

# BIOCHEMICAL EFFECT OF GINGER ON SOME BLOOD AND LIVER PARAMETERS IN MALE NEWZELAND RABBITS

# M.A. LEBDA\*, NABIL M TAHA, MAHDY A KORSHOM, ABD EL-WAHAB A MANDOUR, AMANY M EL-MORSHEDY

Department of Biochemistry, Faculty of Veterinary Medicine, Alexandria University, Egypt

\*E-mail: lebda\_vet@yahoo.com

**ABSTRACT:** The aim of the present study was to investigate the effects of different ginger rhizome treatments on hepatic oxidative stress markers and antioxidant status. Also, the study was extended to show the serum lipid profile, liver and kidney functions and serum glucose. Forty male New Zealand rabbits were allocated into four groups (10 rabbits in each); control, ginger powder, hot extract of ginger and cold extract of ginger. The results revealed that administration of ginger in its different forms significantly reduced malondialdehyde (MDA) level, glutathione peroxidase (GPX) and glutathione-S-transferase (GST) activities, meanwhile, the reduced glutathione (GSH) was significantly increased in liver. Moreover, ginger treatment depleted serum triacylglycerol (TAG), total cholesterol and low density lipoprotein-cholesterol (LDL-c) while the high density lipoprotein-cholesterol (HDL-c) was increased. Ginger administration improved liver functions but unfortunately, the serum creatinine and glucose levels were increased. We concluded that ginger especially hot extract maintain the antioxidant activities, improve liver functions and reduce lipid peroxidation.

Key words: Ginger, Cholesterol, Malondialdehyde, Glutathione

# INTRODUCTION

Plants have been the major source of drugs for the treatment of various diseases in many ancient systems of medicine in the world. Ginger is an underground rhizomes of plant Zingiber officinale belonging to the family Zingiberaceae which is widely consumed as spice for the flavoring of foods (Ajith et al., 2007). It has been reported that ginger and its extracts possess some pharmacological activities including hypoglycemic, insulinotropic and hypolipidemic in human (Huang et al., 2004) and in experimental animals (Kondeit et al., 2005). The anti-inflammatory and antioxidant properties in ginger help to relieve various inflammatory disorders like gout, osteoarthritis and rheumatoid arthritis (Habib et al., 2008). The antioxidants in ginger include gingerols, shogaols, monoterpenes, sequiterpenes, some phenolic derivatives and other phytochemicals which are responsible for their pharmacological activities (Li et al., 2001). Ginger acts as a hypolipidemic agent in cholesterol fed rabbits. Also, Akhani et al. (2004) reported that ginger treatment significantly decreased both serum cholesterol and triacylglycerol. In addition, Fuhrman et al. (2000) reported that ginger decreased LDL-cholesterol and triacylglycerol in apolipoprotein-E deficient mice. Many previous studies investigated the hepatoprotective effects of ginger extract against liver toxicity induced by ethanol, carbon tetrachloride, bromobenzene and acetaminophen with significant decrease in the level of ALT and AST (Mallikarjuna et al., 2008; El-Sharaky et al., 2009).

The present work was conducted to study the effect of ginger on liver antioxidant enzymes and glutathione content, serum lipid profiles and aminotransferases, urea, creatinine and serum glucose.

#### MATERIALS AND METHODS

Animals: Forty male New Zealand rabbits of  $30\pm 2$  days old weighing  $1800\pm 250g$  were kept in clean and disinfected metal cages. Food and water were available *ad libidum*. All animals kept on basal ration composed of 16.3% crude protein, 11.7% crude fiber, 0.4% calcium, 0.32% phosphorus, 1.359% magnesium and of 2580 kcal digestible energy/kg ration. The animals were allowed to acclimatize for a period of two weeks before the commencement of the experiment.

**Medicinal plant:** Ginger (*Zingiber Officinale Roscoea*) was purchased from the market of the herbs in Alexandria and mixed with the basal diet along the period of experiment.

Preparation of ginger extract:

2% Hot extract; 20 g of ginger powder was weighed then dissolved in 1 L of water and boiled, sieved, cooled and presented for animals each day freshly.

2% Cold extract; 20 g of ginger powder was weighed then soaked in 1 L of water for 10 hours, sieved and presented animals each day freshly.

Experimental design: All animals were allocated into four groups 10 rabbits/each as follow; Group (1): control group kept on basal diet. Group (2): ginger powder group received 2% ginger powder in basal diet. Group (3): cold extract group received 2% cold extract of ginger in drinking water. Group (4): hot extract group received 2% hot extract of ginger in drinking water. The experiment was extended for one month.

**Sampling**: Blood samples were collected from ear vein of all animals under the experiment. Samples were centrifuged at 3000 rpm/15 min. the obtained clear, non-hemolyzed sera were kept at -20°C until the time of analysis. The rabbits were slaughtered; eviscerated and liver tissues were harvested from the carcass and washed by normal saline, dried and weighed. The collected livers of each group were kept frozen at -20 °C until the time of analysis.

# **Biochemical analysis**

The determination of liver lipid peroxide as Malondialdehyde were measured spectrophotometrically after the reaction with thiobarbituric acid according to Placer et al. (1966); liver Glutathione peroxidase was determined chemically using cummene hydroperoxide as substrate according to Chiu et al. (1976); Glutathione-S-transferase activity was measured spectrophotometrically at room temperature as a rate of GSH conjugation of CDNB according to Habig et al. (1974); Glutathione was assayed by spectrophotometric technique according to Sedlack and Lindsay (1968).

The serum triacylglycerol was determined according to Fossati (1982); serum total cholesterol according to Thomas (1992); high density lipoprotein cholesterol according to Assmann (1979); serum low density lipoprotein cholesterol according to Assmann (1979); serum low density lipoprotein cholesterol according to Bauer (1982); serum Alanine aminotransferase activity and serum Aspartate aminotransferase activity were determined according to Reitman and Frankel (1957); serum alkaline phosphatase activity according to Kind and King (1954); serum gamma glutamyl transferase activity according to Szasz and Persijn (1974); serum glucose according to Kaplan (1984); serum urea according to Tabacco et al. (1979); serum creatinine according to Henry (1984); serum testosterone concentration according to Demetriou (1987).

# **Statistical analysis**

The data of biochemical parameters were compared among groups within periods using the GLM procedure of the Statistical analysis System computer package SAS, (1987). Means were compared by the LSMEAN of the same program. Data obtained were expressed in Mean  $\pm$  SEM.

# RESULTS

The liver lipid peroxidation (Malondialdehyde) content, glutathione peroxidase and glutathione-S-transferase and reduced glutathione concentration in rabbits fed basal diet supplemented with 2% ginger powder and ginger extract; hot and cold for 30 days are given in Table 1. All treated groups showed significant decrease of MDA concentration, and GST activity. The 2% hot extract of ginger treated group showed significant decrease of GPx activity, the ginger cold extract treated group showed also, significant decrease of GPx activity while, GSH concentration significantly increased as compared to control group.

| Table 1 - Effect of ginger powder, hot and cold extract on liver lipid peroxidation (nmol/g wet tissue), antioxidant enzymes activity (IU/g wet tissue) and Glutathione levels (µmol/g wet tissue) in rabbits liver |              |              |               |              |  |
|---|--------------|--------------|---------------|--------------|--|
|   | MDA          | GPx          | GST           | GSH          |  |
| Control group   | 62.2 ±1.73 ª | 8.26 ±0.66 a | 137.67±19.4 ª | 28.6 ±0.11 ° |  |
| Ginger powder 2%  | 39.5 ±2.67 b | 9.12 ±0.65 ª | 25.11 ±1.99 d | 37.99±0.86 b |  |
| Ginger hot extract 2%   | 31.6 ±2.49 ° | 5.17 ±0.66 b | 60.36 ±5.47 ° | 41.37±0.84 a |  |
| Ginger cold extract 2%  | 38.4 ±3.44 b | 4.32 ±0.53 b | 98.84 ±4.57 b | 37.62±1.15 b |  |
| Values are means ± standard errors. Means in a column without a common small letter differ significantly (P<0.05).  |              |              |               |              |  |

The serum lipid profile in rabbits fed basal diet supplemented with 2% ginger powder and ginger extract; hot and cold for 30 days are given in Table 2. The 2% ginger powder treated group showed significant decrease of triglycerides and total cholesterol while HDL-c significantly increased as compared to control group. The 2% hot extract ginger treated group showed highly significant increase of HDL-c and high decrease of LDL-c as compared to control group. The 2% cold extract of ginger treated group showed significant decrease of LDL-c as compared to control group. The 2% cold extract of ginger treated group showed significant decrease of LDL-c as compared to control group.



| Table 2 - Effect of ginger powder, hot and cold extract on serum lipid profile (mg/dl) in rabbits                  |                        |                        |                        |                               |              |
|--|------------------------|------------------------|------------------------|-------------------------------|--------------|
|  | TAG                    | Chol                   | HDLc                   | LDLc                          | VLDLc        |
| Control group  | 91.3± 6.72 a           | 77.0±0.93 a            | 38.2±1.05 °            | 20.5±2.13 b                   | 18.26±1.04 ª |
| Ginger powder 2%   | 72.0±3.31 <sup>b</sup> | 71.0±0.89 b            | 40.7±0.88 <sup>b</sup> | 16.0±1.98 <sup>b</sup>        | 14.4±1.12 b  |
| Ginger hot extract 2%  | 68.0±2.31 <sup>b</sup> | 70.0±1.15 <sup>b</sup> | 43.2±0.48 <sup>a</sup> | 16.2±1.68 b                   | 13.6±1.06 b  |
| Ginger cold extract 2%   | 88.0±3.46 <sup>a</sup> | 79.0±1.65 ª            | 37.0±0.73 °            | <b>28.4±0.95</b> <sup>a</sup> | 17.6±1.15 ª  |
| Values are means ± standard errors. Means in a column without a common small letter differ significantly (P<0.05). |                        |                        |                        |                               |              |

The serum enzyme activities in rabbits fed basal diet for 30 days supplemented with 2% ginger powder and ginger extract; hot and cold for 30 days are given in Table 3. All treated groups showed significant decrease of serum aspartate and alanine aminotransferase, gamma glutamyl transferase and alkaline transferase activities as compared with control group.

|                        | AST                     | ALT          | ALP                      | GGT                     |
|------------------------|-------------------------|--------------|--------------------------|-------------------------|
| Control group          | 62.2 ±1.73 ª            | 8.26 ±0.66 ª | 137.67±19.4ª             | 28.6 ±0.11 °            |
| Ginger powder 2%       | 39.5 ±2.67 b            | 9.12 ±0.65 ª | 25.11 ±1.99 d            | 37.99±0.86 <sup>t</sup> |
| Ginger hot extract 2%  | 31.6 ±2.49 °            | 5.17 ±0.66 b | 60.36 ±5.47 °            | 41.37±0.84              |
| Ginger cold extract 2% | 38.4 ±3.44 <sup>b</sup> | 4.32 ±0.53 b | 98.84 ±4.57 <sup>b</sup> | 37.62±1.15 <sup>t</sup> |

The serum glucose, urea, creatinine and testosterone hormone concentration in rabbits fed basal diet supplemented with 2% ginger powder and ginger extract; hot and cold for 30 days are given in Table 4. The serum glucose and creatinine concentration were significantly increased, while the serum testosterone concentration was significantly decreased in all ginger-treated groups as compared to control one. The serum urea concentration only significantly decreased in 2% ginger powder treated group as compared to control one.

| Table 4 - Effect of ginger powder, hot and cold extract on serum glucose, urea and creatinine concentration (mg/dl) and serum testosterone concentration (mg/dl) in rabbits |                                |                           |                               |                        |  |
|---|--------------------------------|---------------------------|-------------------------------|------------------------|--|
|   | Glucose                        | Urea                      | Creatinine                    | Testosterone           |  |
| Control group   | 65.0±1.34 °                    | 38.3±0.88 ª               | 0.99±0.03 b                   | 4.72±0.17 ª            |  |
| Ginger powder 2%  | 80.0±1.83 ª                    | 33.3±0.99 b               | 1.21±0.03 a                   | 1.51±0.19 °            |  |
| Ginger hot extract 2%   | 72.2±2.32 b                    | 30.2±1.01 b               | <b>1.14±0.01</b> <sup>a</sup> | 2.72± 0.35 b           |  |
| Ginger cold extract 2%  | 82.7±1.74 ª                    | 38.8±1.05 ª               | 1.22±0.04 <sup>a</sup>        | 0.72±0.08 <sup>d</sup> |  |
| Values are means ± standard errors.   | Means in a column without a co | ommon small letter differ | significantly (P<0.05).       |                        |  |

# DISCUSSION

The present study demonstrated that ginger treatment for thirty days significantly decreased the MDA concentration, GPx and GST activities and significantly increased concentration of GSH as compared to control group. Decreasing lipid peroxidation by ginger treatment may be attributed to its antioxidant activity as it contains many phenolic compounds which have inhibitory effect on lipid peroxidation, these phenolic antioxidants may conserve the antioxidant enzymes but increase SH- containing compounds including glutathione. This explanation was agreed with Ahmed et al. (2000) who reported that ginger significantly lowered lipid peroxidation by ameliorating the activities of the antioxidant enzymes; superoxide dismutase (SOD), catalase and glutathione peroxidase in rats. Moreover, Sujatha and Srinivas (1995) revealed that the aqueous extract of ginger inhibited lipid peroxidation and formation of diene, triene and tetraene conjugates in human erythrocyte membrane. Supplementation with ginger can reduce free radical mediated oxidative stress to the cells, the crude gingerol extract was found to have antioxidant activity (Asnani and Verma, 2009). Also, these results were in harmony with Liu et al., (2003) who recorded that administration of either 2% ginger or 5% ginger containing diets to hyperlipidemic rats showed increased GSH and decreased plasma lipid peroxide levels. The depletion of antioxidant enzymes may be explained as ginger offered protection to cells against oxidative stress by scavenging free radicals (Guo et al., 1997). This may be due to the presence of many antioxidative compounds like gingerols, shogaols, phenolic ketone derivatives, volatile oils and flavonoids in ginger, these antioxidant compounds may modulate spare the antioxidant enzymes (Young et al., 2005).

The hypolipidemic effect of ginger may be attributed to stimulation of the conversion of cholesterol to bile acids, an important pathway of elimination of cholesterol from the body by ginger. The activity of hepatic cholesterol-7- $\alpha$ -hydrolase, the rate limiting enzyme of bile acid biosynthesis from cholesterol was significantly elevated in ginger treated animals (Heeba and Abd-Elghany, 2010). Also, the hypocholesterolemic effects of ginger may be due to the inhibition of cellular cholesterol synthesis, since, ((E)-8 beta,17-epoxyllabed-12-ene-15,16 dial) compound was isolated from ginger and interfered with cholesterol biosynthesis in liver homogenate in hypercholesterolemic mice causing its reduction (Tanabe et al., 1993). Our results were in agreement with

Bhandari et al. (2005) who demonstrated that the ethanolic extract of ginger significantly reduced serum total cholesterol and triglycerides and increased the HDL-c levels, also the extract can protect tissues from lipid peroxidation and exhibit lipid lowering activity in diabetic rats. However, our results were disagree with Rong et al. (2009) who reported that treatment of male and female rats with ginger powder up to 2000mg/ kg for 35 days did not affect serum total cholesterol and triglyceride levels. These differences may be attributed to different dose and sex used in the two experiments.

Administration of ginger improved liver function s as it reduced liver enzymatic activities. These results were in accordance with that of Mallikarjuna et al. (2008) who showed that administration of ginger ethanolic extract (200 mg/kg) orally from day 15 to day 21 along with country-made Liquor (CML) produced significant lowering of AST, ALT, ALP and tissue lipid peroxide levels.

Treatment of ginger significantly decreased serum urea and increased serum creatinine concentration since, ginger contain polyphenols and flavonoids that influence removing certain waste products from plasma. These results agree with Ajith et al., (2007) who reported that the presence of polyphenols and flavonoids in ginger extract might be responsible for the antioxidant nephroprotective activities and the reduction of serum urea and creatinine levels. Creatinine is an organic base formed during muscle protein metabolism as a degradation product of Creatine phosphate. Like many other organic bases, creatinine is filtered at the glomerulus and eliminated from plasma by the kidney. It means that creatinine is filtered only but is not reabsorbed; therefore ginger might have little influence on its excretion, whereas urea is filtered and reabsorbed partly in the nephron. In addition the relation of urea to the water reabsorption may cause extra cellular contraction, which consequently resulted higher concentration of substances such as creatinine in plasma (Mehrdad et al., 2007); this may be the reason for higher significant level of creatinine in rabbits receiving 2% ginger. However, Dias et al. (2006) found that serum creatinine levels were not modified by ginger treatment.

Serum testosterone level significantly decreased, since ginger at higher doses may reduce testicular mass due to feedback reaction while serum glucose level was significantly increased. Our results concerning testosterone were agree with Rong et al. (2009) that oral administration of ginger powder at 2000mg/kg for 35 days slightly but significantly decreased the weight of testes in rats. Also, Morakinyo et al. (2010) reported significant decrease in the weight of testes and serum testosterone concentration in rats given oral aqueous ginger extract (500mg/kg body weight) for 30 days. The decrease in the level of testosterone may be contributed to decrease level of cholesterol as observed in our results which is a precursor of steroid hormone biosynthesis. However, our results were disagree with that of Mallikarjuna et al., (2008) who recorded that aqueous ginger extract administered orally over 8 days significantly increased the weight of testis and the serum testosterone levels in rats. Moreover, Khaki et al., (2009) who reported that serum testosterone level increased significantly in rats received 100 mg/kg body weight for 8 weeks. These discrepancies in the results may be attributed to the dose and the duration of experiment.

Unfortunately, our results regarding blood glucose were disagree with, Sakr, (2007) who reported that Ginger was found to decrease blood glucose in adult male rats. Also, Supplementation with ginger oil significantly reduced the level of blood glucose (9.38%) in non-diabetic rats (Al-Attar and Zari, 2007). However, Weidner and Sigwart, (2000) failed to reproduce the hypoglycemic effect of ginger extract with doses 25, 50 and 100 mg/kg in rats and rabbits. Also Bordia et al. (1997) demonstrated that no effect on blood glucose sugar was observed in healthy human and patients with coronary arterial disease when given 4 gm of ginger daily for 3 months. Even administration of ginger powder to rats up to 2000mg/kg for 35days and 1%, 2%/kg diet for 30 days did not affect serum glucose that suggested that ginger not interfere with glucose metabolism under physiological status (Shanmugam et al., 2011).

#### CONCLUSION

The use of ginger was beneficial in lowering lipid profiles and lipid peroxidation and has hepatoprotective and nephroprotective effects, but its effect on serum sugar and testosterone levels need further more studies.

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