Effect of ginger consumption on serum makers of general metabolism, liver and kidney functions and lipid profiles in ethanol induced withdrawal rats.

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ABSTRACT

Introduction: Routine biochemical assays has led to increased incidental findings of pathogenesis of chronic alcoholism. A thorough history and physical examination, followed by a series of blood tests, are essential for the comprehensive evaluation of the disease. Objective: Chronic intake of high dose alcohol may cause oxidative stress, and associated metabolic abnormalities in the body. The effect of long-term alcohol consumption on the biochemical parameters under withdrawal stress has not been explained well. In this study we investigated the restorative effect of aqueous extract of Zingiber officinale against ethanol induced serological changes in male albino rats. Material and Methods: Male wistar albino rats were maintained for 42 days as follows: I. Control, II. Alcohol-treated group, III. Alcohol-withdrawal group and IV. Ginger treated withdrawal group, with all groups containing 6 animals each and 72 hrs of post treatment in case of withdrawal groups. At the end of treatment period, serum cholesterol, triglycerides, phospholipids, albumin, bilirubin and enzymatic activities of GGT, ALT and AST in the rat serum or plasma were measured by using standard methods. Results: Metabolic markers and lipidic markers were significantly increased in the alcohol-treated group compared to control. A significant reduction in serum TC, LDL-c, TG, and total phospholipids was observed accompanied by an increase in HDL-c levels in ginger extract treated rats. No significant difference between the groups was observed when LFTs and renal damage markers were compared. Conclusions: Ginger supplementation can modulate different toxic effects that arise due to ethanol treatment and restored the normal levels of many altered biochemical parameters in rat serum. Together, our data suggest that consumption of ginger could be useful in the treatment of obesity and other disorders related to cardiovascular diseases (CVD) due to its hypolipidaemic property.

Key words: Ginger, Renal Markers, LFTs, Lipids, Plasma, Ethanol Withdrawal.

INTRODUCTION

Alcohol is generally accepted to be a toxic compound on cells or tissues capable of reacting with nucleophiles including nucleic acids, proteins, peptides, amino acids, lipids, and carbohydrates. Also, oxidation of alcohol generates an excess of NADH, which alters redox state in the cytosol, in turn, is responsible for a variety of metabolic abnormalities such as hyperlactacidemia, hyperuricemia, depressed citric acid cycle activity, enhanced hepatic lipogenesis, decreased hepatic release of lipoproteins, lipolysis of peripheral fat, altered mitochondrial oxidative metabolism, changes in mitochondrial structure and function, protein breakdown, depending on the condition hypo/hyperglycemia, the block of hepatic gluconeogenesis by ethanol [39,38,31,40,12]. Production of excess AcD, NADH, reactive oxygen species, lipid peroxidation and protein oxidation due to alcohol metabolism may result in metabolic chaos within the cell or tissue biochemistry during chronic alcoholism. Toxic compounds (adducts of proteins, lipid peroxides, AcD, free radicals), which have damaging effects on cellular biomolecules, are well documented and their consequences have been implicated in the etiology of a number of human disorders [12,47,2,45,11,48]. While ethanol itself is pro-oxidant because it directly generates reactive oxygen species during its metabolism [88], ethanol withdrawal (EW) i.e., sudden abrupt cessation from ethanol; produces oxidative stress indirectly through the activation of excitatory neurotransmitter receptors and the concomitant alteration of intracellular calcium levels [27]. These events will eventually lead to oxidative stress [23]. Several studies have demonstrated that ethanol withdrawal induces oxidative damage in vivo and in vitro [55, 42, 31,32].

Ginger a common spice with a renowned medical record has an established hypolipidaemic [10,55,9], anti – hypercholesterolemic [23,7,28], Hepatoprotective [44,22],antioxidant properties [60], hypoglycemic [10,3,5] and hypouremic activities [8].

In the light of current knowledge regarding alcoholism biochemistry, it is suggested that blood chemical test levels could be changed after acute or chronic alcohol intake. Indeed some biochemical tests like γ-glutamyl transferase (GGT), alanine transaminase, aspartate transaminase, etc. were used as a laboratory test in the evaluation of clinic alcoholism pathogenesis [41,51,59] but these levels during withdrawal needs to be elucidated. The aim of the present study was to examine changes in certain serological test values and to evaluate biochemical changes in the blood of male rats fed chronically with alcohol and after withdrawal from chronic ethanol intoxication under treatment with ginger extract.

MATERIAL AND METHODS

Chemicals:
All chemicals used in the present study were of Analar grade (AR) unless otherwise mentioned and obtained from the following scientific companies: Sigma (St. Louis, MO, USA), Fisher (Pittsburg, PA, USA), M/s Merck (Mumbai, India), M/s Himedia Laboratories Pvt. Ltd, Mumbai, India, M/s Sisco research Laboratories (Mumbai, India ), M/s Ranbaxy (New Delhi, India), Qualigen (Mumbai, India), M/s Loba Chemie (Mumbai, India). M/s
**Swaroopa, Maralla et al. / Journal of Pharmacy Research 2012,5(1),485-491**

SRL India. Ethanol was obtained from Hyman chemicals company, Egypt. In the present investigation Barnstead Thermoline water purification plant for Double Distillation, HAHNVAPOR Rotary Evaporator HS-2005V, Mini Lyodl lyophilizer, Kubota KR2000T centrifuge and Hitachi U-2800 Spectrophotometer and other standard equipments were used for biochemical/physiological analyses.

Ginger extract Preparation:
The fresh rhizomes of Zingiber officinale were obtained from local market and identified by the herbarium staff of the Botany Department, Sri Venkateswara University, Tirupati, India. Ginger extract was prepared using the method of Akhani et al., (2004), with slight modifications. Fresh rhizomes of ginger (1Kg) were collected and crushed, then Soxhlet extracted with double distilled water, rotavaporated and lyophilized to obtain the aqueous extract, which was stored in deep freezer at -20°C in a well-closed glass container.

Animal Maintenance:
The study involved young (3–4 months old; 200 - 220 g) male albino rats of Wistar strain purchased from Sri Venkateswara Traders Pvt. Limited, Bangalore, maintained in the animal house of the department in polypropylene cages. The animals were allowed to habituate to the animal facilities for at least for two weeks adaptation period upon arrival and were maintained under standard conditions of humidity (50% relative humidity), room temperature (25 - 28°C) and 12 h light/12 h dark cycle (lights off at 6:00 P.M. and lights on at 6:00 A.M.). They were fed with standard rat pellet diet (M/s Hindustan Lever Ltd., Mumbai) ad libitum and had free access to water. Experimental animals were handled according to the University and Institutional Legislation, regulated by the committee for the purpose of Control and Supervision of experiments on Animals (CPCSEA), Ministry of Social Justice and empowerment, Government of India.

Experimental protocol:
The experimental animals were divided into 4 groups; each group contained six animals: Control group G1 (normal controls without treatment), Alcoholic group G2 (injected with 2g/kg b.w. of 20% alcohol, Hyman.), Ethanol withdrawal rats G3, treated with alcohol for 6 weeks abstained from alcohol for 72 hrs before sacrificed, treated withdrawal group G4, treated with ginger for 6 weeks but abstained from alcohol for 72 hrs before they were sacrificed (firstly, the rats were given alcohol along with ginger for 6 weeks but abstained from treating with both for 72 hrs before they were sacrificed). Ginger extract was given orally to the rats through a gastric intubation daily for 6 weeks at a dose of 200mg/kg body weight.

Collection of blood samples:
At the end of the 6 weeks of treatment, all the animals were sacrificed by cervical dislocation, blood samples were collected by cardiac puncture into clean, heparinized microfuge tubes, plasma was separated by centrifugation at 3500 rpm for 10 minutes and stored at -20°C for biochemical analysis. While samples from the ethanol withdrawal rats of both ginger treated & untreated groups were collected by sacrificing after 72 hours of the last dose of ethanol with procedure as mentioned above.

Biochemical analysis:
Serum samples were analyzed for glucose by the methods described by Trinder (1969) and the levels of total proteins in serum was quantified as described by Lowry et al., (1951), the tissue and serum lipids were extracted according to the method described by Folch et al., (1957). The lipid parameters including total cholesterol Zaltkis et al., (1953), triglycerides Foster et.al (1973), free fatty acids Falholt et al., (1973) phospholipids Zifersmit et al., (1950), total lipids analysis according to the method of Woodman and Price (1972) were estimated. Concentrations of plasma HDL- C were measured by standard enzymatic methods of Izzo et al., (1981 ). LDL- C & VLDL- C concentration was calculated using the Friedewald formula (Folch, J., 1957 ), Serum total bilirubin was determined by Walter and Gerard method (1970). The enzymatic activities of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALAT) (Reitman And Frankel, 1957) Lactate Dehydrogenase (LDH) was determined by King(1965), Serum alkaline phosphatase activity was performed using Kind and King (1954) method. Amylase activity by method of Somogyi (1961), γ-Glutamyl transferase activity is estimated according to Rosalki and Rao(1972). Non-protein nitrogen constituents were determined by the methods of Patton and Crouch (1977) for urea, Fossati et al., (1980) for uric acid and Bartels and Bohmer (1972) for creatinine.

Statistical analysis:
Data were statistically analyzed by one-way analysis of variance followed by Dunn’s test (SPSS). Finally, significant difference (L.S.D) was used to test the difference among treatments. Results were considered statistically significant when (P < 0.05).

**RESULTS**

General Metabolic parameters: The administration of ginger extract to the alcoholic rats significantly reduced plasma glucose level when compared with alcoholic group. This reduction was not enough to reach normal rats, but it was still significantly higher when compared with the normal group, as shown in Table 1 and illustrated in (Figs. 1 & 2). On the other pretreated with ginger extract and then induced-dwthdrawal when compared with alcoholic group, but it was still significantly higher than normal group.

**Table I. Effects of withdrawal due to chronic ethanol administration on the general biochemical parameters in rat serum or plasma.**

<table>
<thead>
<tr>
<th>Metabolic parameters</th>
<th>Control group G1</th>
<th>Alcohol-treated group G2</th>
<th>Ethanol Withdrawal group G3</th>
<th>Ginger treated Ethanol Withdrawal group G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>108.8±7.48</td>
<td>195.5±4.79</td>
<td>156.68±22.50</td>
<td>119.31±49.61</td>
</tr>
<tr>
<td>Protein (g/L)</td>
<td>6.41±19.19</td>
<td>6.94±6.67</td>
<td>6.91±0.58</td>
<td>6.32±0.30</td>
</tr>
<tr>
<td>LDH IU/L</td>
<td>847.04±26.27</td>
<td>2099.18±45.43</td>
<td>1475.15±21.82</td>
<td>820.40±16.09</td>
</tr>
<tr>
<td>Amylase(U/L)</td>
<td>1128.51±40.67</td>
<td>1780.96±49.03</td>
<td>1731.17±73.34</td>
<td>1247.25±27.54</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D of 6 animals. Alcoholic control is compared with normal. Withdrawal groups are compared with both normal and Alcoholic control. * Values are statistically significant at P* <0.05 when compared with normal. #Values are statistically significant at P# <0.05 when compared with Alcoholic control.

**Fig. 1: Effect of treatment of ginger extract 200 mg/kg (body weight) on the levels of plasma glucose, lipid profile, Creatinine, uric acid and alcohol abstained rats.**

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In addition to glucose, levels of γ-glutamyl transferase, total amylase and pancreatic amylase were also significantly elevated in the alcohol-treated group. Amylase is a sensitive indicator in pancreatitis diagnosis. In the study, serum total and pancreatic amylase levels were significantly higher in rats of alcohol-treated group but these test levels were elevated in ew ethanol-fed rats compared to control group. Thus, it may be assumed that the high amylase levels serve as a good diagnostic marker in chronic alcoholic pancreatitis, as it is still used as a marker in the clinic evaluation of pancreatitis.

Table II. Effects of ginger extract on the Lipid Profiles during chronic ethanol administration & withdrawal in rat serum or plasma.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control G1</th>
<th>Alcohol-treated G2</th>
<th>Ethanol Withdrawal G3</th>
<th>Ginger treated Withdrawal G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Lipid Content</td>
<td>247.35±16.73</td>
<td>332.53±6.79</td>
<td>338.15±12.27</td>
<td>258.45±11.10</td>
</tr>
<tr>
<td>Phospholipids</td>
<td>76.41±4.66</td>
<td>123.36±15.33</td>
<td>112.92±10.31</td>
<td>94.43±6.55</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>55.15±4.77</td>
<td>137.12±6.10</td>
<td>136.71±11.97</td>
<td>87.01±9.69</td>
</tr>
<tr>
<td>Free Fatty Acids</td>
<td>61.68±4.50</td>
<td>82.24±8.68</td>
<td>79.56±4.87</td>
<td>69.11±8.45</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>103.40±17.53</td>
<td>199.20±14.69</td>
<td>174.05±11.49</td>
<td>112.85±7.68</td>
</tr>
<tr>
<td>HDL c</td>
<td>42.83±3.37</td>
<td>31.03±8.07</td>
<td>33.11±8.34</td>
<td>46.75±2.71</td>
</tr>
<tr>
<td>LDL c</td>
<td>37.03±7.65</td>
<td>71.42±4.52</td>
<td>64.10±6.76</td>
<td>32.36±9.66</td>
</tr>
<tr>
<td>VLDL c</td>
<td>17.07±2.24</td>
<td>33.77±6.61</td>
<td>31.79±3.22</td>
<td>24.38±6.32</td>
</tr>
<tr>
<td>ALAT (IU/L)</td>
<td>79.57±6.95</td>
<td>110.93±15.84</td>
<td>86.91±6.09</td>
<td>88.14±5.61</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D of 6 animals. Alcoholic control is compared with normal. Withdrawal groups are compared with both normal and Alcoholic control. * Values are statistically significant at P* < 0.05 when compared with normal. #Values are statistically significant at P# < 0.05 when compared with Alcoholic control.

On the other hand, as shown in Table, the treatment of rats with ginger extract together with alcohol administration caused a significant reduction in the plasma levels of cholesterol and LDL-cholesterol when compared with alcoholic rats, but HDL-cholesterol level recorded significant elevation when compared with alcoholic rats, while plasma triglycerides statistically did not change when compared with alcoholic rats, but there was a significant increase when compared with normal group. Furthermore, the levels of plasma cholesterol and HDL-cholesterol in rats pretreated with ginger extract recorded a significant increase when compared with normal group, in contrast, LDL-cholesterol recorded a significant decrease when compared with control group as shown in Table 2.

Liver function tests
The present study indicated the adverse effect of chronic ethanol on enzyme activities of ALT, AST and γ-glutamyltransferase (GGT) are considered to be a sign of alcohol abuse. In the present study, the hepatoprotective effect of ginger aqueous infusion when given orally to the rats was evident by significant reduction in ALT, AST, ALP and total bilirubin in rats receiving ginger along with withdrawal when compared to the ethanol withdrawal group only (Table III).

Fig. 2: Effect of treatment with ginger extract 200 mg/kg (body weight) on lipid profiles in ethanol withdrawal rats.

Fig. 3: Effect of treatment with ginger extract 200 mg/kg (body weight) on the levels of markers of liver membrane damage due to chronic ethanol ingestion and during ethanol withdrawal.

Kidney Function Markers:
As shown in Table 1V, the alcohol produced significant increase in the levels of plasma creatinine, urea and uric acid when compared with normal group, while, administration of ginger extract to the alcoholic rats significantly reduced the levels of plasma creatinine, urea and uric acid when compared with the alcoholic group, but no significant changes were observed when compared with the normal rats. This indicates that, treatment with ginger extract normalized the plasma creatinine, urea and uric acid.

On the other hand, the treatment followed by induction of withdrawal decreased significantly the levels of plasma creatinine and uric acids when compared with the alcoholic group. Furthermore, they are still significantly higher than normal rats. In contrast, non-significant increase was observed in plasma urea when compared with alcoholic group, but it was still significantly higher than normal rats as shown in Table 1V.

Table III. Effects of ginger extract on the LFTs during chronic ethanol administration & withdrawal in rat serum or plasma.

<table>
<thead>
<tr>
<th>Markers for Liver damage</th>
<th>Control group G1</th>
<th>Alcohol -treated group G2</th>
<th>Ethanol Withdrawal group G3</th>
<th>Ginger treated Withdrawal group G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALAT (SGPT) I/U L</td>
<td>11.26±3.99</td>
<td>14.95±8.60</td>
<td>13.88±5.47</td>
<td>10.97±2.46</td>
</tr>
<tr>
<td>AsAT (SGOT) I/U L</td>
<td>15.63±8.84</td>
<td>18.27±3.33</td>
<td>17.94±8.06</td>
<td>15.52±6.73</td>
</tr>
<tr>
<td>γ GGT I/U L</td>
<td>10.54±4.35</td>
<td>23.42±6.53</td>
<td>21.56±8.23</td>
<td>13.97±2.24</td>
</tr>
<tr>
<td>Total Bilirubin (mg/dL)</td>
<td>0.63±0.03</td>
<td>0.92±0.12</td>
<td>0.73±0.18</td>
<td>0.67±0.14</td>
</tr>
<tr>
<td>ALP (I/U L)</td>
<td>79.57±6.95</td>
<td>110.93±15.84</td>
<td>86.91±6.09</td>
<td>88.14±5.61</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D of 6 animals. Alcoholic control is compared with normal. Withdrawal groups are compared with both normal and Alcoholic control. * Values are statistically significant at P* < 0.05 when compared with normal. #Values are statistically significant at P# < 0.05 when compared with Alcoholic control.
Triglycerides accumulation can be thought of as resulting from an imbalance between the rate of synthesis and the rate of release of triglycerides by the parenchymal cells into the systemic circulation [49]. The elevated plasma triglycerides levels observed might have been partially due to lipoprotein lipase. Modest hypertriglyceridemia occurs in association with alcohol, virus and drug induced hepatitis [20]. The mechanism of this process may involve reduction of lipolytic enzymes, namely, hepatic triglyceride lipase and lipoprotein lipase [49]. The reduction of these enzymes may lead to decreased removal of triglycerides from plasma and their probable accumulation in tissues. We observed significantly reduced levels of lipids in plasma of ginger treated rats, thus showing the beneficial effect of ginger against ethanol-toxicity.

The serum levels of LDL-C was significantly elevated in ethanol group. The phenolic compounds have been shown to form phenoxyl radicals in the presence of peroxidases. The elevated level of LDL-C was significantly reduced in ginger treated rats may be due to the antioxidant property of ginger which is capable of inhibiting the LDL-C peroxidation. It has been reported that hypolipidemic drugs with antioxidant properties, may prevent LDL-C peroxidation and retard the accumulation [18]. The depleted levels of serum HDL-C in the ethanol rats may be due to hypertriglyceridemia induced by reactive metabolite formed during biotransformation. The HDL-C is a free radical scavenger and prevents peroxidation of beta lipoproteins [14]. Decreased HDL-C may be due to diminished lecithin cholesterol acyl transferase (LCAT) activity and may also contribute to the increased cholesterol level. An increase of LDL-c and VLDL may also cause a greater decrease of HDL-C as there is a reciprocal relationship between the concentration of VLDL-C and HDL-C. In our study, the levels of LDL-C and VLDL-C were found to be increased and HDL-C decreased in ethanol-treated rats. Administration of ginger significantly decreased the levels of VLDL-C and LDL-C and increased HDL-C.

Concerning protein concentration, Doyle et al. [20] supported the present decreased result. They proved it to inhibition of hepatic protein secretion by ethanol that was associated with accelerated catabolism of unsecreted plasma proteins suggesting hepatocellular degradative processes that are usually responsive to the change in the levels of protease activity and/or perturbation of the secretory process. The same harmful lowering effect of ethanol ingestion was proved to be reflected on other liver parameters; on urea [19,61,62], on protein and albumin/globulin ratio [12], Wickramasinghe et al. [18] also found reduction in serum albumin in alcohol toxicity. The lowering of serum albumin level had also been supported by Troitskii et al. [19] demonstrating the modification of rat serum albumin that was attributed to shift to J-fetoprotein during chronic and acute alcoholism. Donohue et al. [19] reported that there was 50% degradation in total plasma protein and a 46% increase in albumin catabolism where the reduction was more severe with malnutrition. In addition, Dinarello [18] stated that the acute phase response caused decreased hepatic albumin synthesis.

The specified factors leading to LDH inhibition in chronic alcoholism were the increased “NADH/NAD” ratio causing shift to the left in the equilibrium of the oxidoreductive couple lactate-pyruvate resulting in hyperlactacidemia [10]. The extracellular release of LDH [10] could lead to liver LDH lowering. This found support the statement that chronic alcoholism caused extracellular release of hepatic LDH raising its activity in plasma [14].

The stimulation of protein synthesis in healthy ginger group may be related to a protein promoting action of ginger. Hipkiss and Chan [20] proved the ability of carnosine to protect the already formed proteins against inactivation. Kang et al. [21,22] stated that the acute phase response caused decreased hepatic albumin synthesis.

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**DISCUSSION**

Chronic consumption of alcohol can result in spectrum of abnormalities in many organ systems [17,21,49]. Our study of alcohol administration was carefully controlled and withdrawal was monitored. In this work we have studied the effect of treatment with ginger extract on blood glucose, lipid profile and kidney functions in ethanol-induced withdrawal rats through 6 weeks of chronic treatment. To examine these effects the levels of plasma glucose, cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, creatinine, urea and uric acid were determined. Furthermore, biological markers of alcohol consumption (GGT), hepatocellular injury (AST and ALT) and protein synthesis (albumin) were measured.

Present study revealed a significant rise in the enzyme markers of liver cell membrane disruption viz, AST, ALT, ALP and GGT level on exposure to ethanol, indicating considerable hepatocellular injury. In our study group, the level of serum marker enzymes were normalized after three days of abstinence, contrary to GGT activity. The observed decrease in the activities of these enzymes shows that ginger, to some extent, preserves the structural integrity of the liver from the toxic effect of ethanol. As regards ALP, the extracellular discharge was also recorded [18]. Decreased protein synthesis as a cause of lowered activities of the two transaminases had long been noticed [16].

Our findings demonstrate that ginger has hepatoprotective and antihyperlipidaemic effect, which is evidenced by the decreased levels of total cholesterol, triglycerides, free fatty acids, phospholipids, low density lipoprotein-C, very low density lipoprotein-C and elevated levels of HDL-C in the plasma of ethanol-toxicity in rats. These properties are comparable to the standard drug silymarin. The 200mg dose of aqueous extract showed promising hepatoprotective and antihyperlipidaemic effect.

### Table IV. Effects of ginger extract on Renal damage Markers of rat serum or plasma during chronic ethanol administration & withdrawal.

<table>
<thead>
<tr>
<th>Renal damage Markers (mg/dl)</th>
<th>Control group G1</th>
<th>Alcohol treated group G2</th>
<th>Ethanol Withdrawal group G3</th>
<th>Ginger treated Ethanol Withdrawal Group G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.758±0.45</td>
<td>4.616±0.41</td>
<td>3.981±0.21</td>
<td>3.631±0.52</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.310±0.026</td>
<td>0.451±0.074</td>
<td>0.397±0.087</td>
<td>0.342±0.064</td>
</tr>
<tr>
<td>Urea</td>
<td>19.38±2.96</td>
<td>23.58±2.96</td>
<td>22.42±3.15</td>
<td>18.11±1.37</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>1.167±0.18</td>
<td>1.955±0.37</td>
<td>1.033±0.25</td>
<td>1.090±0.24</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D of 6 animals. Alcoholic control is compared with normal. Withdrawal groups are compared with both normal and Alcoholic control. *Values are statistically significant at P* <0.05 when compared with normal. #Values are statistically significant at P# <0.05 when compared with Alcoholic control.

### Fig. 4: Effect of treatment with ginger extract 200 mg /kg (body weight) on the levels of Renal damage Markers in ethanol withdrawal and chronic ethanol fed rats.
drawal rats. These results are in agreement with the study of Akhani et al.,[5] who found that post-treatment and pretreatment of streptozotocin-induced diabetic rats with ginger extract significantly decreased the blood glucose level and increased the insulin level. Kar et al.,[14] reported that, the inorganic part of a medicinal plant contains many mineral elements, which are responsible for the hypoglycemic activity. In support of this view, a number of essential minerals (Ca, Zn, K, Mn and Cr), are known to be associated with the mechanisms of insulin release and its activity in different animals and in human beings.[15]

The results indicate, injection of ethanol caused an increase of plasma lipid profile. These results are similar to the study of Martinez-conde et al.,[19], who reported that ethanol have lipolytic action on adipocytes, increasing plasma levels of free fatty acids. Srinivasan and Sambayal[52] reported that feeding rats with ginger significantly elevated the activity of hepatic cholesterol 7-alpha-hydroxylase which is a rate-limiting enzyme in the biosynthesis of the bile acids and stimulates the conversion of cholesterol to bile acids leading to the excretion of cholesterol from the body. In support of this view, the study of Bhandari et al.,[13] revealed that posttreatment with ginger extract to the cholesterol-fed rabbits for 70 days resulted in less marked hyperlipidemia. Hypolipidaemic and anti-atherosclerotic effects of ginger extract were also demonstrated in cholesterol-fed rabbits[40]. It was concluded that the hypocholesterolaemic effect of ginger could have possibly resulted from the inhibition of cellular cholesterol biosynthesis after the consumption of the extract.[21] Furthermore, Neess et al.,[41] reported that the reduction of cellular cholesterol biosynthesis is associated with increased activity of the LDL receptor, which in turn leads to enhanced removal of LDL from plasma, resulting in reduced plasma cholesterol concentration.

In the present study the effect of ginger on the kidney functions was assessed by the determination of the levels of plasma creatinine, urea and uric acid, and the study revealed that post-administration of ginger extract to the diabetic rats reduced and normalized the levels of plasma creatinine, urea and uric acid. Moreover, the study of Ajith et al.,[14] demonstrated that ethanol extract of ginger rendered significant protection against induced nephrotoxicity, which was evident from the lowered serum urea, and creatinine levels in the mice that pre-treated with ginger extract, and this study concluded that ginger extract significantly protected the elevation of serum creatinine and urea levels. In addition, Ajith et al.,[14] 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.

From the data obtained, it is concluded that treatment with ginger extract produced a significant anti-hyperglycemic, hypocholesterolaemic, anti-atherosclerotic, and antihepatotoxic effects. Furthermore, ginger is capable of improving hyperlipidemia and the impaired kidney functions in ethanol-induced withdrawal rats.

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