Original Article

Comparative Study of Ginger, Methi, Garlic & Drug Atorvastatin on Hyper-cholesterolemic Animals

Zingiber Officinale Rosc (Ginger), Trigonella Foenum Graecum (Methi) and Allium Sativum Linn (Garlic) on Lipid Profile and Liver Enzyme Activities in Hypercholesterolemic Rats in Comparision with Drug Atorvastatin

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ABSTRACT

Objective: To evaluate and compare the hypolipidemic and hepatoprotective effects of Zingiber officinale (ginger), Trigonella faenumgraecum (Methi) and Allium sativum (Garlic) in hypercholesterolemic animal model (albino rats) in comparison with 3-hydroxy 3- methyl glutaryl Co A reductase inhibitor (Atorvastatin)

Study Design: Experimental study.

Pace and Duration of Study: This study was conducted at Biochemistry Department, Al Tibri Medical College, Isra University, Karachi Campus from January 2016 to December 2016.

Materials and Methods: Thirty six albino rats (wistar strains) of both gender were taken and divided into six groups namely (A) Normal control (B) Hypercholesterolemic (C) Zingiber 5% (D) Fenugreek 5%, (E) Allium sativum 5% supplemented groups and (F) Atorvastatin supplemented group. The blood was analyzed for lipid profile and serum liver enzymes after 8 weeks of supplementation.

Results: The serum cholesterol, LDL-C, triacylglycerol,Alanine aminotransferase (ALT), Aspartate amino-transferase (AST) and Alkaline phosphatase (ALP) were increased in hypercholesterolemic rats as compared to normal control rats. Zingiber officinale, Fenugreek and Allium sativum supplemented groups, when compared with hypercholesterolemic group showed lowering of lipid profile and also lowering of serum liver enzyme activities. Zingiber officinale, Fenugreek and Allium sativum supplemented rats had shown no significant difference in the serum level of total cholesterol, HDL- C, LDL-C among the three groups. The triacylglycerol level was markedly decreased in Zingiber officinale supplemented group as compared with Atorvastatin supplemented group. ALT, AST level had shown no significant difference in Zingiber officinale supplemented group as compared to Atorvastatin supplemented rats.

Conclusion: The data obtained from this study concluded that the Zingiber officinale, Fenugreek and Allium sativum had shown the preventive role in hyperlipidemia. Zingiber oficinale is more effective in lowering serum triacylglycerol level and also potent hepatoprotective effect as compared to Fenugreek, Allium sativum and Drug Atorvastatin.

Key Words: Hyperlipidemia, Allium sativum, Fenugreek, Atorvastatin, Zingiber.

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INTRODUCTION

Hyperlipidemia is a main hazard for ischaemic heart disease (IHD). The prevalence of hyperlipidemia as well as its complications are increasing in the world. Moreover alteration in lipid profile results in a diversity of long standing diseases such as diseases of arteriesof heart and atherosclerosis. It is a common disorder in developed as well as under developed countries. Hyperlipidemia is among main factors which causes disabilities and deaths[1].

There arenumber of antihyperlipidemic agents for controlling hyperlipidemia. Lipid lowering treatment using different types of statins effectively reduce the lipoproteinsparticularly low density lipoprotein (LDL) and cholesterol[2]. Statins can inhibit 3-hydroxy-3-methyl glutaryl CoA (HMG-CoA) reductase, which mediates cholesterol production[3]. However the use of statin is restricted due to enhanced undesired effects theyposses along with their thereapeutic efficacy[4].

Recent studies have directed towards the protective effect of plants on hyperlipidemia. Hence it was felt worth wise to explore role of commonly used herbs in

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experimental animals for controlling hyperlipidemia. Herbs have been known to be used as traditional medicines in various diseases from ancient times in many parts of the world including Pakistan. The use of herbal medicine is cost effective with few side effects as compared to the modern medicines[4].

Zingiber officinale (ginger) contain a number of bioactive substances namely 6- gingerol, 6- shogaol, sesqueterpene and Zingeberene[5]. Ginger posses antihyperlipidemic effects and the response of ginger constituents rely upon the amount taken[6]. The oral administration of ginger extract with daily dose of 25mg /kg for 6 weeks caused significant reduction in blood glucose and triacylglycerol while it could not reduced the increased level of total cholesterol and LDL- C to normal level[7].

Fenugreek seeds are good source of soluble dietary fiber; their consumption has shown the reduction in serum and liver cholesterol levels.[8] Ferugreek seeds and its phytocompounds –trigonelline and diosgenin exhibit protective role in liver and the elevated level of liver enzymes decreased by using Fenugreek[9]. Fenugreek seeds administration to high cholesterol diet (HCD) group lowered the amount of total cholesterol, triacylglycerol and lowdensity cholesterol where as HDL-Clevel was significantly increased in hypercholesteolemic diet (HCD) fed rats[10].

Garlic contains sulphur compounds δ-glutamyl -s - allyl –L -cysteines and S –allyl –L–cysteine sulfoxide and other garlic components possess hypocholesterolemic properties[11]. Garlic (Allium sativum) decreases total cholesterol and triacylglycerol and lower LDL in hypercholesterolemic group as compared to control group[12].

The use of medicinal plants is advocated in treatment of hypercholesterolemia because of their negligible side effects, and easy availability. The aim of this study is to assess the comparative hypocholesterolemic effects of Zingiber offcinale Rosc, Fenugreek (Trigonella fenum greecum linn) and Allium sativum. It is also planned to assess the side effects of these medicinal plants on hepatic enzymes.

MATERIALS AND METHODS

It is a Descriptive Comparative Experimental study, conducted at Department of Biochemistry Al-Tibri Medical College and Hospital Karachi during January 2016 to December 2016. Thirty six albino rats of either gender with average weight of 150-200 grams were used for this study. The rats were obtained from animal house of Al-Tibri Medical College and Hospital. The rats were kept in good conditions and adlibitum. Rats were randomly divided into six groups (A, B, C, D, E, and F. In each group six rats (n=6) were included.

Group A was given normal rat diet and served as normal control while group B was given hypercholesterolemic diet containing 20% fat and 1% cholesterol. Remaining groups were given the diet according to diet chart All group of animals were fed the diet for 8 weeks. Group C was Supplemented with 5% zingeber officinale powder with hypercholesterolemic diet, Group D was supplemented with 5% Trigonella foenum graecum seed powder with hypercholesterolemic diet. Group E was supplemented with 5% Allium sativum cloves (Crushed) with hypercholesterolemic diet. Group F was supplemented with 10 mg of Atorvastatin in 1 Kg of hypercholesterolemic diet.

Ginger, Fenugreek and Garlic were procured locally from bazaar. These were sun dried, powdered and stored until required for diet preparation. All chemical used for study were of analytical grade (ANALAR). The ingredients were mixed thoroughly in warm water and then baked in the oven .The diet was prepared separately for each group according to the diet chart.

At the end of study period rats were exposed to anaesthesia and blood samples collected from the heart into specimen tubes. These were cenrtrifuged; serum was separated and kept into labeled apendorff tubes in deep freezer till used for estimation of total cholesterol, triacylglycerols, high density cholesterol and liver enzymes.

The values within the group were analyzed by student 'T' test, whereas the values between the groups were analyzed by Analysis of variance (ANOVA). SPSS version 18 was used for calculation. P Value < 0.05 is taken as statiscally significant.

RESULTS

The rats obtained from animal house of AL-Tibri medical college were kept under standard environment (25±1 ^{0}C), relative humidity 40-60% and 12/12 hour light / dark cycle) for 8 weeks experimental period. The rats were given free access to food and drinking water during the entire experimental period.

In hypercholesterolemic rats the Total cholesterol (TC), Triacylglycerols (TAG), Low density Lipoproteins (LDL) and LDL/HDL ratio were increased but satistically non-significantly, where as HDL level was decreased in hypercholesterolemic rats as compared to normal control rats. Moreover the serum enzymes level of Alanine amino Transferase (ALT), Aspartate amino Transferase (AST) and Alkaline phosphatase (ALP) were increased in hypercholesterolemic as compared to normal control rats.

Table 1 and Figure 1 shows the comparison of lipid profile in different groups of rats after taking supplementation with 5% Zingiber officinale (C), Fenugreek (D) and Allium sativum (E) with hypercholesterolemic diet and atorvastatin 10mg/kg of diet (Group F). There is significant decrease of triacylglycerol of group C (Zingiber officinale) as compared to group D, E and F (atorvaststin 10mg /kg of diet) group. LDL-C is significantly decreased in group

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F (atorvastatin 10mg /kg of diet), as compared to C (5% Zingiber officinale) D and E.

The serum lipid profile and serum enzyme activities of 5% Zingiber supplemented groups were compared with 5% Fenugreek and 5% Allium sativum and 10 mg/kg Atorvastatin group. The values are given as Mean±S.E.M. The number of animals is given in parenthesis.

Table No.1: Comparison of Serum lipid profile and serum liver enzyme of 5% Zingiber supplemented group with 5% Fenugreek and 5% Allium sativum supplemented groups.

Parameter	Supplementation with 5% Zingiber C (6)	Supplementation with 5% Fenugreek D (6)	P Value	Supplementation with 5% Allium sativum E (6)	P Value	Supplementation with 10 mg /kg Atorvastatin F (6)	P Value
TC (mg/dl)	164.66 ± 1.92	159.66 ±6.03	0.989	167.16 ±5.02	0.999	127.00* ±3.91	0.001
TAG (mg/dl)	79.33 ±1.54	107.78* ±2.25	0.001	129.33* ±2.67	0.001	105.16* ±2.79	0.001
HDL-C (mg/dl)	41.16 ±1.60	39.83 ±2.03	0.998	35.66 ±1.85	0.356	38.50 ±1.62	0.942
LDL-C (mg/dl)	107.83 ±2.52	99.00 ±5.74	0.804	103.66 ±5.27	0.994	67.50* ±4.02	0.001
ALT (IU/L)	39.33 ±1.54	43.16 ±1.37	0.757	48.66* ±1.83	0.016	33.16 ±2.74	0.240
AST (IU/L)	98.33 ±3.65	112.66 ±3.92	0.090	117.00* ±2.67	0.011	91.83 ±3.66	0.847
ALP (IU/L)	247.50 ±10.54	256.66 ±5.57	0.972	263.00 ±2.63	0.744	230.66 ±5.04	0.667

*P<0.05 values are statistically significant as compared to 5% supplementation of Zingiber

Table No.2: Comparison of Serum lipid profile and serum liver enzyme of 5% Fenugreek supplemented group with 5% Allium sativum supplemented groups.

Parameter	**Supplementation with 5% Fenugreek D (6)**	**Supplementation with 5% Allium sativum E (6)**	**P value**	**Supplementation with 10 mg /kg Atorvastatin F (6)**	**P value**
TC (mg/dl)	159.66±6.03	167.16±5.02	0.92	127.00*±3.91	0.001
TAG (mg/dl)	107.78±2.25	129.33*±2.67	0.001	105.16±2.79	0.991
HDL-C (mg/dl)	39.83±2.03	35.66±1.85	0.673	38.50±1.62	0.998
LDL-C (mg/dl)	99.00±5.74	103.66±5.27	0.989	67.50*±4.02	0.001
ALT (IU/L)	43.16±1.37	48.66±1.83	0.366	33.16*±2.74	0.008
AST (IU/L)	112.66±3.92	117.00±2.67	0.975	91.83*±3.66	0.003
ALP (IU/L)	256.66±5.57	263.00±2.63	0.996	230.66±5.04	0.186

*P<0.05 values are statistically significant as compared to 5% Fenugreeksupplemented group

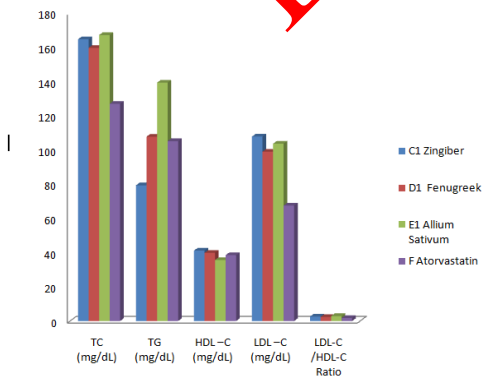

Figure No.1: Comparison of serum lipid profile with 5% Zingiber, Fenugreek, Allium sativum and Atorvastatin.

The graph shows the mean value of serum lipid profile of 5% Zingiberofficinale, Fenugreek, Allium sativum and Atorvastatin (10mg/kg of diet) supplemented rats.

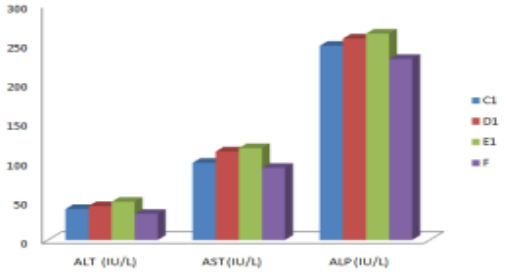

Figure No.2: Comparison of serum liver enzymes with 5% Zingiber, Fenugreek, Allium sativum and Atorvastatin.

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In group F, ALT is significantly decreased as compared to D (5% Fenugreek) and E (5% Allium sativum). Aspartate aminotransferase (AST) level is significantly increased in group E (5% Allium sativum) as compared to C (5% Zingiberofficinale). AST is significantly decreased in group F (atorvastatin 10mg/kg of diet) as compared to group D (5% Fenugreek) and E. Alkaline phosphatase (ALP) is significantly increased in group E (5% Allium sativum) as compared to group F (Atorvastatin 10 mg / kg of diet) as shown in Table-2 and Figure 2.

The graph shows the comparison of mean values of serum liver enzymes of 5% Zingiberofficinale, Fenugreek, Allium sativum and Atorvastatin (10mg/kg of diet) supplemented rats.

DISCUSSION

Hyperlipidemia is a predisposing factor to vascular disease which eventually leads to diabetes mellitus, cardiac diseases, inflammation and other associated disorders. Antihyperlipidemic drugs are usually used for the treatement of dyslipidemia and other related metabolic disorders.

Hypercholesterolemia is treated by many drugs, of which statins are most frequently prescribed[13]. The most adverse effect of statins are toxicity to liver and muscles. The hazardous factors associated with hypercholesterolemia are renal insufficiency, hypothyrodisom, liver dysfunction[14] and diabetes[15].

Use of plant products have been advocated as substitute for the treatment of dyslipidemia. Spices are dietary supplementary herbs widely used in Indian and Pakistani foods as flavouring agent, colouring agent and preservative from thousands of years.

Ginger, Garlic and Fenugreek are used as food supplements/ additives without toxic effects. They have the added advantage of possessing medicinal properties in general and potential benefits for patients with cardiovascular disease in particular. In the present study, the hypercholesterolemic rats had shownincreased level of serum TAG, LDL-C and Total Cholesterol, and a low level of HDL-C as compared to normal control. This may be due to increased exogenous synthesis of cholesterol, due to consumption of high fat diet, and the increase in LDL-C may be because of the of reduction of LDL – receptor sites[16]. Paul et al also had shown that total cholesterol, LDL – C and triacylglycerols were increased by the administration of Vanspati ghee[17]. The increase in plasma TAG with this diet is due to the over production of VLDL[18].

The level of LDL- cholesterol (as calculated by Friedwald equation)[19], was elevated in hypercholesterolemic rats. Administration of ginger with hypercholesterolemic diet had decreased LDL-Cholesterol, total cholesterol and triacylglycerol, but HDL- Cholesterol had been increased which shows that ginger has a beneficial influence on cholesterol metabolism which is supported by many researchers [17,20-22].

The groups treated with Zingiber showed significant reduction in triacylglycerolcompared to hypercholesterolemic group, Isa Y et al[23] had shown the up regulation of adiponectin by 6 – shogaol and 6 – gingerol, which increases the oxidation of fatty acid and subsequently level of serum triacylglycerolis decreased[23,24]. Our finding on the effectiveness of ginger in decreasing serum triacylglycerol is in accordance of the finding of El-Rokh et al[25].

The serum enzymes AST, ALT were significantly decreased in all treatment groups with ginger as compared to hypercholesterolemic group in the present study. These results are in agreement with those obtained by many workers[26].

The present work has been done to manifest the effect of Fenugreek on lipid profile and hepatic enzymes. A significant decrease was observed in the blood level of cholesterol, Triacylglycerol, LDL-Cholesterol and an increased HDL-Cin 5% and 10% Fenugreek supplemented rats as compared to hypercholesterolemic group. Similar observations were demonstrated in experimental animals by previous worker[27].

In the present study the 5% Allium sativum was supplemented in the diet of rats, had shown hypolipidemic effect as was found by Dalal et al[28] and has caused a significant reduction in serum total cholesterol as was found by Farnaz[29]. HDL-Cholesterol had significantly increased in Allium sativum supplemented group as compared to hypercholes-terolemic group in the present study as was reported by previous study[30].

It was observed that the level of serum triacylglycerol was significantly decreased in Zingiber supplemented group as compared to Fenugreek, Allium sativumand Atorvastatin (Table –IV-4), but Islam and Choi had found no significant difference in the lipid profile between the ginger supplemented and Garlic supplemented groups[31].

The serum enzyme activities after 8 week treatment of hypercholesterolemic rats with Allium sativum, Fenugreek and Zingiber officinalehas shown significant decrease in the activities of ALT, ASTand ALP as compared to hypercholesterolemic rats.In contrast to this Gazuwa et al reported that when onion and Garlic were compared there was no significant difference in TAG, HDL-C and VLDL-C as compared to control, but animals in test group showed higher activities of transaminases as well as alkaline phosphatase, which shows that onion andGarlic caused some level of damage[32].

CONCLUSION

Zingiber officinale, Trigonella foenum graecum and Allium sativum all showed hypolipidemic and

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hepatoprotective effects as compared to drug Atorvastatin on hyperlipidemic rats. The LDL-C lowering effect is more prominent in Atorvastatin treated group.

It is concluded that triacylglycerol lowering effect of Zingiber is more than that of Atorvastatin, but Zingiber did not give LDL-C lowering effect as compared to Atorvastatin. So it is concluded that Zingiber has more efficacy among the three herbs in lowering serum triacylglycerol level in addition it have more potent hepatoprotective effect as compared to Fenugreek and Allium sativum.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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