http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 14 (3): 219-225, 2011
ISSN 1028-8880 / DOI: 10.3923/pjbs.2011.219.225

Effects of Taurine on Glutathione Peroxidase, Glutathione Reductase and Reduced Glutathione Levels in Rats

[1]P. Anand, [1]D. Rajakumar, [1]Mathew Jeraud, [2]A. John William Felix and [1]T. Balasubramanian
[1]Department of Physiology, Rajah Muthiah Dental College,
[2]Department of Community Medicine, Rajah Muthiah Medical College,
Annamalai University, Annamalainagar-608 002, Tamilnadu, India

Abstract: The aim of the present study is to investigate the effects of oral administration of taurine on endogenous glutathione peroxidase (GPx) and Glutathione Reductase (GR) activities and reduced glutathione (GSH) level in normal rats. Normal saline (Group I) or 5% taurine in normal saline was administered in dose of 50 mg (Group II), 250 mg (Group III) or 500 mg kg^{-1} of body weight (Group IV) through intragastric intubation for 60 days. GPx and GR enzyme activities and GSH and taurine levels were determined in liver, heart, stomach, kidney and plasma of normal Wistar rats. GPx activity showed an increase in liver, heart, stomach and plasma. GR activity increased in kidney and decreased in liver and plasma. GSH levels increased in liver, stomach and decreased in kidney. Liver showed an increase and heart, stomach and kidney a decrease in taurine level in taurine administered rats when compared to control rats. The results varied from organ to organ and the observed variations among organs might be related to their respective enzymatic, non-enzymatic antioxidant potential and its functions. From the present study it may be concluded that long term oral administration of taurine affects GPx, GR and GSH levels in normal rats.

Key words: Glutathione enzyme, free radical, taurine, redox-state, oxidative stress, prophylactic agents

INTRODUCTION

In tissues, the oxidation-reduction state also called the redox state depends on the delicate balance between oxidants and antioxidants status at any given time. The oxidants are the free radicals and reactive oxygen or nitrogen species (ROS and RNS , respectively) produced in the body as a result of regular intermediary metabolism and other oxidative processes like respiratory bursts seen in neutrophil during phagocytosis. Apart from their roles in the intermediary metabolism and body defence, the oxidants also play a major role as regulatory mediators in signalling processes (Seifried *et al*., 2007). However, at high concentration, oxidants can damage all major cellular constituents and is termed as oxidative stress (Valko *et al*., 2007). The oxidative stress is implicated in the pathogenesis of various disorders like cancer, diabetes, cardiovascular diseases, autoimmune diseases and neurodegenerative disorders (Nakagawa and Miyata, 2008; Mates *et al*., 1999; Gwarzo *et al*., 2010; Kayode *et al*., 2009; Vaghasiya and Chanda, 2010). Potentially damaging oxidative stress is kept in check by endogenous cellular antioxidant mechanisms, which include antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) and nutrient derived antioxidant small molecules (vitamin C, vitamin E, carotenes, flavonoids, glutathione, uric acid and taurine (Devasagayam *et al*., 2004).

Unfortunately, the public has become too familiar with the term antioxidant and equates it to a chemical that is good for our wellbeing. Antioxidant foods, drinks (often in parallel unhealthily rich in sugars and colourants), cosmetics and creams abound the market. As a result, numerous vitamins trace elements and micronutrients often with well-defined biochemical functions (such as ascorbate, a known cofactor for several enzymes) have been re-branded as universal antioxidants. This implies that because they are antioxidants, the more one consumes the better it is for your health (Gutteridge and Halliwell, 2010). Excessive intake of antioxidants could down-regulate important endogenous antioxidants (Halliwell and Gutteridge, 2007; Gutteridge, 1999). It is also found to depress parts of the immune system and increase microbial damage. The normal cellular protective responses to tissue damage may also be altered (Gutteridge, 1999; Ristow *et al*., 2009; Childs *et al*., 2001; Leulier and Royet, 2009; Ha *et al*., 2009).

In recent years, antioxidants have gained a lot of importance because several antioxidants like SOD, CAT, lycopene, co-enzyme Q10, vitamin C and vitamin E have

Corresponding Author: P. Anand, Department of Physiology, Rajah Muthiah Dental College, Annamalai University, Annamalainagar-608 002, Tamilnadu, India Tel: 91-09894446555/04144-238071

been found to be pharmacologically active as prophylactic and therapeutic agents for various clinical disorders (Ratnam *et al*., 2006). Taurine (2-aminoethane sulfonic acid), a conditionally essential amino acid is a well-documented antioxidant agent. Clinically taurine has been used with varying degrees of success in the treatment of a wide variety of conditions including cardiovascular diseases, hypercholesterolemia, epilepsy and other seizure disorders, macular degeneration, Alzheimer's disease, hepatic disorders, alcoholism and cystic fibrosis (Birdsall, 1998). Taurine was reported to be beneficial in preventing experimental diabetic neuropathy (Obrosova *et al*., 2001), lead-induced oxidative damage (Gurer *et al*., 2001), CCl_4-induced oxidative stress (Vohra and Hui, 2001), cerulein-induced acute pancreatitis (Ahn *et al*., 2001), nonylphenol-induced toxicity (Karafakioglu *et al*., 2011), aluminium-induced oxidative stress (Al-Kahtani, 2010) and early changes in experimental diabetic kidney (Ha *et al*., 1999) through antioxidant mechanisms. Protective effects on lens (Devamanoharan *et al*., 1998) and modulating effects on human endothelial cell death are among its other effects (Wu *et al*., 1999).

Taurine is one of the key ingredients in energy drinks which are widely available in the grocery stores and convenience stores for easy access (Smith *et al*., 2011). Taurine is marketed as a dietary supplement for promotion of biliary health, eye health and prevention and treatment of congestive heart failure (Babu *et al*., 2008). Little is known regarding the effects of high-dose or long-term taurine use in children and adolescents (Babu *et al*., 2008).

Despite its extensive use, clinical and animal studies conducted with various doses of taurine on normal endogenous antioxidant system are not reported in literature. In light of this context, the present study was designed to investigate the effects of oral administration of graded doses of taurine on endogenous glutathione peroxidase, glutathione reductase and reduced glutathione levels in plasma, liver, heart, stomach and kidney in normal Wistar rats.

MATERIALS AND METHODS

Experimental animals: Forty albino Wistar rats (150-200 g; 20 weeks old) of either sex were obtained from the Central Animal House, Rajah Muthiah Medical College, Annamalai University during February 2009 and August 2010. The animals were maintained with standard rat chow and tap water ad libitum under standard laboratory conditions. The experiment was conducted in accordance with the accepted principles and guidelines of the Committee for the purpose of control and supervision on experiments on animals (CPCSEA), India after obtaining necessary approval.

Chemicals and reagents: Taurine, homoserine, dowex resins, o-phthalaldehyde and mercaptoethanol were obtained from Sigma-Aldrich, St. Louis, MO. The assay kits for glutathione (GSH) (Cat No. 703002), glutathione peroxidase (GPx) (Cat No. 703102) and glutathione reductase (GR) (Cat No. 703202) were purchased from Cayman chemicals company USA. Qualigens chemicals, India supplied the methanol (HPLC grade). All other chemicals used were of analytical grade.

Experimental design: Forty albino Wistar rats were divided into 4 groups of 10 rats each. Animals in Group 1 (Control) were administered 2.5 mL of 0.9% saline orally through intragastric intubation for 60 days. Animals in Group 2 (Low dose-Taurine), Group 3 (Medium dose-Taurine) and Group 4 (High dose-Taurine), were given 5% taurine in 0.9% saline orally at a dose level of 50, 250 and 500 mg kg^{-1} of body weight, respectively through intragastric intubation for 60 days (Anand *et al*., 2010). At the end of 60 days blood samples were collected and liver, heart, stomach and kidney were dissected out for analysis.

Collection of blood samples: All the experimental procedures were performed between 08:00 and 10:00 h. following a fasting period of 12 h, blood samples were withdrawn from retro-orbital sinus using fine capillary tube into the heparinised tubes. The heparinized blood was centrifuged at 1000xg for 10 min at 4°C. The supernatant plasma was separated out and stored at -80°C until assay.

Tissue preparation: After collection of the blood, animals were sacrificed by cervical decapitation and liver, heart, stomach and kidney were quickly dissected out into ice-cold Phosphate Buffered Saline (PBS). Prior to removal of the tissues, they were rinsed with PBS (pH 7.4) containing 0.16 mg mL^{-1} heparin to remove any blood clots. The tissues were homogenised and centrifuged as per the instructions from the suppliers of the kit. The resulting supernatant was removed and stored at -80°C until the assay was carried out.

Glutathione assay: GSH levels were measured following the procedure (Zhu *et al*., 2007) provided by the suppliers of the assay kit Optimized enzymatic recycling method-using GR is the basic principle of this assay kit.

Briefly, 100 μL of supernatant of tissue homogenate was added to an equal volume of the metaphosphoric acid and then centrifuged at 2,000xg for 2 min to remove protein. Then 50 μL of 4 M triethanolamine per mL of the supernatant was added to increase the pH of the sample. For total GSH assay, 50 μL of sample was added to 150 μL of a reaction mixture containing 0.4 M 2-(N-morpholino) ethanesulphonic acid, 0.1 M phosphate (pH 6.0), 2 mM EDTA, 0.24 mM NADPH, 0.1 mM 5, 5'-dithiobis-2-nitrobenzoic acid (DTNB) and 0.1 unit GR. The absorbance was measured using a microplate reader at 5 min intervals for 30 min. Reduced glutathione (GSH) concentration were expressed as μmol g^{-1} of wet tissue and μmol mL^{-1} of plasma.

Glutathione peroxidase assay: GPx activity was measured following the procedure (Zhu *et al*., 2007) provided by the suppliers of the assay kit. This assay kit measures GPx activity indirectly by a coupled reaction with GR. Oxidised glutathione (GSSG) produced upon reduction of hydroperoxide by GPx is recycled to its reduced state by GR in the presence of NADPH. The oxidation of NADPH to $NADP^+$ is accompanied by a decrease in absorbance at 340 nm and is directly proportional to the GPx activity in the sample. The decrease in absorbance was read with microplate reader and the activity is reported as nmol/min/mL of plasma or nmol/min/g of wet tissue.

Glutathione reductase assay: GR activity was measured following the procedure (Zhu *et al*., 2007) provided by the suppliers of the assay kit. GR activity was assayed spectrophotometrically by monitoring the oxidation of NADPH to $NADP^+$ by GR at 340 nm. Briefly, 200 μL of reaction mixture contained 50 mM potassium phosphate (pH 7.5), 1 mM EDTA, 1 mM GSSG and 0.1 mM NADPH. The reaction was initiated by addition of 20 μL of supernatant of tissue homogenate. The decrease in absorbance at 340 nm was recorded at 60 sec intervals for 6 min. Each assay was performed in duplicate and enzyme units were reported as nmol NADPH oxidized/min/g of wet tissue or ml of plasma.

Estimation of taurine levels: The 0.45 gram of tissue was weighed and stored at -80°C until the assay. Taurine was assayed by the method described by Waterfield (1994) using high performance liquid chromatography with fluorimetric detection.

Statistical analysis: Differences among control and experimental groups were tested using one-way ANOVA with Scheffe multiple comparisons test (for significant ANOVA) after logarithmic transformation of the data to correct for normality (Rosner, 2000; Hair, 1998). Differences of $p<0.05$ were considered statistically significant.

RESULTS

Effects on reduced glutathione (GSH) levels: The GSH level is estimated in μM g^{-1} of wet tissue or μM mL^{-1} of plasma. Oral administration of taurine in rats (Group II, III and IV) resulted in a significant increase in liver GSH level compared with control rats at $p<0.05$ level. A significant dose dependent increase was observed in the stomach GSH level of the taurine administered rats (Group II, III and IV) compared to control rats (Group I) at $p<0.05$. In kidney the level of GSH was significantly decreased in the taurine administered groups (Group II, III and IV) compared to control group (Group I) at $p<0.05$. There was no significant difference in the heart or plasma GSH levels between the taurine administered rats (Group II, III and IV) and the control rats (Group I) (Table 1).

Effects on glutathione peroxidase (GPx) activity: The GPX activity is expressed as μM/min/g of wet tissue or μM/min/mL of plasma. GPx activity in liver showed a significant difference between Group I (Control) and Group III and IV (Medium dose-taurine and High dose-taurine) but not Group II (Low dose-taurine) The activity of GPx in the heart showed a significant increase in the taurine administered groups (Group II, III and IV) when compared to the control group (Group I) at $p<0.05$. A significant increase was observed in stomach GPx activity of the taurine administered groups (Group II, III and Group IV) compared to control rats (Group I) at $p<0.05$. A significant increase in the plasma GPx activity was observed in the Group III (Medium dose-taurine) and Group IV (high dose-taurine) compared to the Group I and II at $p<0.05$. There was no significant difference in the kidney GPx activity between the taurine administered rats (Group II, III and IV) and the control rats (Group I) (Table 2).

Effects on glutathione reductase (GR) activity: The GR activity is expressed as μM/min/g of wet tissue or μM/min/mL of plasma. Oral administration of taurine resulted in a significant decrease in the liver GR activity for the taurine administered rats (Group II, III and IV) compared to the control rats (Group I) at $p<0.05$. The GR activity in the kidney was significantly increased in the taurine groups (Group II, III and IV) compared to control rats at $p<0.05$. In plasma a significant decrease in GR activity was observed between the control (Group I) and taurine administered groups (Group II, III and IV) at

Table 1: Effects of exogenous taurine on GSH level in tissue and plasma

	Group			
Tissue/plasma	I	II	III	IV
Liver (μmol g^{-1} of wet tissue)	50.510±2.52	103.02±41.40[a]	105.78±44.69[b]	107.86±10.29[c]
Heart (μmol g^{-1} of wet tissue)	53.362±27.26	80.186±54.14	90.557±72.60	108.66±14.34
Stomach (μmol g^{-1} of wet tissue)	26.812±11.54	123.192±7.49[a]	147.107±12.73[b]	180.203±58.50[c]
Kidney (μmol g^{-1} of wet tissue)	48.88±2.79	1.964±1.49[a]	6.628±6.463[b, d]	6.463±3.09[c, e]
Plasma (μmol mL^{-1} of plasma)	1.480±0.97	1.549±0.524	1.155±0.24	1.155±0.981

Group I: Control; Group II: Low dose taurine; Group III: Medium dose taurine; Group IV: High dose taurine; a- Group I vs Group II; b- Group I vs Group III; c- Group I vs Group IV; d-Group II vs Group III; e- Group II vs Group IV; f- Group III vs Group IV; a to f represents the significant difference at $p<0.05$

Table 2: Effect of exogenous taurine on GPx activity in tissue and plasma

	Group			
Tissue/plasma	I	II	III	IV
Liver (μmol/ming of wet tissue)	11.06±3.87	14.85±9.27	16.79±1.81	18.85±5.79[c]
Heart (μmol/min/g of wet tissue)	3.06±2.68	32.31±25.02[a]	41.15±20.32[b]	66.00±51.39[c]
Stomach (μmol/min/g of wet tissue)	6.75±2.26	12.39±3.47[a]	36.71±2.99[b, d]	74.08±20.35[c, e, f]
Kidney (μmolmin/g of wet tissue)	11.24±9.04	10.41±4.51	11.28±3.83	15.06±5.94
Plasma (μmol/min/mL of plasma)	2.845±2.00	2.452±1.88	7.189±4.69[b, d]	19.769±1.91[c, e, f]

Group I: Control; Group II: Low dose taurine; Group III: Medium dose taurine; Group IV: High dose taurine; a- Group I vs Group II; b- Group I vs Group III; c- Group I vs Group IV; d- Group II vs Group III; e- Group II vs Group IV; f- Group III vs Group IV; a to f represents the significant difference at $p<0.05$

Table 3: Effect of exogenous taurine on GR activity in tissue and plasma

	Group			
Tissue/plasma	I	II	III	IV
Liver (μmol/min/g of wet tissue)	58.621±29.15	12.795±7.56[a]	12.401±1.93[b]	14.008±10.01[c]
Heart (μmol/min/g of wet tissue)	57.791±11.85	55.865±22.55	55.820±21.00	51.302±5.47
Stomach (μmol/min/g of wet tissue)	7.371±3.90	6.646±3.94	6.761±3.53	8.305±5.27
Kidney (μmol/min/g of wet tissue)	2.577±0.64	5.245±1.34[a]	6.125±2.12[b]	20.223±12.95[c, e, f]
Plasma (μmol/min/mL of plasma)	4.833±1.75	3.007±0.87[a]	3.235±0.96[b]	3.307±0.48[c]

Group I: Control; Group II: Low dose taurine; Group III: Medium dose taurine; Group IV: High dose taurine; a-Group I vs Group II; b- Group I vs Group III; c- Group I vs Group IV; d- Group II vs Group III; e- Group II vs Group IV; f- Group III vs Group IV; a to f represents the significant difference at $p<0.05$

Table 4: Effect of exogenous taurine on taurine level in tissue and plasma

	Group			
Tissue/plasma	I	II	III	IV
Liver (umol g^{-1} of wet tissue)	23.620±5.54	140.52±80.98[a]	334.85±122.5[b, d]	695.68±105.33[c, e, f]
Heart (umol g^{-1} of wet tissue)	629.30±388.39	524.47±117.68	506.74±54.43	148.31±16.24[c, e, f]
Stomach (nmol g^{-1} of wet tissue)	357.22±190.46	332.0±157.94	233.43±162.32[b, d]	122.98±42.73[c, e,
Kidney (umol g^{-1} of wet tissue)	381.92±35.47	52.806±18.39[a,	71.191±22.33[b, d]	134.932±9.61[c, e, f]
Plasma (nmol mL^{-1} of plasma)	5.317±0.36	5.445±0.32	5.409±0.28	5.401±0.41

Group I: Control; Group II: Low dose taurine; Group III: Medium dose taurine; Group IV: High dose taurine; a- Group I vs Group II; b- Group I vs Group III; c- Group I vs Group IV; d- Group II vs Group III; e- Group II vs Group IV; f- Group III vs Group IV; a to f represents the significant difference at $p<0.05$

$p<0.05$. There was no significant difference in the heart and stomach GR activity between the taurine administered rats (Group II, III and IV) and the control rats (Group I) (Table 3).

Effects on taurine levels in tissue and plasma: The taurine levels in the tissue and plasma were expressed as nM g^{-1} of wet tissue and nM mL^{-1} of plasma, respectively. In liver taurine level a significant dose dependent increase was observed in the taurine administered groups (Group II, III and IV) compared to control rats at $p<0.05$. A significant decrease in the levels of taurine in the heart was observed in the group IV (High dose-taurine) rats when compared to control rats (Group I) at $p<0.05$. The taurine levels in stomach was significantly lowered in taurine administered groups when compared to the control group (Group I) at $p<0.05$. The taurine level in the kidney was significantly decreased in the taurine administered groups than control at $p<0.05$. There was no significant difference in the plasma taurine level between the taurine administered rats (Group II, III and IV) and control rats (Group I) (Table 4).

DISCUSSION

In the present study a dose dependent increase in GSH levels following taurine administration was observed in liver, heart and stomach. GSH levels in the tissue are primarily dependent upon the rates of biosynthesis and utilization in oxidation/reduction reactions (Rebrin *et al*., 2005). Cetiner *et al*., (2005) studied on effect of taurine on methotrexate induced toxicity in rat livers and reported that taurine does not have a known direct effect on GSH biosynthesis but it reduces the consumption of GSH by

inhibiting the LPO reactions, a marker for free radical induced damage. Similarly, Miyazaki *et al.* (2004) also reported that administration of taurine (TAU) increased the GSH levels in rats due to the inhibition of GSH oxidation to prolong the exercise performance. TAU and GSH biosynthesis have the common precursor cysteine (Rebrin *et al.*, 2005; Dawson *et al.*, 2002). In a study on sulfur containing amino acids on ageing (Benedetti *et al.*, 1991) and in another study on cyclosporine-A induced oxidative stress and hepatotoxicity in rats (Hagar, 2004) it has been pointed out that TAU increased the GSH levels as a result of directing more amount of cysteine into GSH biosynthesis. Schaffer *et al.* (2003) also agreed to the above statement in their review on cytoprotective role of taurine. However, in kidney, GSH level was significantly decreased in the taurine administered animals and plasma GSH level remained unchanged. Harris (1992) reviewed on regulation of antioxidant enzymes had pointed out that the antioxidant enzymes levels also depend on factors such as organ specificity, age of the organism etc. The decrease in kidney GSH contrary to the increase observed in liver, heart and stomach in the present study could be due to the organ specificity and presently the mechanism for this decrease is not known.

Similarly, a dose dependent increase in GPX activity of liver, heart, stomach and plasma in the taurine administered rats is seen. Sinha *et al.* (2008) have shown that taurine increased the GSH levels, GPX and GR activity of erythrocytes in cadmium induced toxicity rats by inhibiting the lipid peroxidation. Yildirim *et al.* (2007) have reported that taurine is effective in decreasing liver MDA levels and increasing GSH content and GPx activity when given to 13-14 months old rats at a dose of 200 mg kg/day ip for a week. An increase in GPX activity and GSH level following taurine administration similar to our study is reported by Comhair *et al.* (1999) in individuals with chronic beryllium disease and suggested that the increase in GPx may be mediated through redox mechanisms which lead to increase in GSH levels. Similarly, Sudheesh *et al.* (2010) reported that treatment with Palladium α-lipoic acid formulation (POLY-MVA) significantly increased the heart mitochondrial GSH level and GPx activity and pointed out that the enhanced activity of GPx can be attributed with the high level of GSH.

In the present study, GR activity showed a significant decrease in liver and plasma. Ulusu *et al.* (2003) in their study using streptozotocin induced diabetic rats have pointed out that GR is responsible for the regeneration of GSH and the decrease in GR activity in brain and heart may be due to the decline in production and availability of GSH to overcome H_2O_2. In kidney, GR activity was significantly increased and remained unchanged in heart and stomach of the taurine administered rats. Mallikarjuna *et al.* (2008) has reported that the increased GR activity is an indicative of increased GSH concentration via GSSG reaction at cellular level. Antioxidant enzyme activity is tissue dependent and varies from tissue to tissue and the duration and severity of the pathological conditions (Ulusu *et al.*, 2003). In alloxan induced diabetic rabbits, Winiarska *et al.* (2009) also showed that the effect of taurine on the activity of the enzymes of glutathione metabolism appear to be tissue dependent. In our study also GR activity varied from tissue to tissue and this might be due to the tissue specificity or glutathione availability. The kidney is the organ that excretes any excessive intake of the taurine (Sved *et al.*, 2007). The high intake of taurine may act as a stimulus for the greater excretion of taurine by the kidney resulting in low levels of taurine in kidney (Table 4). The low level of taurine's antioxidant activity is probably compensated by the GSH resulting in a decreased GSH level in kidney (Table 1). The low level of GSH may stimulate the GR activity. The threshold for maximum stimulation may be reached at the concentration administered in high dose group and hence responsible for the sharp rise in GR activity seen in Group IV (Table 3).

Liver taurine levels were significantly increased in a dose dependent manner in taurine administered animals. Parildar-Karpuzoglu *et al.* (2007) and Parildar *et al.* (2008) observed that administration of taurine in old and young rats depleted of taurine using β-alanine pre-treatment resulted in significant increase in liver and heart taurine levels. In the study of Eppler and Dawson (2001), 18 month old male Fischer rats were treated with taurine (1.5% in drinking water) for 8 months and reported that taurine concentration in liver and kidney was significantly higher in supplemented rats. Dawson *et al.* (1999) observed that TAU supplementation (1.5% of TAU in drinking tap water) in old rats can significantly increase TAU content in liver and kidney of aged male Fischer rats. Similarly, in the present study we observed that taurine levels in the kidney were significantly increased in the taurine administered animals.

CONCLUSION

The present study suggests that long term oral administration of taurine may affect the GSH level, GPx and GR activity of organs and the effects vary from organ to organ. Apparently, more studies are necessary to establish the role of oral administration of antioxidants like taurine in normal rats on physiological functions.

ACKNOWLEDGMENTS

I am grateful to Mrs. Radhika Balasubramanian for her help in preparing this manuscript.

REFERENCES

Ahn, B.O., K.H. Kim, G. Lee, H.S. Lee and C.D. Kim *et al.*, 2001. Effects of taurine on cerulein-induced acute pancreatitis in the rat. Pharmacology, 63: 1-7.

Al-Kahtani, M.A., 2010. Renal damage mediated by oxidative stress in mice treated with aluminium chloride: Protective effects of taurine. J. Biol. Sci., 10: 584-595.

Anand, P., D. Rajakumar, A.J.W. Felix and T. Balasubramanian, 2010. Effects of oral administration of antioxidant taurine on haematological parameters in wistar rats. Pak. J. Biol. Sci., 13: 785-793.

Babu, K.M., R.J. Church and W. Lewander, 2008. Energy drinks: The new eye-opener for adolescents. Energy drinks: The new eye-opener for adolescents. Clin. Pediatric Emergency Med., 9: 35-42.

Benedetti, M.S., A. Russo, P. Marrari and P. Dostert, 1991. Effects of ageing on the content in sulfur-containing amino acids in rat brain. J. Neural. Transm. Gen. Sect., 86: 191-203.

Birdsall, T.C., 1998. Therapeutic applications of taurine. Altern. Med. Rev., 3: 128-136.

Cetiner, M., G. Sener, A.O. Sehirli, E. Eksioglu-Demiralp and F. Ercan *et al.*, 2005. Taurine protects against methotrexate-induced toxicity and inhibits leukocyte death. Toxicol. Applied Pharmacol., 209: 39-50.

Childs, A., C. Jacobs, T. Kaminski, B. Halliwell and C. Leeuwenburgh, 2001. Supplementation with vitamin C and N-acetyl-cysteine increases oxidative stress in humans after an acute muscle injury induced by eccentric exercise. Free Radic. Biol. Med., 31: 745-753.

Comhair, S.A., M.J. Lewis, P.R. Bhathena, J.P. Hammel and S.C. Erzurum, 1999. Increased glutathione and glutathione peroxidase in lungs of individuals with chronic beryllium disease. Am. J. Respir. Crit. Care Med., 159: 1824-1829.

Dawson, R. Jr., M. Biasetti, S. Messina and J. Dominy, 2002. The cytoprotective role of taurine in exercise-induced muscle injury. Amino Acids, 22: 309-324.

Dawson, R. Jr., S. Liu, B. Eppler and T. Patterson, 1999. Effects of dietary taurine supplementation or deprivation in aged male Fischer 344 rats. Mech. Ageing Dev., 107: 73-91.

Devamanoharan, P.S., A.H. Ali and S.D. Varma, 1998. Oxidative stress to rat lens *In vitro*: Protection by taurine. Free Radic. Res., 29: 189-195.

Devasagayam, T.P., J.C. Tilak, K.K. Boloor, K.S. Sane, S.S. Ghaskadbi and R.D. Lele, 2004. Free radicals and antioxidants in human health: Current status and future prospects. J. Assoc. Physicians India, 52: 794-804.

Eppler, B. and R. Dawson Jr., 2001. Dietary taurine manipulations in aged male Fischer 344 rat tissue: Taurine concentration, taurine biosynthesi and oxidative markers. Biochem. Pharmacol., 62: 29-39.

Gurer, H., H. Ozgunes, E. Saygin and N. Ercal, 2001. Antioxidant effect of taurine against lead-induced oxidative stress. Arch. Environ. Contam. Toxicol., 41: 397-402.

Gutteridge, J.M., 1999. Does redox regulation of cell function explain why antioxidants perform so poorly as therapeutic agents. Redox Rep., 4: 129-131.

Gutteridge, J.M.C. and B. Halliwell, 2010. Antioxidants: Molecules, medicines and myths. Biochem. Biophys. Res. Commun., 393: 561-564.

Gwarzo, M.Y., V.A. Nwachuku and A.O. Lateef, 2010. Prevention of alloxan induced diabetes mellitus in rats by vitamin a dietary supplementation. Asian J. Anim. Sci., 4: 190-196.

Ha, E.M., K.A. Lee, Y.Y. Seo, S.H. Kim and J.H. Lim *et al.*, 2009. Coordination of multiple dual oxidaseregulatory pathways in responses to commensal and infectious microbes in drosophila gut. Nat. Immunol., 10: 949-957.

Ha, H., M.R. Yu and K.H. Kim, 1999. Melatonin and taurine reduce early glomerulopathy in diabetic rats. Free Radic. Biol. Med., 26: 944-950.

Hagar, H.H., 2004. The protective effect of taurine against cyclosporine A-induced oxidative stress and hepatotoxicity in rats. Toxicol. Lett., 151: 335-343.

Hair, J.F., R.L. Tatham, R.E. Anderson and W. Black, 1998. Multivariate Data Analysis. 5th Edn., Prentice Hall, New Delhi, pp: 775-777.

Halliwell, B. and J.M.C. Gutteridge, 2007. Free Radicals in Biology and Medicine. 4th Edn., Oxford University Press, Oxford.

Harris, E.D., 1992. Regulation of antioxidant enzymes. FASEB J., 6: 2675-2683.

Karafakioglu, Y.S., I.H. Cigerci and A.F. Fidan, 2011. The effects of taurine on aminolevulinic acid dehydratase activity in nonylphenol-induced toxicity. Asian J. Anim. Vet. Adv., 6: 96-100.

Kayode, A.A.A., O.T. Kayode and A.A. Odetola, 2009. Anti-ulcerogenic activity of two extracts of *Parquetina nigrescens* and their effects on mucosal antioxidants defence system on ethanol-induced ulcer in rats. Res. J. Med. Plant, 3: 102-108.

Leulier, F. and J. Royet, 2009. Maintaining immune homeostasis in fly gut. Nat. Immunol., 10: 936-938.

Mallikarjuna, K., K. Nishanth, T.B. Reddy and K.S. Reddy, 2008. Amendments of antioxidant enzyme status in different skeletal muscle fibers under age induced oxidative stress conditions with reference to exercise training. Asian J. Exp. Sci., 22: 117-128.

Mates, J.M., C. Perez-Gomez and I.N. De Castro, 1999. Antioxidant enzymes and human diseases. Clin. Biochem., 32: 595-603.

Miyazaki, T., Y. Matsuzaki, T. Ikegami, S. Miyakawa, M. Doy, N. Tanaka and B. Bouscarel, 2004. Optimal and effective oral doses of taurine to prolong exercise performance in rat. Amino Acids, 27: 291-298.

Nakagawa, H. and N. Miyata, 2008. 2,2,6, 6-tetramethylpiperidin-1-oxyl probes for evaluating oxidative stress on the cell membrane and mitochondria. Methods Mol. Biol., 477: 99-112.

Obrosova, I.G., L. Fathallah and M.J. Stevens, 2001. Taurine counteracts oxidative stress and nerve growth factor deficit in early experimental diabetic neuropathy. Exp. Neurol., 172: 211-219.

Parildar, H., S. Dogru-Abbasoglu, G. Mehmetcik, G. Ozdemirler, N. Kocak-Toker and M. Uysal, 2008. Lipid peroxidation potential and antioxidants in the heart tissue of beta-alanine or taurine-treated old rats. J. Nutr. Sci. Vitaminol. (Tokyo), 54: 61-65.

Parildar-Karpuzoglu, H., S. Dogru-Abbasoglu, J. Balkan, G. Aykac-Toker and M. Uysal, 2007. Decreases in taurine levels induced by beta-alanine treatment did not affect the susceptibility of tissues to lipid peroxidation. Amino Acids, 32: 115-119.

Ratnam, D.V., D.D. Ankola, V. Bhardwaj, D.K. Sahana and M.N.V.R. Kumar, 2006. Role of antioxidants in prophylaxis and therapy: A pharmaceutical perspective. J. Controlled Release, 113: 189-207.

Rebrin, I., S. Zicker, K.J. Wedekind, I. Paetau-Robinson, L. Packer and R.S. Sohal, 2005. Effect of antioxidant-enriched diets on glutathione redox status in tissue homogenates and mitochondria of the senescence-accelerated mouse. Free Radic. Biol. Med., 39: 549-557.

Ristow, M., K. Zarse, A. Oberbach, N. Kloting and M. Birringer *et al*., 2009. Antioxidants prevent health-promoting effects of physical exercise in humans. Proc. Natl. Acad. Sci. USA., 106: 8665-8670.

Rosner, B., 2000. Fundamentals of Biostatistics. 5th Edn., Duxbury Publications, UK., pp: 527-532.

Schaffer, S., J. Azuma, K. Takahashi and M. Mozaffari, 2003. Why is taurine cytoprotective. Adv. Exp. Med. Biol., 526: 307-321.

Seifried, H.E., D.E. Anderson, E.I. Fisher and J.A. Milner, 2007. A review of the interaction among dietary antioxidants and reactive Oxygen species. J. Nutr. Biochem., 18: 567-579.

Sinha, M., P. Manna and P.C. Sil, 2008. Taurine protects the antioxidant defense system in the erythrocytes of cadmium treated mice. BMB Rep., 41: 657-663.

Smith, L.A., I. Habib, S. Shirkey, B. Talon, A. Milne and J. Nadolski, 2011. Sexual dimorphism in the effect of a taurine supplemented diet on life span in adult *Drosophila melanogaster*. Int. J. Zool. Res., 7: 34-48.

Sudheesh, N.P., T.A. Ajith, K.K. Janardhanan and C.V. Krishnan, 2010. Effect of POLY-MVA, a palladium alpha-lipoic acid complex formulation against declined mitochondrial antioxidant status in the myocardium of aged rats. Food Chem. Toxicol., 48: 1858-1862.

Sved, D.W., J.L. Godsey, S.L. Ledyard, A.P. Mahoney and P.L. Stetson *et al*., 2007. Absorption, tissue distribution metabolism and elimination of taurine given orally to rats. Amino Acids, 32: 459-466.

Ulusu, N.N., M. Sahilli, A. Avci, O. Canbolat and G. Ozansoy *et al*., 2003. Pentose phosphate pathway, glutathione-dependent enzymes and antioxidant defence during oxidative stress in diabetic rodent brain and peripheral organs: Effects of stobadine and vitamin E. Neurochem. Res., 28: 815-823.

Vaghasiya, Y. and S. Chanda, 2010. Antimicrobial and free radical scavenging activity of different solvent extracts of *Mangifera indica* L. seeds. Res. J. Microbiol., 5: 1207-1212.

Valko, M., D. Leibfritz, J. Moncol, M.T.D. Cronin, M. Mazur and J. Telser, 2007. Free radicals and antioxidants in normal physiological functions and human disease. Int. J. Biochem. Cell Biol., 39: 44-84.

Vohra, B.P. and X. Hui, 2001. Taurine protects against carbon tetrachloride toxicity in the cultured neurons and *in vivo*. Arch. Physiol. Biochem., 109: 90-94.

Waterfield, C.J., 1994. Determination of taurine in biological samples and isolated hepatocytes by high-performance liquid chromatography with fluorimetric detection. J. Chromatogr., 657: 37-45.

Winiarska, K., K. Szymanski, P. Gorniak, M. Dudziak and J. Bryla, 2009. Hypoglycaemic, antioxidative and nephroprotective effects of taurine in alloxan diabetic rabbits. Biochimie, 91: 261-270.

Wu, O.D., J.H. Wang, F. Fennessy, H.P. Redmond and D. Bouchier-Hayes, 1999. Taurine prevents high-glucose-induced human vascular endothelial cell apoptosis. Am. J. Physiol., 277: 1229-1238.

Yildirim, Z., N. Kilic, C. Ozer, A. Babul, G. Take and D. Erdogan, 2007. Effects of taurine in cellular responses to oxidative stres in young and middle-aged rat liver. Ann. N.Y. Acad. Sci., 1100: 553-561.

Zhu, Y., P.M. Carvey and Z. Ling, 2007. Altered glutathione homeostasis in animals prenatally exposed to lipopolysaccharide. Neurochem. Int., 50: 671-680.