THE PROTECTIVE EFFECT OF TAURINE AGAINST DIAZINON OXIDATIVE STRESS IN RATS

ABSTRACT:
Diazinon (DZN) is one of the most widely used organophosphates in agriculture. The objective of this study was to investigate the propensity of subacute exposure of diazinon to induce oxidative stress, changes in biochemical parameters and enzyme activities in the liver and kidney of male rats and to explore its possible attenuation by taurine. The protective effects of taurine (50 mg/kg body weight, B.W.) given 30 min before and after administration of diazinon were investigated. The results demonstrated that the oral administration of 10 mg/kg diazinon significantly caused elevation in lipid peroxidation (LPO) level in liver and kidney when compared to control groups. Levels of reduced glutathione (GSH) and activities of superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST) and glutathione peroxidase (GSH-Px) were found to be decreased, while glutathione reductase (GSH-Rd) remained unchanged in rat’s liver and kidney treated with diazinon. Taurine treatment to diazinon intoxicated rats decreased LPO level and normalized GSH, SOD, CAT, GST and GSH-Px activities. Also pre-treatment with taurine ameliorated the increase in enzymatic activities of aminotransferases (AST and ALT), lactate dehydrogenase (LDH), creatinine and urea levels in plasma caused by diazinon intoxication. In conclusion, taurine significantly reduces diazinon-induced oxidative stress in rat’s liver and kidney and the protective effect of the pre-treatment with taurine is better than the post-treatment, suggested a significant contribution of its antioxidant property to these beneficial effects.

KEY WORDS:
taurine, diazinon, liver, kidney, oxidative stress

INTRODUCTION:
Pesticides are occasionally used indiscriminately in large amounts causing environmental pollution, and therefore, are of a major concern. Residual amounts of organophosphate (OP) and organochlorine (OC) pesticides have been detected in the soil, water bodies, vegetables, grains and other foods products (John et al., 2001). Organophosphates are known to cause inhibition of acetylcholinesterase activity in the target tissues (Abu-Quare and Abou-Donia, 2001; Kappers et al., 2001). Toxicities of OP pesticides cause adverse effects on many organs and systems (Sultatos, 1994; Hagar and Fahmy, 2002) like immune system (Handy et al., 2002; Neishabouri et al., 2004), urinary system (Rodrigo et al., 2001), reproductive system (Joshi et al., 2003) and haematological and biochemical changes (de Blaquiere et al., 2000).

Diazinon (o,o - diethyl -o - [2 - isopropyl-6 –methyl - 4 - pyrimidinyl] phosphorothioate) is an OP insecticide with a broad range of activities. It has been widely and effectively used throughout the world with applications controlling insects in crops, ornamentals, lawns, fruit and vegetables and as a pesticide in domestic and agricultural bodies (Garfitt et al., 2002). Some reports have been published with respect to diazinon (DZN) and its effects on biochemical and hematological parameters of rats, rabbits, and mice (Kalender et al., 2006; Yehia et al., 2007; El-Shenawy et al., 2009). In addition, diazinon was shown to affect mitochondrial membrane transportation in rat liver (Nakagawa and Moore, 1999) and disturbs cytochrome P450 system in human liver (Kappers et al., 2001; Sams et al., 2003).

Estimation of lipid peroxidation has been found to have predictive importance from a number of studies as a biomarker for oxidative stress (Amirkabirian et al., 2007). It can also occur as a consequence of imbalance between antioxidant system and pro-oxidant state generated by pesticide toxicity. Endogenous enzymatic and non-enzymatic antioxidants are essential for the conversion of reactive oxygen species (ROS) to harmless metabolites as well as to protect and restore normal cellular metabolism and functions (Bebe and Panemangalore, 2003).
ROS can be detoxified by an enzyme defense system, comprising superoxide dismutase (SOD), catalase (CAT), and selenium-dependent glutathione peroxidase, or non-enzymatic systems by the scavenging action of reduced glutathione, while organic peroxides can be detoxified by the activity of glutathione S-transferase; GST (Halliwell and Gutteridge, 1999).

Taurine (2-aminoethanesulfonic acid) is one of the major intracellular free β-amino acids, which is normally present in most mammalian tissues. It has several functions in cell metabolism including osmoregulation, membrane stabilization, detoxification and regulation of cellular calcium homeostasis (Huxtable, 1992; Gurer et al., 2001). Taurine has been demonstrated to function as a direct antioxidant by scavenging reactive oxygen radicals, inhibition of lipid peroxidation and as an indirect antioxidant by preventing changes in membrane permeability resulting from oxidant injury in many tissues including liver (Timbrell et al., 1995; Hagar, 2004; Waters et al., 2001). A number of investigators reported that taurine protects several organs in the body against toxicity and oxidative stress due to heavy metals and other toxins as well as drugs (Hwang et al., 1998; Dogru-Abbasoglu et al., 2001; Hagar et al., 2006; Tabassum et al., 2006; Jagadeesan and Sankarsami Pillai, 2007; Manna et al., 2008 a&b; Parildar-Karpuzoglu et al., 2008). But, there is no knowledge in the literature on the protective effects of taurine in organophosphate pesticide regarding remedy of oxidative damage.

This study is planned to evaluate the role of taurine as a protective agent against diazinon-induced hepatotoxicity and nephrotoxicity by measuring some antioxidant parameters including lipid peroxidation, GSH and antioxidant enzyme systems such as SOD, CAT, GSH-Px, GST and GSH-Rd, as well as some biochemical parameters indicative of liver and kidney functions.

MATERIAL AND METHODS:
Chemicals and reagents:
Diazinon, technical form of purity 99% was obtained from El-Watanya Company, Egypt. All chemicals were analytical reagent grade and chemicals required for all biochemical assays were obtained from Sigma–Aldrich Chemicals Co (St. Louis, MO, USA), and Merck (Darmstadt, Germany).

Animals and Treatment:
Male albino rats weighing 120-160 g were obtained from a colony raised in the Faculty of Agriculture, Alex. Univ. Animals were housed in stainless steel cages and maintained on a 12 h. light/dark cycle, 20 ± 2°C and 50–70% relative humidity. Food and water were provided ad libitum. Rats serving as control received corn oil. The rats were divided into five groups, each including six animals. The test substances were administered in the morning (between 09:00 and 10:00 h) to non-fasted rats and treated as follows:

Group 1:
Corn oil at a dose of 10 mg/kg B.W. per day was given through gavage to rats once a day and used as control.

Group 2:
Diazinon-treated group: Diazinon at a dose of 10 mg/kg B.W. per day in corn oil was given through gavage to rats once a day for four weeks. Standardization of exposure levels in the present experiment based on the sub acute oral LD<sub>50</sub> of diazinon (125 mg/kg) on male rats (WHO, 1998).

Group 3:
Taurine at the dose of 50 mg/kg B.W. in distilled water (0.5 ml per animal) was applied to rats i.p. once a day for four weeks. Dose selection of taurine (50 mg/kg B.W.) was based on the published studies which showed that this dose was effective against the toxicity induced by various xenobiotics. (Getiner et al., 2005; Sener et al., 2005 a, b&c).

Group 4:
Taurine (50 mg/kg B.W.), 30 min before administration of diazinon once a day for four weeks and used as pre-treatment group.

Group 5:
Taurine (50 mg/kg B.W.), 30 min after administration of diazinon once a day for four weeks and used as post-treatment group.

Collection of Samples:
At the end of the experimental period, the animals in different groups were sacrificed by cervical decapitation to avoid stress conditions. Blood was collected into EDTA tubes and centrifuged (3000g for 15min) for the separation of plasma. The liver and kidney samples were dissected out, washed, and weighed using saline solution (0.9% NaCl) and parts of the both tissues immediately stored at -20°C until biochemical analysis. The hepatic and renal tissues were minced and homogenized (10% w/v) in an appropriate phosphate buffer saline (100 mM Na<sub>2</sub>HPO<sub>4</sub>/NaH<sub>2</sub>PO<sub>4</sub>, pH 7.4) and centrifuged at 10,000 g for 15 min. The resulting supernatant was used for various biochemical assays.

Biochemical Assays:
Lipid peroxidation assay:
Lipid peroxidation process is determined by the thiobarbituric acid (TBA) method which estimates the malondialdehyde formation (MDA) according to Nair and Turner (1984). Briefly, a 0.33 ml of liver and kidney homogenate was mixed well with 3 ml of TBA reagent. The mixture was incubated for 20 min in a boiling water bath. After cooling, the mixture was centrifuged at 3000g for 20 min. The supernatant was
measured at 532 nm. Lipid peroxidation is expressed as n moles MDA/g tissue.

**Reduced glutathione (GSH) assay:**

Levels of GSH were determined in the liver and kidney homogenates (10%) according to the method of Ellman (1959). One millilitre of supernatant was treated with 0.5 ml of Ellman’s reagent (19.8mg of 5,5’dithiobisnitro benzoic acid in 100 ml of 0.1% sodium citrate) and 3.0 ml of phosphate buffer (0.2 M, pH 8.0). The absorbance was read at 412 nm in spectrophotometer. To prevent the autoxidation of GSH, the samples were reduced with potassium borohydride prior to analysis (Kleinman and Richie, 2001).

**Assay of antioxidant enzymes:**

Superoxide dismutase (SOD) activity was determined by the method of Kakkar et al. (1973). Superoxide radicals react with nitroblue tetrazolium in the presence of NADH and produce formazan blue. SOD removes the superoxide radicals and inhibits the formation of formazan blue. The intensity of colour is inversely proportional to the activity of the enzyme. The activity of catalase (CAT) was determined by the method of Sinha (1972). Dichromate in acetic acid was converted to perchromic acid and then to chromic acetate, when heated in the presence of H₂O₂. The chromic acetate formed was measured at 620 nm. Glutathione peroxidase (GSH-Px) was estimated by the method of Rotruck et al. (1973). A known amount of enzyme preparation was allowed to react with hydrogen peroxide in the presence of GSH for a specified time period. Then the remaining GSH was measured by the method of Ellman (1959). The glutathione S-transferase (GST) activity was determined spectrophotometrically by the method of Habig et al. (1974) in which 1-chloro-2,4-dinitrobenzenewas used as a substrate. Activity of glutathione reductase (GSH-Rd) was performed in the liver and kidney homogenates by monitoring the oxidation of NADPH in the presence of oxidized glutathione according to the method of Beutler (1969).

**Protein assay:**

Contents of protein were measured in the liver and kidney homogenates (10%) according to the method of Lowry et al. (1951) using bovine serum albumin as standard.

**Plasma enzymes activities and markers of renal function:**

ALT, AST and LDH were assessed in plasma with a commercially available enzymatic-kinetic kit (SpinReact-CECMAN, Germany) and analyzed by autoanalyzer (Bayer ope-RA) by the method of Martinek (1972). Urea, uric acid and creatinine levels were estimated spectrophotometrically using commercial reagent kits (refs. 20143, 20092, and 20151, respectively. Biomaghreb diagnostics by the methods of Patton and Crouch (1977) and Henry et al. (1974), respectively.

**Statistical Analyses:**

All data were expressed as mean ± standard deviation (SD). The data was analyzed using one-way analysis of variance (ANOVA) followed by the Student–Newman–Keuls test to determine significance between different groups. The criterion for statistical significance was set at P < 0.05. These tests were performed using a computer software CoStat program, version 6.2, CoHort Software (798 Lighthouse Ave. PMB 320, Monterey, CA 93940, USA).

**RESULTS:**

No death was observed in any of the experimental groups. The in vivo effects of diazinon (10 mg/kg B.W.) on lipid peroxidation and the antioxidant defense system in the male rat liver and kidney and also, the protective effects of taurine against oxidative damage induced by diazinon were given in figures 1–7. As shown in all experiments, taurine treatment in the absence of diazinon produced no significant effect on all of these tested parameters when compared to control rats.

**LPO level:**

MDA is a marker of oxidative lipid damage and it is a major oxidative product of peroxidized polyunsaturated fatty acid (Amirkabirakibirian et al., 2007). As shown in Fig. 1, MDA level in the rats treated with diazinon was significantly (p < 0.05) increased by 71.5% and 27.5% in liver and kidney, respectively when compared to the control group. Pre- or post-treatment with taurine to the rats intoxicated with diazinon significantly decreased the content of hepatic and renal MDA level when compared to the diazinon group, but still was more than that of the control.
GSH Content:

Conversely, as depicted in figure 2, the level of GSH in the rats treated with diazinon was significantly decreased in liver (25%, \( p < 0.05 \)) and kidney (36.5%, \( p < 0.05 \)) when compared to the control group. However, a significant increase of hepatic and renal GSH content was observed in pre-treatment with taurine to diazinon-intoxicated rats, without reaching the control level. On the other hand, post-treatment with taurine could not do any changes in the pesticide effect (Fig. 2).

Fig. 2. GSH content in hepatic and renal tissues of male rats orally treated with diazinon (10 mg/kg) and/or taurine (50 mg/kg B.W.). Values are expressed as mean ± SD for six animals per group; a, b, &c different superscripts indicate statistical significant differences between groups (\( P < 0.05 \)).

Antioxidant enzymes:

As presented in figure 3, the activity of CAT in the diazinon group was significantly decreased in liver (38%, \( p < 0.05 \)) and kidney (42.5%, \( p < 0.05 \)) when compared to the control group. As depicted in figure 4, the activity of SOD in the diazinon group was significantly decreased in liver (27%, \( p < 0.05 \)) and kidney (22%, \( p < 0.05 \)) when compared to the control group. Pre- and post-treatment with taurine can recover the inhibition of liver and kidney CAT and SOD completely to reach the control level. (Figs 3&4). Statistically there were no significant differences between pre- and post-treatments with taurine and the control group. As shown in figure 5, the activity of GSH-Px in the diazinon group was significantly decreased in liver (45%, \( p < 0.05 \)) and kidney (38%, \( p < 0.05 \)) when compared to the control group. However, the activity of GSH-Px in rats pre- or post-treated with taurine did not record significant change when compared with the control. Oral administration of diazinon caused a significant decrease in hepatic (36%, \( p < 0.05 \)) and renal GST (42%, \( p < 0.05 \)) activity compared to the control. Pre- or post-treatment with taurine showed slightly increase in GST activity (Fig. 6). As shown in figure 7, the activity of GSH-Rd in the diazinon group was remained unchanged in liver and nonsignificantly decreased in kidney (6%) when compared to the control group. Pretreatment with taurine showed no change in the activity of GSH-Rd in liver and kidney when compared to the diazinon group.

Fig. 3. CAT activity in hepatic and renal tissues of male rats orally treated with diazinon (10 mg/kg) and/or taurine (50 mg/kg B.W.). Values are expressed as mean ± SD for six animals per group; a, b, &c different superscripts indicate statistical significant differences between groups (\( P < 0.05 \)).

Fig. 4. SOD activity in hepatic and renal tissues of male rats orally treated with diazinon (10 mg/kg) and/or taurine (50 mg/kg B.W.). Values are expressed as mean ± SD for six animals per group; a, b, &c different superscripts indicate statistical significant differences between groups (\( P < 0.05 \)).

Fig. 5. GSH-Px activity in hepatic and renal tissues of male rats orally treated with diazinon (10 mg/kg) and/or taurine (50 mg/kg B.W.). Values are expressed as mean ± SD for six animals per group; a, b, &c different superscripts indicate statistical significant differences between groups (\( P < 0.05 \)).
Plasma enzymes activities and markers of renal function:

Table 1 shows a significant increase (p < 0.05) in plasma levels of AST, ALT, LDH, creatinine and urea by 23.5%, 21.5%, 20.3%, 12.8%, and 36.45% associated with a decrease of uric acid level by 56% in diazinon-treated rats when compared with control group. Pretreatment with taurine restored significantly (p < 0.05) the levels of these markers when compared to diazinon-treated rats. Taurine alone did not produce any significant changes in the level of these biochemical parameters.

Table 1. Effect of taurine (50 mg/kg B.W.) on diazinon-induced changes in plasma enzymes activities and markers of renal function in male rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Diazinon</th>
<th>Taurine</th>
<th>Pre treatment</th>
<th>Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (U/L)</td>
<td>60.61±</td>
<td>74.81±</td>
<td>62.32±</td>
<td>63.45±</td>
<td>69.03±</td>
</tr>
<tr>
<td></td>
<td>1.23 a</td>
<td>1.9 b</td>
<td>5.12 a</td>
<td>2.23 a</td>
<td>2.11 c</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>66.82±</td>
<td>81.24±</td>
<td>65.32±</td>
<td>65.21±</td>
<td>77.56±</td>
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<tr>
<td></td>
<td>0.86 a</td>
<td>2.6 b</td>
<td>2.82 a</td>
<td>3.01 a</td>
<td>3.16 c</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>931.21±</td>
<td>1120.13±</td>
<td>911.56±</td>
<td>928.01±</td>
<td>1040.53±</td>
</tr>
<tr>
<td></td>
<td>44.26 a</td>
<td>63.81 b</td>
<td>32.18 a</td>
<td>31.23 a</td>
<td>42.82 c</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.86±</td>
<td>0.97±</td>
<td>0.83±</td>
<td>0.84±</td>
<td>0.92±</td>
</tr>
<tr>
<td></td>
<td>0.04 a</td>
<td>0.03 b</td>
<td>0.02 a</td>
<td>0.06 a</td>
<td>0.02 c</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>31.52±</td>
<td>43.01±</td>
<td>29.31±</td>
<td>32.61±</td>
<td>40.54±</td>
</tr>
<tr>
<td></td>
<td>1.12 a</td>
<td>2.71 b</td>
<td>2.11 a</td>
<td>1.37 a</td>
<td>1.66 c</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>3.74±</td>
<td>1.65±</td>
<td>3.52±</td>
<td>3.62±</td>
<td>2.21±</td>
</tr>
<tr>
<td></td>
<td>0.47 a</td>
<td>0.13 b</td>
<td>0.21 a</td>
<td>0.52 a</td>
<td>0.03 c</td>
</tr>
</tbody>
</table>

- Values are expressed as mean ± SD for six animals per group.
- a, b, c different superscripts indicate statistical significant differences between groups (P < 0.05) (one way ANOVA).

DISCUSSION:

Environmental pollution with pesticides such as organochlorines, organophosphates and carbamates induced embryotoxicity, genotoxicity, teratogenicity and tissues damages (Sinha et al., 1998; Cavas and Ergene-Gozukara, 2003; Soni and Bhatnagar, 2005; Tisch et al., 2005). Oxidative stress caused by increased generation of reactive oxygen species (ROS) has been suggested to play the major role of this toxicity (Banerjee et al., 2001; Abdollahi et al., 2004). Diazinon which is one of the most widely used OP is readily absorbed from the gastrointestinal tract and is rapidly metabolized within a few hours (FAO/WHO, 1971; Garfitt et al., 2002).

Organophosphorous (OP) can induce oxidative stress by generation of free radicals that can cause lipid peroxidation, alternations in membrane fluidity, DNA damage and finally carcinogenic processes (Bindhumol et al., 2003; Banudevi et al., 2006). In the present study, four weeks oral administration of diazinon resulted in significant increase in the hepatic and renal content of MDA, indicating increased lipid peroxidation caused by administration of diazinon. These results are in agreement with other studies (Ogutcu et al., 2006, Amirkabirkabirian et al., 2007). The toxic manifestations induced by diazinon may be associated with the enhanced production of ROS or the increase in MDA levels which is induced by the pesticide itself (degradation of phospholipids and ultimately result in cellular deterioration) or by a possible increase in free radicals caused by diazinon. Lipid peroxidation has been suggested as one of
the molecular mechanisms involved in OP-induced toxicity (Kehrer, 1993). LPO, a reactive oxygen species-mediated mechanism, has been implicated in the pathogenesis of various liver and kidney injuries.

Glutathione dependent defense against xenobiotic toxicity is a multifaceted phenomenon that has been well characterized in animals (Ningaraj et al., 1998). GSH play a key role in the detoxification of the reactive toxic metabolites and liver necrosis is shown to be initiated when reserves of GSH are depleted. In the present study, the renal and hepatic levels of GSH were found to be decreased significantly in diazinon treated rats compared to control rats. These findings are in accordance with the previous studies showed that other organophosphates significantly decreased GSH levels in many organs (Tsukamoto et al., 2002). The mechanism of GSH depletion involves the diminishment of the overall antioxidant potential of liver and kidney as a result of increased lipid peroxidation following diazinon treatment.

Antioxidant enzymes, mainly CAT, SOD and GSH-Px are the first line of defense against free radical induced oxidative stress. CAT is responsible for the catalytic decomposition of hydrogen peroxide to molecular oxygen and water (Aebi, 1984). SOD is responsible for catalytic dismutation of highly reactive and potentially toxic superoxide radicals to hydrogen peroxide (McCord and Fridovich, 1969). GSH-Px, responsible for enzymatic defense against hydrogen peroxide, is strictly linked with the concentration of GSH because it catalyses the reaction between glutathione and hydrogen peroxide, resulting in the formation of glutathione disulphide (Halliwell and Gutteridge, 1999). In present study, diazinon caused a significant decrease in activities of CAT, SOD and GSH-Px in rat liver and kidney confirming the increased production of free radicals caused by administration of diazinon. These findings are in accordance with those of Sarabia et al. (2009) who reported that diazinon caused a decrease in these antioxidant enzymes activities in mouse testis. Yarsan et al. (1999) reported that other pesticides such as aldicarb decreased activities SOD, CAT and GSH-Px activities in rat erythrocytes. The present data show that the depletion of SOD, CAT and GSH-Px which was directly mediated by diazinon, proved the role of these enzymes in accelerated the conversion of superoxide radicals to hydrogen peroxide, then decomposition of hydrogen peroxide to molecular oxygen and water.

GST is a detoxifying enzyme that catalyzes the conjugation of a variety of electrophilic substrates to the thiol group of GSH, producing less toxic forms (Hayes et al., 2005). The results of the present study showed that the GST activity was significantly decreased in liver and kidney of rats treated with diazinon. These results showed disturbances in the activities of the enzyme regulating glutathione metabolism. The results are consistent with the previous studies as reported for other organophosphates (Singh et al., 2006).

GSH-Rd is an important secondary antioxidant enzyme required to maintain high GSH/GSSG ratios (Carlberg and Mannervik, 1985). In present study, GSH-Rd remained unchanged in rat liver and kidney after diazinon treatment. These findings are compatible with study of Dwivedi et al. (1998) who found no difference in GSH-Rd activity in rat liver and brain after 60 days treatment with 1/50 LD50 dose of quinalphos.

It is well known that reactive oxygen species are persistently produced by normal oxidative metabolism, mainly from mitochondrial respiration (Sohal, 1997). As the use of oxygen varies with cell type, it is expected that damages induced by reactive oxygen species are tissue specific. The present study demonstrated that the final product of membrane lipid peroxidation content of kidney was higher than the liver as shown by Subramanian et al. (2000), previously. This observed variations of oxidative damage among organs might be related to their respective enzymatic (Sani et al., 2006) and non-enzymatic (Choi et al., 2004) antioxidant potential. In present study, the decrease of renal GSH level (35%) was more than the decrease of hepatic GSH level (25%), confirming that liver has more antioxidant potential than kidney. Based on all of these data, it might be suggested that diazinon intoxication caused oxidative injury in kidney more than liver due to high antioxidant capacity of the liver cells defended against the oxidative injury, while kidney cells could not.

In the present study, increases in aminotransferase activities in plasma of diazinon-intoxicated rats could be expected to occur in association with a pathology involving necrosis of the liver (El-Demerdash, 2004). Plasma AST increases in such cases and escapes to the plasma from the injured hepatic cells. In addition, plasma ALT level is also useful in indicating the existence of liver diseases, as this enzyme is present in large quantities in the liver. It increases in plasma when cellular degeneration or destruction occurs in this organ (Hassoun and Stohs, 1995). The kidney is the critical target organ for xenobiotic compounds which produce a variety of renal toxic effects involving tubular cells and glomerulus (Mohamed et al., 2003). These compounds inhibit the incorporation of amino acid into protein causing an increase in urea levels which is the major nitrogen-containing metabolic product of protein.
metabolism (Pollak, 1982). In the present study, increased plasma creatinine and urea levels in diazinon-intoxicated rats reflect the diagnosis of renal failure (Donadio et al., 1997). Moreover, elevated blood urea is known to be correlated with an increased protein catabolism in mammals and/or the conversion of ammonia to urea as a result of increased synthesis of arginase enzyme involved in urea production. Recently, Rulíope and García-Puig (2007) reported that hyperuricemia is a renal prognostic factor. In this sense, the decrease of plasma uric acid levels, observed in this study, may reflect the response to an increased production of endogenous oxygen species since uric acid is a potent scavenger compound of peroxynitrite (Hooper et al., 1998).

In the present study, treatment with taurine was significantly mitigated diazinon-induced oxidative stress in liver and kidney. This might be manifested by the improvement of some or all of the biochemical variables determining diazinon toxicity. In addition, taurine inhibited lipid peroxidation, abrogated GSH depletion, enhanced the activities of endogenous antioxidants, and ameliorated the decrease in antioxidant enzymes activities induced by diazinon in liver and kidney. The protective effects of taurine on liver and kidney could be attributed to the role of taurine in maintaining a normal enzyme levels, stabilization in the intracellular defense systems (Chen, 1993) and its antioxidant action against lipid peroxidation, thus conserving the internal antioxidants system. The stimulatory effect of taurine on endogenous antioxidants was reported by others (Huxtable, 1992; Saad and Al-Rikabi, 2002). Biochemical investigations of the present study were demonstrated for the first time that taurine has a prominent protective effect against organophosphate toxicity as well. Consistent with our finding, taurine has been demonstrated to protect against hepatic and renal toxicity induced by several free radicals, generating insults including lipopolysaccharide (Kim and Kim, 2002), acetaminophen (Waters et al., 2001; Saad and Al-Rikabi, 2002), thioacetamide (Dogru-Abbasoglu et al., 2001), and ischemia/reperfusion (Chen, 1993). Moreover, the antioxidant effect of taurine was shown in other organs including the lung (Banks et al., 1992) and heart (Milei et al., 1992). Taurine has been demonstrated to function as a direct antioxidant that scavenges or quenches oxygen free radicals, thus inhibiting lipid peroxidation, and as an indirect antioxidant that prevents the increase in membrane permeability resulting from oxidant injury in many tissues including liver (Chen, 1993). The possible explanation for the protective effects of pretreatment with taurine against diazinon-induced increase in LPO is its ability to react with the oxygen metabolites. Taurine might stimulate S-nitrosylation of GSH producing S-nitrosoglutathione, which is approximately 100 times more potent than the classical GSH. In addition, S-nitrosylation of cysteine residues by nitrosoglutathione can inactivate caspase-3, thus preventing hepatic cell apoptosis (Chiueh and Rauhala, 1999). It is clear from this study that the activities of the antioxidant enzymes, in rats pretreated with taurine, were significantly higher compared to the rats treated with diazinon, and were very similar to the values noted in normal control rats indicating the antioxidant effects of taurine. Upon pretreatment with taurine, radicals might be scavenged especially in the kidney tissue where more reactive oxygen species generation is occurred.

Administration of taurine protects the liver and kidney function from diazinon intoxication as indicated by the significant restoration of plasma AST, ALT, LDH, creatinine, urea and uric acid. As an indirect antioxidant, taurine has been proposed as a membrane stabilizer that can maintain membrane organization, prevent ion leakage and water influx, and subsequently, avoid cell swelling (Milei et al., 1992). The stabilizing effect of taurine on cellular membrane has been suggested to be associated with the interaction between taurine and polyunsaturated fatty acids in the membrane, which results in an increase in the affinity of taurine for its carrier transport and the interaction between taurine and the sites related to anion transport and water influx. This property of taurine may also partly account for its protection against diazinon-induced liver damage. On the other hand, taurine can also function as a regulator of intracellular calcium homeostasis (Huxtable, 1992) that can be disturbed due to diazinon toxicity.

The results of the present study demonstrate that administration of taurine has a therapeutic role in preventing diazinon-induced hepatic and renal toxicity, possibly through its unique cytoprotective properties such as antioxidant activity.

In conclusion, biochemical evaluations demonstrated that exposure of diazinon results in the induction of lipid peroxidation and changes in antioxidant system in rat liver and kidney. All data indicate that reactive oxygen species might be associated with the diazinon-induced toxicity. Moreover, results of the present study showed that pretreatment of taurine may attenuate diazinon-induced oxidative damage by decreasing lipid peroxidation and altering antioxidant defense system in rat liver and kidney. It may be tractable to consider applying taurine, at least in agricultural practice, to minimize hepatotoxicity and nephrotoxicity effects elicited by pesticide exposure.
REFERENCES:


