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The Effects of Taurine on Aminolevulinic Acid Dehydratase Activity in Nonylphenol-Induced Toxicity

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ABSTRACT

The aim of this study was to investigate the effects of taurine on blood aminolevulinic acid dehydratase (ALAD) activity in nonylphenol-induced rats. Forty rats were divided into 5 groups each containing 8 Wistar-albino male rats: control group (C) by standard rat feed, taurine group (T) by standard rat feed+3% taurine (v/w) in drinking water, nonlyphenol group (NP) by standard rat feed+50 μg kg^{-1} diet Nonlyphenol, Nonlyphenol+ Taurine group (NPT) by standard rat feed+50 μg kg^{-1} diet Nonlyphenol+3% taurine (v/w) in drinking water and alcohol group (A) by standard rat feed +50 μL kg^{-1} diet alcohol were fed *ad libitum* for 30 days during the study. The blood ALAD activity significantly increased in T group compared the other experimental groups. Nonlyphenol treatment significantly decreased the blood ALAD activity as compared to control. Decreased levels of blood ALAD activity in NP group were significantly increased in NPT group. The ALAD activity significantly decreased in A group compared the T groups. The results demonstrate that taurine could provide great advantages against to side effects of nonlyphenol toxication on ALAD activity in rats those exposed to Nonylphenol.

Key words: Nonlyphenol, taurine, ALAD, toxicity

INTRODUCTION

Nonylphenol, an environmental contaminant, is the final degradation product of alkylphenol polyethoxylates, which are widely used in industrial processes (Junk *et al*., 1974). The NP is classified by the U.S. Environmental Protection Agency as an inert of toxicological concern that must be identified on pesticide labels (Brigs and Council, 1992). Nonylphenol is probably diverse routes of human exposure; not only via contaminated foods and drinking water, but also via dermal absorption or inhalation (Clark *et al*., 1992; Ahel *et al*., 1993). Nonylphenol has weak estrogenic activity. It has been demonstrated that nonylphenol could interfere with reproduction in fish, reptiles and mammals and induce the cell death in gonads and changes to other reproductive parameters (Gong and Han, 2006).

Aminolevulinic acid dehydratase (ALAD) is the second enzyme in the heme biosynthetic pathway, which is cytosolic and nonlimiting in heme synthesis in healthy cells. The enzyme catalyzes the condensation of two molecules of aminolevulinic acid to form one molecule of the

monopyrrole porphobilinogen. Activity of this enzyme is markedly inhibited by environmental toxins, insecticides carcinogens and heavy metals (Conner and Fowler, 1994). After this inhibition the formation of porphobilinogen, therefore hemoglobin and other hemoproteins is obstructed, deteriorate the formation of oxygen storage, transportation and P450 detoxification system by causing accumulation of aminolevulinic acid (Ozmert, 2005).

Taurine is a ubiquitous sulphur containing amino acid which is normally present in most mammalian tissues has been proposed to be an antioxidant (Eppler and Dawson, 2001). It plays various important physiological functions including osmoregulation, bile acid conjugation, pharmacological actions, pathological states and prevention of oxidant induced injury in many tissues (Lallemand and de Witte, 2004). The useful effects of taurine as an antioxidant in biological systems have been attributed to its capability to stabilize biomembranes, to scavenge reactive oxygen species and to decrease the peroxidation of unsaturated membrane lipids (Banks *et al.*, 1992; Kilic and Yildirim, 2008). According to our knowledge, there are some studies regarding the effects of nonylphenol and taurine in humans and some animal species (Aslan and Karafakioglu, 2010). However, there have been no published articles investigating the effects of nonylphenol on ALAD activity. The aim of this experimental animal study was to investigate the effects of taurine on ALAD activity in nonylphenol-induced rats.

MATERIALS AND METHODS

Fourty same-age male Wistar albino rats weighing 175±375 g were used in the study. The study was conducted in 2007. All the animals were carefully monitored and maintained. The investigation conformed to the principles outlined in the Declaration of Helsinki. The rats were randomly divided into five experimental groups each containing 8 rats: control group (C); taurine group (T); nonylphenol group (NP); Nonylphenol+ Taurine group (NPT) and alcohol group (A). C group by standard rat feed, T group by standard rat feed+3% taurine (v/w) in drinking water, NP group by standart rat feed+50 μg kg^{-1} diet Nonlyphenol, NPT group by standard rat feed+50 μg kg^{-1} diet Nonlyphenol+3% taurine (v/w) in drinking water and A group by standard rat feed+50 μL kg^{-1} diet alcohol were fed *ad libitum* for 30 days during the study. At the end of the experimental period, the rats were anaesthetized and killed by cervical dislocation. Blood samples were taken into heparinized tubes in the fasting state in all subjects from heart, to measure ALAD activity.

The activity of blood ALAD was assayed according to the procedure of Berlin and Schaller (1974). Briefly, 0.2 mL of heparinized blood was mixed with 1.3 mL of distilled water and incubated for 10 min at 37°C for complete hemolysis. After adding 1 mL of standard aminolevulinic acid, the tubes were incubated for 60 min at 37°C. Enzyme activity was stopped after 1 h by adding 1 mL of 10% trichloroacetic acid. After centrifugation (1500x g for 10 min at 25°C) of reaction mixture, reaction mixture, equal volume of Ehrlich reagent was added to the supernatant and the absorbance was recorded at 555 nm after 5 min.

All data were presented as Mean±SE for parametric variables. Parametric variables were compared using one-way analysis of variance with post-hoc analysis using the Duncan test. Data were analyzed using the SPSS® for Windows computing program (Version 10.0) and $p<0.05$, was considered statistically significant (Sokal and Rohlf, 1969).

RESULTS AND DISCUSSION

As shown in Table 1, the blood ALAD activity significantly increased in T group compared the other experimental groups ($p<0.05$), moreover the level of the T group almost reached the control

Table 1: Aminolevulinic acid dehydratase activity in control and experimental groups

	Group				
Activity	C	NP	T	NPT	A
ALAD (μmol/min/mL erythrocytes)	5.13±0.4^{b}	3.83±0.4^{c}	7.42±0.37^{a}	5.06±0.24^{b}	4.23±0.17^{b,c}
		(-25.34)	(+44.64)	(-1.36)	(-17.54)

Values with different superscript letters show statistically significant differences ($p<0.05$); (+) % Increase/stimulatory rate and (-) % decrease/inhibitory rate from control. Results are expressed as Means±SE

group level. Nonlyphenol treatment (50 μg kg^{-1} diet Nonlyphenol) significantly decreased the blood ALAD activity as compared to control ($p<0.05$). Decreased levels of blood ALAD activity in NP group were significantly increased in NPT group ($p<0.05$). In addition NPT group level was as high as at the control group level. On the other hand, the blood ALAD activity significantly decreased in A group compared the T groups ($p<0.05$).

Alkylphenol Polyethoxylates have been widely used as plastic additives and components of surfactants, paints, herbicides and insecticides (Messina and Dawson, 2000). Approximately, 80% of these chemicals are reported to be nonlyphenol (Naylor, 1996). Most research to date on nonlyphenol has focused on the growth of reproductive organs in animals (Laws *et al*., 2000; Lee and Lee, 1996). The multigeneration studies in rats showed that nonlyphenol affected not only reproductive organs but also nonreproductive organs (Chapin *et al*., 1999; Nagao *et al*., 2001). Nonlyphenol has been shown to produce oxidative stress, enhancing ROS generation in human blood neutrophils (Okai *et al*., 2004). Furthermore, nonlyphenol administration increased reactive oxygen species level and lipid peroxidation and depressed the activity of antioxidant enzymes such as superoxide dismutase and glutathione reductase in rat testis (Chitra and Mather, 2004). Recently, treatment of rats with nonlyphenol was found to induce hydroxyl radical formation in the brain (Obata and Kubota, 2000). Gong and Han (2006) reported that 10-40 μM nonlyphenol for 24 h caused intracellular accumulation of reactive oxygen species, in testicular sertoli cells. Nonlyphenol has been shown to affect the activity of cytochrome P450 in rats. Aslan and Karafakioglu (2010) reported that nonylphenol induced oxidative stress in rat blood by decreasing the activities of antioxidant enzymes and generation of free radicals in rats.

The ALAD is the second enzyme in the heme biosynthesis pathway and catalyzes condensation of two molecules of aminolevulinic acid to a porphobilinogen. ALAD possesses thiol (SH) groups, which are essential for its activity (Goyer, 1996). The ALAD is highly sensitive to the presence of toxic metals having high affinity for SH group (Flora, 1999). The generation of radicals can affect the thiol groups of proteins. Consequently, ALAD activity is fundamental for oxidative metabolism and ALAD is extremely sensitive to oxidative stress (Rocha *et al*., 2005). Furthermore, Gurer-Orhan *et al*. (2004) reported, significant negative correlation between ALAD activity and erythrocyte malondialdehyde concentrations.

The useful effects of taurine as an antioxidant in biological systems have been attributed to its capability to stabilize biomembranes, to scavenge reactive oxygen species and to decrease the peroxidation of unsaturated membrane lipids (Banks *et al*., 1992). Taurine is a well known substance that has antioxidant properties in peroxidatively damaged tissues. Decreased malondialdehyde level, which is an indicator of lipid peroxidation, increases in taurine deficiency (Cakatay *et al*., 2003). In an earlier study, the rat liver MDA level was significantly reduced by age after 7 days treatment with 200 mg/kg/day taurine (Yildirim *et al*., 2007).

In present study, we found that nonlyphenol treatment (50 μg kg^{-1} diet Nonlyphenol) significantly decreased the blood ALAD activity. Compared with published studies, this report is the first to indicate that the blood ALAD activity is lower in nonylphenol-induced rats. On the other hand, we found that the decreased levels of blood ALAD activity in nonylphenol-induced rats were increased by taurine application. We could not find a similar result in the literature on the blood ALAD activity in nonylphenol-induced rats. But Flora *et al.* (2008) reported that combined administration of a higher dose of taurine (100 mg kg^{-1}) with monoisoamyl dimercaptosuccinic acid led to more pronounced beneficial effects on ALAD activity and GSH levels in arsenic exposed rats. Aslan and Karafakioglu (2010) reported taurine treatment decreases the oxidative stress in nonylphenol-induced oxidative damage by maintaining the GSH recycling activity, increasing the SOD activity and free radical scavenging potential. Present results suggest that decreased the blood ALAD activity may lead to severe effects in nonylphenol-induced rats. Nonylphenol treatment decreased the blood ALAD activity in this study. Although, taurine treatment incrases the blood ALAD activity in nonylphenol-induced rat by free radical scavenging potential. Moreover, the results demonstrate that taurine could provide great advantages against to side effects of nonlyphenol toxication on ALAD activity in animals exposed to nonylphenol.

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