrombotic[11], anti-tumorigenic[12], radio protective[13], antimicrobial[14], antifungal[14] actions. Considering the vast variety of actions, this study has been done to evaluate the effect of Zingiber officinale powder on serum lipids and atherogenesis in high fat fed adult albino rats.

Materials and Methods

Experimental herb: Zingiber officinale Roscoe (Ginger). Ginger for experimental purpose was dried and aqueous extract of the same was prepared. Dose administered was 500mg/kg[5], orally (p.o)

Atorvastatin: Crude powder of Atorvastatin obtained from Biocon Pharmaceuticals, Bangalore. Human dose 80 mg, which is 7.2 mg/kg in rats[19].

High Fat Diet: Mixture of coconut oil (from Marico Industries Ltd, Mumbai) and vanaspathi ghee (from Ruchi industries, Mumbai) procured from market.

Vehicle: Normal saline (0.9%).

Experimental animals used in the study

Study was carried out in healthy albino rats of Wistar strain (Rattus norvegicus) procured from the Central Animal House, Mahadevappa Rampure Medical College, Gulbarga, Karnataka. Animals used were of either sex weighing between 150-200 gms. They were housed in polypropylene cages in room where the congenial temperature 27°C ±1°C and 12 hrs light and dark cycles were maintained. The animals were allowed to acclimatize to the environment for 7 days before the experiment and supplied with a standard pellet diet and water in sufficient quantity, as per the recommendation of CPCSEA (Committee for the purpose of control and supervision of experiment on animals) for laboratory animal facilities.

Experimental Design

For the experiment, the animals were weighed, recorded, numbered and randomly divided into 6 groups of 5 animals each.

Group-A: Normal Control Group (Received normal saline 10 ml/kg body weight/ day)

Group-B: Received Atorvastatin and normal diet

Group-C: Received Zingiber Officinale and normal diet

Group-D: Received high fat diet only Group-E: Received high fat diet and Atorvastatin.

Group-F: Received high fat diet and Zingiber Officinale

All the animals used for the experiment were kept under observation for daily food intake. The drugs were administered to the animals in the doses mentioned by means of an intra-gastric feeding tube. Duration of study was 8 weeks. At the end of the 8th week, all the animals were taken group wise and blood collected from each of them for assessing the various parameters of lipid profile.

Collection of blood: At the end of 8 weeksblood was collected by retro-orbital sinus puncture using capillary tube under mild ether anesthesia.

Biochemical Estimation: After overnight fasting 2ml blood was collected in plain bulbs without anticoagulant, from orbital sinuses[20] of all animals. Plain bulbs containing blood are kept at room temperature for 30-45 minutes for serum separation. After separation of serum from blood, the biochemical parameters (total cholesterol, serum LDL, Triglycerides and HDL) were estimated.

Results

The study was carried out to evaluate the effects of Zingiber Officinale Roscoe, on serum lipids and atherogenesis in adult albino rats fed with high fat diet, as compared to that of a standard hypolipidaemic agent, Atorvastatin. The results obtained are summarized in tables. Results are reported as Mean ± SEM (standard error of mean) of 5 animals at a time from each group. The statistical significance between groups was analyzed by using one-way ANOVA, followed by Dunnet's multiple comparison test. The significance was expressed by 'p" values, as mentioned in the table. 'p' values of <0.01was considered significant.

Total serum cholesterol: Table 1 Shows total serum cholesterol level in different groups. The total cholesterol level of rat treated with Z. Officinale extract (Group C), at the end of 8th week, was 80.4±5.75 ($p<0.01$).

Table 1. Total serum cholesterol (in mg/dl) results expressed in Mean ± SEM (n=5)

Group		Results (8th week of experiment)
Group A	Normal control	88.7±5.52
Group B	Atorvastatin	61.2±2.4
Group C	Z. Officinale extract	80.4±5.5[a]
Group D	High fat diet	267.0±7.56[a]
Group E	High fat Diet + Atorvastatin	77.5±4.7[b]
Group F	High fat diet + *Z. Officinale* extract	99.1±1.47[b]

One way ANOVA, p <0.01, [a]: p <0.01 when compared with normal control group, [b]:p<0.01 when compared with hyperlipidaemic control group (ANOVA followed by Dunnet's multiple comparison test). From the results obtained, it is clear that, as compared to group A i.e. control, group C has shown decreased level of serum cholesterol i.e. hypolipidaemic activity. When compared to group D, F and A, group F has shown decreased level of Sr. cholesterol, than group D but slightly more than group A, i.e antihyperlipidaemic activity. When compared group A, E and F, group E has shown significant hypolipidaemic activity.

Serum Triglyceride: Table-2 shows serum triglyceride level in different groups.

Table 2. Serum Triglyceride level (mg/dl) results expressed in Mean ± SEM (n=5)

Group		Results (8th week of experiment)
Group A	Normal control	66.76±3.02
Group B	Atorvastatin	54.03±1.89
Group C	Z. Officinale	57.5±1.39[a]
Group D	High fat diet	218.48±9.19[a]
Group E	High fat Diet + Atorvastatin	57.03±3.26[b]
Group F	High fat diet + *Z. Officinale*	83.6±1.88[b]

One way ANOVA, p <0.01, [a]: p <0.01 when compared with normal control group, [b]:p<0.01 when compared with hyperlipidaemic control group (ANOVA followed by Dunnet's multiple comparison test). From the results obtained, it is evident that, as compared to group A i.e. control, group C has shown decreased level of serum triglyceride i.e. hypolipidaemic activity. When compared group D, F and A; group F has shown decreased level of serum triglyceride, than group D but slightly more than group A i.e. antihyperlipidaemic activity. When compared group A, E and F; group E has shown significant hypolipidaemic activity.

Serum LDL: Table-3 Shows serum LDL level in different groups.

Table 3. Serum LDL level (mg/dl) results expressed in Mean ± SEM (n=5)

Group		Results (8th week of experiment)
Group A	Normal control	48.98±2.96
Group B	Atorvastatin	29.2±1.31
Group C	Z. Officinale	32.70±1.21[a]
Group D	High fat diet	207.25±7.81[a]
Group E	High fat Diet + Atorvastatin	29.0±3.92[b]
Group F	High fat diet + *Z. Officinale*	50.13±3.92[b]

One way ANOVA, p <0.01, [a]: p <0.01 when compared with normal control group , [b]:p<0.01 when compared with hyperlipidaemic control group (ANOVA followed by Dunnet's multiple comparison test). Above result shows that, as compared to group A i.e. control group, group C has decreased level of serum LDL i.e. hypolipidaemic activity. When compared group D, F and A, group F has shown decreased level of serum LDL than group D but slightly more than group A i.e. antihyperlipidaemic activity. As compared to group A, E and F; group E has displayed significant hypolipidaemic activity.

Serum HDL: Table 4: Shows serum HDL levels in different groups.

Table 4. Serum HDL level (mg/dl) results expressed in Mean ± SEM (n=5)

Group		Results (8th week of experiment)
Group A	Normal control	26.35±1.68
Group B	Atorvastatin	36.8±1.7
Group C	Z. Officinale	35.3±1.28[a]
Group D	High fat diet	16.0±0.19[a]
Group E	High fat Diet + Atorvastatin	37.05±1.4[b]

Group F	High fat diet + Z. Officinale	25.7±1.5[b]

One way ANOVA, p <0.01, [a]: p <0.01 when compared with normal control group, [b]:p<0.01 when compared with hyperlipidaemic control group (ANOVA followed by Dunnet's multiple comparison test). From the above result it is evident that, as compared to group A, i.e. control, group C has shown increased level of Serum HDL. When compared group d, F and A, group F has shown increased level of Serum HDL, then group D but slightly less than group A. When compared, Group A, E and F; group E has shown significant rise in serum HDL slightly more than group F.

Atherogenic Index: Table 6 shows atherogenic index in different groups

The atherogenic index[21] was calculated using the formula and is another way of identifying dyslipidemia and risk of complications arising out of it.

Total Cholesterol — HDL

Atherogenic Index =

HDL

Table 5. Atherogenic index (as ratio) results expressed in Mean ±SEM (n=5)

Group		Results (8th week of experiment)
Group A	Normal control	2.42±0.20
Group B	Atorvastatin	1.06±0.12
Group C	Z. Officinale	1.27±0.04[a]
Group D	High fat	15.92±1.06[a]
Group E	High fat + Atorvastatin	1.11±0.16[b]
Group F	High fat + *Z. Officinale*	2.91±0.23[b]

One way ANOVA, p <0.01, [a]: p <0.01 when compared with normal control group, [b]:p<0.01 when compared with hyperlipidaemic control group (ANOVA followed by Dunnet's multiple comparison test). The above results show that, as compared to group A, i.e. control, group C has shown low atherogenic index. When compared to group D, F and A; group F has shown low atherogenic index than group D, but slightly more than group A. As compared to group

Table 6. Effect of aqueous extract of Z. Officinale on serum lipids at the end of 8th week of experiment

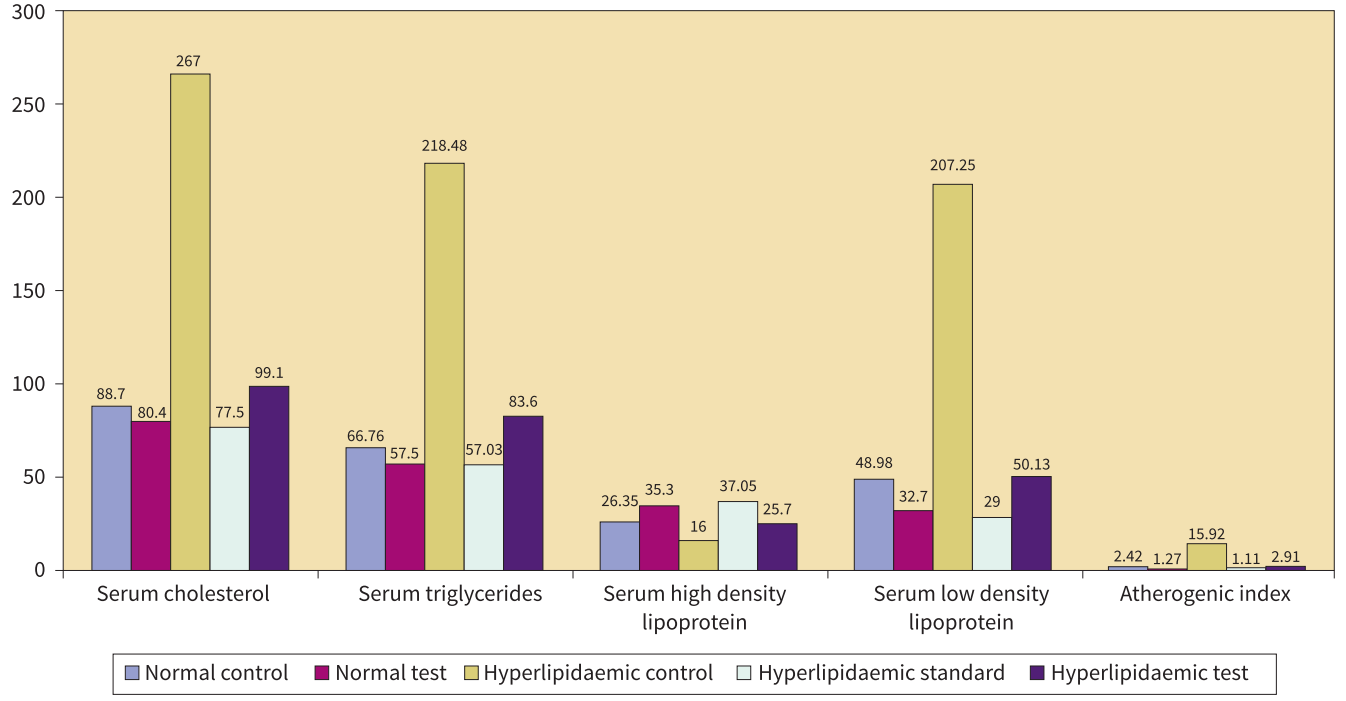
Group	Drug	Dose Oral, Single Dose	Test Result (Mean±SEM) in mg/dl)				Test Result (Mean± SEM) (in ratio)
			Serum total cholesterol	Serum triglycerides	Serum High Density Lipoprotein	Serum Low Density Lipoprotein	Atherogenic Index
Group-A (Normal control)	Normal saline	10m/kg	88.7± 5.52	66.76± 3.02	26.35± 1.68	48.98± 2.96	2.42± 0.20
Group-B (Standard control)	Atorvastatin	7.2mg/kg	61.2± 2.4	54.3± 1.89	36.8± 1.7	29.2± 1.31	1.06± 0.12
Group-C (Hypolipidaemic)	Z.Officinale	500mg/kg	80.4± 5.75[a]	57.5± 1.39[a]	35.3± 1.28[a]	32.70± 1.21[a]	1.27± 0.04[a]
Group-D (Hyperlipidaemic control)	High fat diet	10ml/kg	267.0± 7.56[a]	218.48± 9.19[a]	16.0± 0.90[a]	207.25± 3.92[a]	15.92± 1.06[a]
Group-E (Standard)	High fat diet + Atorvastatin	10ml/kg + 7.2mg / kg respectively	77.5± 4.7[b]	57.03± 3.26[b]	37.05± 1.4[b]	29.0± 4.0 b	1.11± 0.16 b
Group-F (Antihyperlipidaemic)	High fat diet + Z. Officinale	10ml/kg+ 500mg/kg respectively	99.1± 1.47[b]	86.6± 1.88[b]	25.7± 1.5[b]	50.13± 3.92 b	2.91±. 23 b
One way ANOVA		F	330.01	219.80	44.28	312.84	149.97
		p	<0.01	<0.01	<0.01	<0.01	<0.01

[a]:p<0.01 when compared with normal control group.

[b]:p<0.01 when compared with hyperlipidaemic control group.

(ANOVA followed by Dunnet's multiple comparison test)

Ggraph 1. Shows the different serum lipid parameters at the end of 8th week of experiment



A, E and F, group E has shown very low atherogenic index.

Summary of result: Table 7 and Graph 1 shows the summary results of the experiment.

Discussion

The purpose of the present study was to evaluate the effect of Zingiber Officinale extract on serum lipids, and atherogenesis in adult albino rats fed with high fat diet, in comparison to a standard hypolipidaemic agent Atorvastatin

Hyperlipidaemia was induced by administering high fat diet to the albino rats. High fat diet was prepared by mixing edible coconut oil and vanaspathi ghee in a ratio of 2:3, v/v as described by Shyamala MP et al. The authors stated that hyperlipidaemia is the result of an oxidative abuse due to free radicals, formed by the interaction of high fat diet. They further stated that, enhancement in concentrations of serum cholesterol and triglycerides of hyperlipidaemic rats may be as a result of lipid peroxidation evoked by high fat diet. In the present study hypolipidaernic activity

*Z.*Officinale extract was tested in albino rats. Atorvastatin, a potent hypolipidaemic agent, at a dose of 7.2 mg/kg body weight was used as the standard drug in the present study. The study was conducted for a period of 8 weeks.

Group - C, which was treated with *Z.*Officinale extract for studying hypolipidaemic effect. When compared with normal control group, showed a significant decrease in the levels of the total serum cholesterol 80.4 ± 5.75 ($p<0.0l$), serum triglycede 57.5 ± 1.39 ($p<0.0l$), serum LDL 32.70±1.21 ($p<0.0l$), while there was a significant increase in the level of the serum HDL 35.3 ± 1.28 ($p<0.0l$) when compared to the normal control group i.e. *Z.*Officinale extract has got hypolipidaemic activity.

In this study hyperlipidaemia produced by high fat diet was confirmed by analysis of different levels of lipid parameters when compared with the control group. Here the high fat diet treated group (Group-D) showed a significant rise in the level of total serum cholesterol 267.0 ± 7.56 ($p<0.0l$), serum triglyceride 218.48 ± 9.19 ($p<0.01$), serum LDL 207.25 + 7.81 ($p<0.01$), as well as a significant decrease in serum HDL level 16.0 + 0.90 ($p<0.0l$), when compared to the normal control group. At the end of the 8th week of the experiment, such changes in lipid parameters by production of hyperlipidaemia by high fat diet were also reported by Shyamala MP et al .

Group-F, which was treated with high fat diet supplemented with *Z.Officinale* extract, when

compared with the hyperlipidaernic control group (Group-D), showed a significant decrease in the levels of the total serum cholesterol 99.1 ± 1.47 (p<0.0l), serum triglyceride 83.6 ± 1.88 (p<0.0l), serum LDL 50.13 ± 3.92 (p<0.0l), while there was a significant increase in the level of serum HDL cholesterol 25.7 ± 1.5 (p<0.0l) at the end of the experimental period of 8 weeks. The reduction in serum lipids has shown significant fall (p<0.0l) which confirms that *Z.Officinale* extract has got significant antihyperlipidaemic activity also.

The group receiving high fat diet along with Atorvastatin simultaneously (Group-E), showed a significant decrease in the levels of total serum cholesterol 77.5±4.7 (p<0.0l), serum triglyceride 57.03 ± 3.26 (p<0.0l), serum LDL 29.0±4.53 (p<0.0l), while there was a significant increase in the level of serum HDL cholesterol 37.05 ± 1.40 (p<0.0l) at the end of the 8th week of experiment.

Group - C which was treated with *Z.Officinale* extract alone, showed a significant decrease in the level of atherogenic index 1.27 ± 0.04 (p<0.0l) as compared to the normal control group 2.42 + 0.20. The high fat diet treated group (Group-D), showed a significant rise in the level of atherogenic index 15.92 ± 1.06 (p<0.01). Group-F which was treated with high fat diet supplemented with *Z.Officinale* extract, when compared with the hyperlipidaemic control group (Group-D) showed a significant decrease in the level of atherogenic index 2.91±0.23 (p<0.01). The group receiving high fat diet along with Atorvastatin (Group-E), showed a significant decrease in the level of atherogenic index 1.11±0.16 (p <0.01). A similar change in the value of atherogenic index was reported by Mukherjee B et al. In the hyperlipidaemic group, there was a significant increase in the value of atherogenic index 6.1±1.51, while the group receiving C. roseus, methanolic extract along with high fat diet, showed a significant decrease in atherogenic index, comparable to the normal control group 1.4±0.88. A decrease in the atherogenic index is believed to be beneficial, since the HDL level is inversely related with coronary heart disease and its elevation is considered as an antiatherosclerotic factor .

Z.Officinale extract administration in hyperlipidaemic rats can elicit a profound influence on lipid metabolism. An enhancement in concentration of total serum cholesterol, serum triglyceride, serum LDL and atherogenic index of hyperlipidaemic rats was observed which was probably due to lipid peroxidation evoked by high fat diet. Lipid peroxidation is a free radical mediated process which has been implicated in a variety of disease states. HDL cholesterol concentration and HDL ratio would be useful in diseases like diabetes mellitus and coronary heart disease, because of their inverse relationship. High LDL levels are usually associated with atherosclerosis.

Hypertriglyceridemia is associated in metabolic consequences of hypercoagul ability, hyperinsulinemia, insulin resistance and glucose resistance and is one of the risk factors in coronary heart disease. Hypolipidaemic efficacy of

Z.Officinale extract is revealed by the attainment of values below normal in lipid profile of Group-C rats. Antihyperlipidaemic activity of *Z.Officinale* extract is established by the attainment of near normal values in lipid parameters of Group-F rats. The hypolipidaemci effect of *Z.Officinale* extract may have a protective mechanism against the development of atherosclerosis.

The present study was done, to evaluate the effects of Zingiber officinale on serum lipids and atherogenesis in albino rats, is in agreement with other studies[15,16]. In the present study *Z.Officinale* aqueous extract was used, which is easily available and inexpensive. In previous studies

Z.Officinale methanolic and ethanolic extract has been used. Present study was carried out over longer duration of time i.e. 8 weeks as compared to previous studies. As atherosclerosis is closely associated with hyperlipidaernia and inflammation, all the effects are studied together in the present study and also compared with standard drug Atorvastatin. Such comparative study was not done before. Ginger has shown to possess, significant hypolipidaemic and antiatherogenic activity slightly lesser as compared to Atorvastain. But if we compare Ginger with Atorvastain in terms of adverse effect profile, Atorvastatin causes severe adverse effects like rhabdornyolysis to mention one of them. So ginger can be safely used in treatment of mild to moderate cases of hyperlipidaemia considering

its easy availability, cost effectiveness and other beneficial effects.

Conclusion

The present study was undertaken to assess the effects of Z.Officinale extract on serum lipids and atherogenesis in adult albino rats fed with high fat diet. Effect was compared with standard hypolipidaemic agent Atorvastatin. The study indicated that *Z.*Officinale extract at a dose of 500mg/kg body weight, has significant hypolipidaemic activity, comparable to that of Atorvastatin. This can be concluded from the data that levels of lipid parameters-total serum cholesterol, serum triglycerides, LDL and atherogenic index which are actually raised with high fat diet, are seen to be lowered significantly with concurrent administration of Z.Officinale extract. The study also showed that, *Z.*Officinale extract at a dose of 500mg/kg body weight, exerted anti-atherogenic activity as evidenced by the decreased level of atherogenic index near to normal values, in rats fed with high fat diet and *Z.Officinale* extract concurrently, at the end of the experimental period.

Zingiber Officinale (Ginger) is the most commonly used traditional, household spice, which is safe, cost-effective and easily available. It can be utilized for providing dietary management in hyperlipidaemic patients, for prevention and treatment of atherosclerosis.

Not many studies have been undertaken, to fully evaluate the molecular and biochemical basis of the hypolipidaemic action of Ginger. Thus, ginger

*Z.*Officinale a commonly used natural product, deserves further evaluation from the stand point of itshypolipidaemic effect in therapy. Today there is widespread interest in drugs derived from plants. The shortcomings of the drugs available today, propel the discovery of new pharmacotherapeutic agents in medicinal plants. So emphasis should be laid upon, discovery of different active principles in Ginger for the control of various diseases.

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