

HYPOLIPIDEMIC EFFICACY OF ZINGIBER OFFICINALE EXTRACT IN COMPARISON WITH FENOFIBRATE, ROSUVASTATIN AND EZETIMIBE IN HYPERLIPIDEMIC RATS



Kawa F. Dizaye ^a and Hani H. Mohammed ^b

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ABSTRACT

Background

Zingiber officinale (Ginger) is the most common used herb worldwide due to its great medicinal and culinary properties. The medicinal properties come from its antihyperlipidemic, anti-inflammatory, antiemetic, antimicrobial, anticancer and carminative actions.

Objectives

The present study was designed to evaluate and compare the effectiveness of different doses of Ginger decoction with, rosuvastatin, fenofibrate and ezetimibe on lipid profile, liver function test and MDA level in hyperlipidemic rats.

Methods

Fifty-four rats were divided into two groups. The first group included 18 rats and have subdivided into three subgroups each having 6 rats. The first subgroup served as a control. The second and the third subgroup received (2 ml and 4 ml) of ginger extract (10% W/V) daily respectively. The second group included 30 hyperlipidemic rats and they were subsequently subdivided into six subgroups each of 6 rats. The first subgroup served as positive control. The second subgroups received single doses of ginger (10% W/V). The third, fourth and sixth subgroups received Rosuvastatin (15 mg /kg), Fenofibrate (30mg/kg) and Ezetimibe (1mg/kg) respectively. At the end of treatment period (six weeks), all of these groups were subjected to various biochemical analysis of blood.

Results

After six weeks of therapy, ginger extract significantly reduced serum total cholesterol, TG and LDL-C of hyperlipidemic rats, while it significantly increased serum HDL in both normal and hyperlipidemic rats. Daily administration of fenofibrate for six weeks caused a significant reduction in serum TG and LDL-C and significantly increased serum HDL of hyperlipidemic rats. Whereas using of rosuvastatin (15mg/kg) and ezetimibe (1mg/kg) for six weeks lead to significant reduction in serum total cholesterol, TG, LDL-C and significantly increase in serum HDL in hyperlipidemic rats. Dose of 2 ml ginger 10% (W/V) decoction significantly reduced MDA level in normal rats. Furthermore, Ginger extract and the other antihyperlipidemic drugs significantly decreased serum MDA level of hyperlipidemic rats. After 6 weeks of daily ingestion of different doses of ginger decoction, serum ALP was significantly increased in normal rats. However, liver function test of hyperlipidemic rats was not significantly affected by ginger decoction. On the other hand, rosuvastatin caused a significant elevation in serum ALP, while ezetimibe significantly reduced AST of hyperlipidemic rats.

Conclusion

Zingiber officinale decoction was effective as the other antihyperlipidemic agents in improving lipid profile. Although ginger has an antioxidant effect, but prolonged administration may have a hazardous hepatic side effect.

Keywords: *Hyperlipidemia, Ginger, Rosuvastatin, Fenofibrate, Ezetimibe.*

^a College of Medicine, Hawler Medical University.

Correspondence: kawa.dizaye@hmu.edu.iq

^b Department of Pharmacology, College of Medicine, University of Sulaimani, Kurdistan Region, Iraq.

INTRODUCTION

Hyperlipidemia also known as dyslipidemia to cover all abnormalities in lipoprotein metabolism since some of these lipoproteins elevated like LDL-C and the other may be decrease for instance high density lipoprotein (HDL-C) ⁽¹⁾.

The dyslipidemia may be primary or secondary, the primary one resulted from genetic defect related to the patient's family history this in combination with some environmental factors, examples about this type of hyperlipidemia are: primary hypercholesterolemia like familial hypercholesterolemia which characterized by elevation in LDL-C level, primary mixed (combined) hyperlipidemias in which both LDL-C and triglyceride (TG) is elevated, primary triglyceridemias like type 3 hyperlipoproteinemias which characterized by lipoprotein lipase deficiency. The secondary hyperlipidemia occur as result of other disease such as diabetes mellitus, and hypothyroidism ⁽²⁾.

Hyperlipidemia or dyslipidemia can be treated with changing life style like diet, exercise, weight reduction and in some cases pharmacological intervention is needed. Many drug groups are available for this purpose for instance: Statins group, Fibrates, Niacin, Bile acid sequestrants, Omega 3 fatty acid ^(3, 4). In addition many natural drugs and herbs also used as medicine to counteract the dyslipidemia example such as Fenugreek seeds (*Trigonella Foenum*), Garlic (*Allium sativum*) and Ginger (*Zingiber officinale*) is the ground rhizome of plant zingiber officinale belong to the family Zingiberaceae, it's abundant in Asia ^(5, 6).

Zingiber officinale is the most common used herb worldwide due to its great medicinal and culinary properties, it has antioxidant, anticancer, and anti-inflammatory effects ^(7, 8). Ginger used as antiemetic agent especially in chemotherapy induced emesis, it blocks 5-hydroxytryptamine (5-HT) receptor, Oleoresin and Zingibrene which are the main components responsible for specific smell of ginger. Other aroma contributing constituents include Gingediol, Diarylheptanoid, Vitamins and Phytosterol ⁽⁹⁾.

The present study was designed to evaluate and compare the effectiveness of different doses of *Zingiber officinale* extract, Rosuvastatin, Fenofibrate and Ezetimibe on lipid profile, liver function test and Malondialdehyde level in hyperlipidemic rats after six weeks of administration.

MATERIAL AND METHODS

Plant material

Ginger rhizome were used and obtained from private local vegetables and fruits market. The rhizome was cleaned, and cut to small pieces, and boiled for 30 minutes to get decoction, which were used in the study.

Animals

A total of forty five rats of male gender were used in the study, their weight ranged from 200 gm to 225 gm. The rats obtained from College of Veterinary in University of Sulaimani. They kept in animal house of veterinary college under controlled conditions of light and temperature of 25 °C.

Experimental design

Fifty four rats were divided into two groups. The first group included 18 rats and received standard diet throughout the experimental period, and have subdivided into three groups each contain 6 rats. The first subgroup served as control. The second and the third subgroup received (2 ml and 4 ml) of ginger extract (10% W/V) daily respectively by oral gavage tube.

The second group included 36 hyperlipidemic rats. Hyperlipidemia was induced by feeding the rats with high cholesterol (Atherogenic) diet (79% standard diet and 21% ghee fat) for six weeks. The hyperlipidemic rats were subsequently subdivided into six subgroups each contain 6 rats. The first subgroup served as positive control. The second and the third subgroups received single and double doses (2cc, 4cc) of ginger (10% W/V). The fourth, fifth and sixth subgroups received daily single dose of Rosuvastatin (15 mg/kg), Fenofibrate (30 mg/kg) and Ezetimibe (1 mg/kg) orally respectively.

The Ginger decoction (10% W/V), Rosuvastatin (15 mg/kg), Fenofibrate (30mg/kg), and Ezetimibe (1mg/kg) were freshly prepared and were given to rats by oral gavage tube every day.

At the end of treatment period to all these groups, the animals were used for various biochemical parameters. The rats anesthetized using light dose of chloroform and sacrificed by using surgical blade. Blood samples were collected from the rats for determination of the following parameters:

Lipid profile; Serum total cholesterol, high-density

lipoprotein (HDL), low-density lipoprotein (LDL) cholesterol and triglyceride (TG).

Liver function test; Serum alanine aminotransferase (ALT), Serum aspartate aminotransferase (AST) and serum alkaline phosphatase (ALP). Malondialdehyde (MDA)

Statistical analysis

All data are expressed as Mean \pm Standard error mean (M \pm SEM) and the statistical analysis was carried out by using statistical available software (SPSS version 23). Data analysis was made using one-way analysis of variance (ANOVA). The comparison among the groups done by using Duncan test and unpaired T-test. P<0.05 considered as statistical significance.

RESULTS

Lipid profile of normal and hyperlipidemic rats

Comparing to the normal rats, there were marked and significant increase in the level of cholesterol; Triglycerides and LDL in animals treated with atherogenic diet for six weeks, while a significant reduction in level of HDL were observed (Table 1).

Effects of different doses of Ginger on lipid profile of normal rats

Daily administration of 2 ml ginger (10% W/V) for six consecutive weeks induced a significant reduction in serum TG, LDL, and significant increase in HDL level in normal rats. No significant difference was obtained between low and high dose of ginger (10% W/V) in all parameters of lipid profile. (Table 2). Therefore, low dose of ginger was considered as an effective dose to determine its effect on lipid profile in hyperlipidemic rats

Effect of 2ml Ginger (10% W/V), Fenofibrate, Rosuvastatin and Ezetimibe on lipid profile of hyperlipidemic rats

Compared to hyperlipidemic rats model, 2 ml of ginger 10% (W/V), Rosuvastatin and Ezetimibe produced significant reduction in serum cholesterol, whereas daily administration of Fenofibrate has no significant effect on serum cholesterol of hyperlipidemic rats (Table 3).

Two ml of ginger (10% W/V) decoction and the other antihyperlipidemic drugs induced significant reduction in triglycerides of hyperlipidemic rats (Table 3).

All antihyperlipidemic drugs and 2ml ginger decoction significantly reduced serum LDL in hyperlipidemic rats; however, the effect of fenofibrate on serum LDL was significantly less efficacious than ginger and the other antihyperlipidemic drugs (Table 3).

Daily administration of 2 ml ginger 10% (W/V) decoction, rosuvastatin, fenofibrate and ezetimibe significantly changed serum HDL of hyperlipidemic rats (Table 3).

Effects of different doses of Ginger (10% W/V), Fenofibrate, Rosuvastatin and Ezetimibe on MDA of hyperlipidemic rats.

Serum MDA level of rats treated with atherogenic diet was significantly increased when compared with control group. Daily administration of 2ml ginger 10% (W/V) decoction, rosuvastatin, fenofibrate and ezetimibe significantly reduced MDA when compared to hyperlipidemic rats (Figure 1).

Effects of different doses of Ginger (10% W/V), Fenofibrate, Rosuvastatin and Ezetimibe on liver enzymes of hyperlipidemic rats.

AST and ALT of rats on atherogenic diet have slightly and non-significantly increased when they compared with normal rats, while the ALP significantly increased.

No significant change in ALT and AST were observed in rats treated with ginger decoction, fenofibrate and rosuvastatin in hyperlipidemic rats, although ezetimibe has no significant effect on the ALT of hyperlipidemic rats but significantly could reduce AST of hyperlipidemic rats.

Ginger decoction, fenofibrate and ezetimibe have no significant effect on serum ALP of hyperlipidemic rats. However daily administration of rosuvastatin in hyperlipidemic rats significantly increased serum ALP (Table 4).

Table 1. Lipid profile in normal and hyperlipidemic rats.

Parameter	Normal rats	Hyperlipidemic rats	p-value
Cholesterol (mg/dl)	56.33±7.79	95.83±3.85	0.001
Triglyceride (mg/dl)	46±9.72	103.16±8.24	0.001
LDL (mg/dl)	19±6.42	53±6.43	0.004
HDL (mg/dl)	25±1.84	17.60±1.029	0.008

Table 2. Effects of different doses of ginger (10% W/V) on lipid profile of normal rats (n=18).

Parameter	Normal rats	Rats received low dose of ginger	Rats received high dose of ginger
Cholesterol mg/dl	56.33±7.79 a	35.20±6.20 a	47.80±4.97 a
Triglyceride mg/dl	46±9.72 a	8.2±2.48 b	9.5±6.88 b
LDL mg/dl	19±6.4 a	4.8±0.80 b	8.6±1.72 ab
HDL mg/dl	25±1.84 a	39.60±3.07 ab	33.60±6.44 b

Table 3. Effect of different doses of Ginger, Rosuvastatin, Fenofibrate and Ezetimibe on lipid profile of hyperlipidemic rats

Parameter	Normal rats	Hyperlipidemic rats	Effective dose of ginger	Rats received fenofibrate	Rats received rosuvastatin	Rats received ezetimibe
Cholesterol mg/dl	56.33±7.8 a	95.83±3.8 b	72±5.4 a	103.12±4.3 b	71.98±8.9 a	67.52±8.4 a
Triglyceride mg/dl	46±9.7 a	103.16±8.2 b	63.60±7.2 a	58.78±5.63 a	38.72±11.8 a	63.18±9.4 a
LDL (mg/dl)	19±6.4 a	53±6.43 c	15.40±1.96 a	39±2.9 b	12±2.7 a	11.60±3.7 a
HDL mg/dl	25±1.8 a	17.60±1. a	51.50±1.2 b	52.50±3.6 b	52.30±7.5 b	43.56±8.6 b

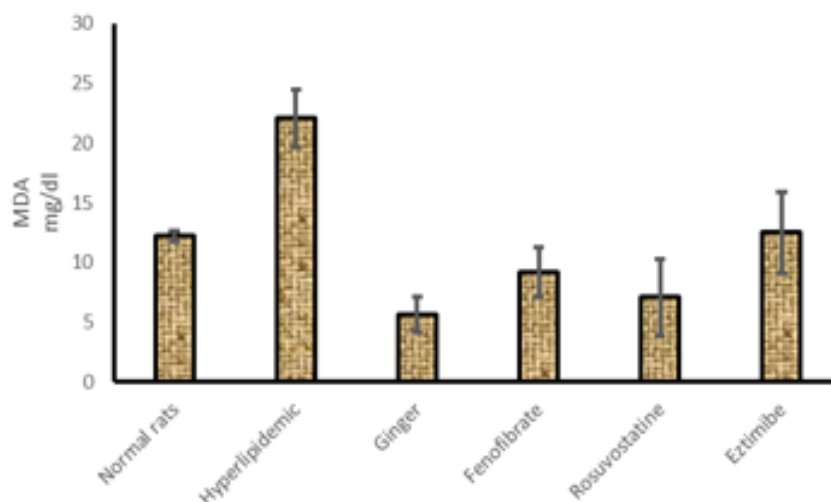


Figure 1. Effects of different doses of Ginger (10% W/V), Fenofibrate, Rosuvostatin and Ezetimibe on MDA of hyperlipidemic rats (n=36).

Table 4. Effects of different doses of Ginger (10% W/V), Fenofibrate, Rosuvostatin and Ezetimibe on liver enzymes of hyperlipidemic rats (n=36).

Parameter	Normal rats	Hyperlipidemic rats	Effective dose of ginger	Rats received fenofibrate	Rats received rosuvostatin	Rats received ezetimibe
ALT	31.6±6.6 a	68.8±5.4 ab	74.4±24.8 ab	38.3±1 ab	85.2±22.8 b	82.9±13.6 b
AST	169.2±5 ab	192.1±13.3 b	169.6±10.7 ab	198.2±16.9 b	252±24.6 b	79.3±53.7 a
ALP	50.8±8.3 a	264.06±17.8 b	169.44±37.5 b	257.66±29.9 b	287±15.5 c	254.3±62.5 b

DISCUSSION

The present study showed that serum cholesterol, TGs and LDL hyperlipidemia in the rats induced by atherogenic diet have significantly increased, while level of HDL was significantly decreased when they compared with the control. These results were in accordance with the findings obtained from Mani et al. 2012, ⁽¹⁰⁾ who found that the atherogenic diet containing (30% vegetable oil and 3% pure cholesterol) given to 28 adults female Charles Foster rats for 28 days have significantly changed lipid profile by increasing level of serum cholesterol, TG and LDL and simultaneously decreased the level of serum HDL. Other published study ⁽¹¹⁾ has obtained similar results of our study and hyperlipidemia has been induced in Wistar rats by using atherogenic diet which containing (Vanaspati ghee and coconut oil in the ratio of 3:1 V/V) for 7 weeks.

Hyperlipidemia induced by atherogenic diet is attributed to an increase in the level of cholesterol biosynthesis

precursor (Acetyl CoA) which lead to increase in HMG-CoA reductase activity, in addition the atherogenic diet lead to down regulation LDL receptor either by changing hepatic LDL receptor activity or by changing rate of LDL production or by both ⁽¹²⁾.

In the present study, the *Zingiber officinale* decoction showed beneficial effects on lipid profile of normal rats, it reduced the level of serum cholesterol, TG, LDL-C and increased serum HDL after six weeks of administration. This result is in agreement with the study of Prasad et al, ⁽¹³⁾ who concluded that using ginger juice (4 ml/rat P.O) for about 21 days showed significant reduction in the level of serum cholesterol and significant increase in serum HDL, however in contrast to the present study, Prasad et al. ⁽¹³⁾ did not observe significant changes in level of serum LDL and TG. These differences indicated that using ginger for 21 days is not sufficient to induce significant changes in serum TG and LDL levels.

The present study found that both doses of ginger (10% W/V) decoction 2 ml and 4ml significantly reduced levels of serum TG, LDL-C, total cholesterol and increased serum HDL in hyperlipidemic rats when they compared with normal rats. These results were in agreement with other experimental study⁽¹⁴⁾ which carried out on 40 rats received ethanolic extract of ginger (500 mg/kg/day) during 9 weeks, showed significant reduction in the serum of total cholesterol, TGs, LDL-C and significant increase in serum HDL. These results were in agreement with the finding of our study. On another hand, the study of Tabibi et al.⁽¹⁵⁾ emphasizes the results of the current study in which daily administration of ginger (1000 mg) by hyperlipidemic peritoneal dialysis patients for 10 weeks show significant reduction in serum level of TG.

The mechanism behind the antihyperlipidemic effect of the ginger comes from its ability to activate cholesterol 7 α -hydroxylase, which is a rate limiting enzyme in biosynthesis of bile acid. It induces conversion of cholesterol to bile acid, thus lead to enhance clearance VLDL and reduce TGs level⁽¹⁶⁾. Moreover niacin component in ginger may play a role in ginger antihyperlipidemic effect through increase in VLDL clearance, reduction of TGs level, increase hepatic uptake of LDL-C and inhibit cholesterogenesis⁽¹⁷⁾.

Results from the present study appeared that six weeks of fenofibrate (30 mg/kg/day) treatment in hyperlipidemic rats significantly increased serum HDL and significantly reduced TGs, LDL-C when compared with non-treated hyperlipidemic rats. This result was similar to the finding of Sun et al,⁽¹⁸⁾ who concluded that different doses of fenofibrate (50-100 mg/kg/day) for two weeks significantly reduced serum TGs while it significantly increased serum HDL of hypertriglyceridemic rats induced by administration of (10 mg/day of 10% fructose) for one week.

The current study showed that fenofibrate (30 mg/kg) treatment for six weeks lead to significant increase in serum HDL and significant reduction in serum TGs, LDL-C in hyperlipidemic rats, when compared to non-treated hyperlipidemic rats. These results were comparable to the findings of Li W et al.⁽¹⁹⁾ who showed that treating healthy male Wistar rats fed on high fat diet with fenofibrate (80 mg/kg/day) for 8 consecutive weeks lead to significant reduction in the level of serum TGs, LDL-C and significant increase in the level of serum HDL. However, the present study disagreed with Li W et al.⁽¹⁹⁾ in which serum total cholesterol was not

affected by fenofibrate during six weeks. This disparity might be related to difference in dose and duration of fenofibrate treatment.

The outcome of the influence of fenofibrate on lipid profile in hyperlipidemic rats is in accordance with findings of Oikawa et al.⁽¹⁹⁾ who concluded that hyperlipidemic patient treatment with fenofibrate 200mg/day for 6 weeks have reduced serum TGs, LDL and increased serum HDL significantly. On the other hand, our study disagreed with Oikawa et al.⁽²⁰⁾ in that fenofibrate (30 mg /kg) didn't significantly changed serum total cholesterol in hyperlipidemic patients. This disparity is related to the fact that longer time is required to reduce total serum cholesterol.

In the present study serum cholesterol, TGs and LDL-C are significantly reduced, while the serum level of HDL is significantly increased of hyperlipidemic rats treated with rosuvastatin (15 mg/kg). These results were in accordance with observations recorded by Ansari et al.⁽²¹⁾ who noticed that administration of rosuvastatin (10mg/kg/day) for 21 days with high fat diet significantly reduced serum level of total cholesterol, TGs, LDL-C and significantly increased serum level of HDL in hyperlipidemic rats when compared to non-treated hyperlipidemic group. Furthermore, results obtained from the study of Rosenson et al.⁽²²⁾ confirmed the results of the present study as they recorded significant reduction in serum LDL-C and significant increasing in serum level of HDL.

The present study exhibited that ezetimibe (1mg/kg) significantly reduced serum cholesterol, TGs, LDL-C and significantly increased serum HDL. This result is identical with the study of Ruggenenti et al.⁽²³⁾ who detected significant reduction in serum cholesterol, TGs and LDL-C when ezetimibe (10mg/day) was given to 108 type 2 diabetic patients with hyperlipidemia for 2 months. In contrast to our results, the study of Ruggenenti et al.⁽²³⁾ recorded reduction in the level of serum HDL. This dissimilarity might be related to the variation in the effect of ezetimibe on rats and human. The results of current study were in accordance to the results of Kumagai et al.⁽²⁴⁾ who observed that hyperlipidemic patients with or without metabolic syndrome treated with ezetimibe (10 mg/day) for 16 weeks induced significant reduction in serum cholesterol, TGs, LDL-C. However, it disagreed with present the study in that the HDL level was not affected by ezetimibe.

Ezetimibe act as anti-hyperlipidemic agent by inhibiting intestinal cholesterol absorption through selectively blocking NPC1L1 protein in jejunal brush border. Depletion of hepatic cholesterol induced by ezetimibe lead to upregulation of LDL receptors on surface of hepatocyte resulting in reduction in serum level of LDL-C⁽²⁵⁾.

Malondialdehyde (MDA) is stable product of lipid peroxidation, evaluation of MDA is to decide whether lipid peroxidation take place or not⁽²⁶⁾. Lipid peroxidation is series of reactions occur during oxidative stress which eventually lead to cellular damage⁽²⁶⁾. Lipid peroxidation is thought to be involved in various pathological conditions, like platelet activation, tissue destruction and various inflammatory processes⁽²⁷⁾.

In the current study two different doses of ginger (10% w/v) decoction, 2 ml and 4ml have been used, to evaluate its effect on MDA of normal rats, both doses of ginger caused significant reduction in serum MDA. Although higher dose caused greater effect. However, no statistically significant difference was detected between large and small doses of ginger extract. These results were in agreement with the study of Ahmad et al.⁽²⁸⁾ who found that using of ginger extract (100 mg/kg) for 8 weeks caused significant reduction in the level of serum MDA of normal rats.

In contrast to our results, Abd-allah et al.⁽²⁹⁾ observed that using of ginger solution for 6 days in 40 rats showed no effect on MDA level of normal rats. The variation in the influence of ginger conforms that the plant decoction needs more than one week to exert its effect on MDA.

In this study, malondialdehyde was significantly higher in hyperlipidemic rats than that of control group. This result is in agreement with study of Yang et al.⁽³⁰⁾ who reported that MDA was elevated significantly in hyperlipidemia patients when they compared to normolipidemic patients.

The present study demonstrated that ginger (10% w/v) decoction significantly reduced serum malondialdehyde of hyperlipidemic rats. This result was in agreement with the determination of Shanmugam et al.⁽³¹⁾ which detected that ginger extract (200 mg/kg) administration for 30 days reduced the MDA level significantly in diabetic rats. These outcomes are supported by the study Taha et al.⁽³²⁾ which exhibited that administration of ethanolic extract of ginger for 3 weeks caused significant reduction in serum MDA of hyperlipidemic rats when

compared to normal group. The reduction of MDA in hyperlipidemic rats induced by ginger is related to its antioxidant and anti-hyperlipidemia activities⁽³²⁾. The antioxidant effect of Zingiber officinale is contributed to the presence of zingibrene and zingerone which are the main components of Zingiber officinale^(33, 34).

In this study fenofibrate has decrease level of MDA significantly after six weeks of administration, and this comes in agreement with the result obtained from Sun et al.⁽¹⁸⁾ in which 2 weeks of fenofibrate therapy (two different doses 50 and 100 mg/kg) in 30 hypertriglycemic rats initiated reduction in the level of MDA and TGs.

The present study revealed that rosuvastatin (15 mg/kg) significantly reduced serum MDA of hyperlipidemia rats. This result is in agreement with the finding of Yu et al.⁽³⁵⁾ who detected that rosuvastatin treatment for 4 weeks lead to significant reduction in serum MDA and regulate expression of oxidized LDL. Furthermore Elhemely et al.⁽³⁶⁾ observed that hyperlipidemic-myocardial infarction rats model received (10 mg/kg/day) of rosuvastatin for 7 weeks result in reduction in MDA level by 34.5%.

In the current study ezetimibe (1 mg/kg/day) significantly reduced serum MDA of hyperlipidemic rats when compared to non-treated hyperlipidemia rats. This result was in accordance with observations obtained from Yunoki et al.⁽³⁷⁾ who found that giving (10 mg/day) of ezetimibe to hyperlipidemic patients for 4 weeks lead to significant reduction in serum MDA when compared with non-treated hyperlipidemic patients.

In the present study, daily administration of different doses of ginger decoction (10% w/v) for six weeks lead to significant increase in serum ALP without significant changes in serum AST and ALT. In the present study, effect of ginger on ALP is comparable to the findings obtained from DN et al.⁽³⁸⁾ who also detected significant increase in ALP of normal rats. However unlike to this study, DN et al.⁽³⁷⁾ exhibited significant elevation in serum AST and ALT. Therefore, ginger should not be used in patients with hepatic disorder. In contrast to present study.. Present study is disagreed with results of Attia et al.⁽³⁹⁾ who found that 50 days of ginger (160 mg/kg) administration by female albino rats (n=24) caused no changes in hepatic enzymes AST, ALT and ALP.

The results of present study exhibited significant

increase in the level of ALT and ALP, while no change observed regarding AST of rats taking high fat diet for six weeks. Our results are in agreement with the findings obtained from ⁽⁴⁰⁾ studies which showed that hepatic enzymes ALT and ALP were increased significantly in rats received high fat diet, while it disagreed with our results in that AST was increased significantly. Results of our study is in accordance with the findings obtained from Shalaby et al. ⁽⁴⁰⁾ who concluded that rats treated with two different doses of ginger extract (200-400 mg/kg) for 6 weeks showed reduction in serum AST and ALP at same time their results disagreed with our findings in that the serum ALT was decreased.

The present study indicated that fenofibrate caused no significant changes in hepatic enzymes AST, ALT and ALP. However, fenofibrate showed non-significant reduction in level of serum ALT and ALP and non-significant increase in serum AST of hyperlipidemic rats. In contrast to the present study, Santiago et al. ⁽⁴¹⁾ reported that treating Spargue-Dawley rats with fenofibrate (10 mg/kg) for two weeks showed significant reduction in serum AST and ALT.

Findings from study of Gandhi et al. ⁽⁴²⁾ disagreed with results of our study as they displayed that dyslipidemia patients treated with fenofibrate caused significant reduction in serum ALT and ALP. The discrepancy in these results could be related to the variation in effect of fenofibrate between human and rats.

In the current study, daily administration of rosuvastatin for six weeks lead to non-significant increase in serum AST and ALT, while it significantly increased ALP. This result comparable to the findings obtained from Sowmya et al. ⁽⁴¹⁾ who found that 6 months of rosuvastatin treatment in dyslipidemic patients of both gender caused non-significant increase in serum AST and ALT. However in contrast to present the study, Sowmya et al. ⁽⁴²⁾ recorded non-significant increase in serum ALP. This disparity may be related to the variation in effect of rosuvastatin between human and rats.

In the present study daily administration of ezetimibe (1 mg/kg) in hyperlipidemic rats for six weeks lead to non-significant increase in serum ALT, significant decrease in serum AST and non-significant decrease in serum ALP. Reports of Almutairi et al. ⁽⁴³⁾ is in agreement with results of the present study. They concluded that using of ezetimibe 10 mg/day in hyperlipidemic patients (n=25) for 6 months induced non-significant

elevation in serum ALT, while it disagreed with our result in that it caused non-significant increase in serum ALP. In contrast to our results, Bays et al. ⁽⁴⁴⁾ recorded that hyperlipidemic patients (n=432) treated with two different doses of ezetimibe (5, 10 mg/day) caused statistically non-significant increase in serum AST.

In conclusion, Zingiber officinale decoction was effective as the other antihyperlipidemic agents in improving lipid profile. Although ginger has an antioxidant effects, but prolonged administration may have a hazardous hepatic side effect.

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