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Short-Term Effect of Deltamethrin Treatment on Oxidative Stress Biomarkers in Anatolian Water Buffaloes

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Abstract: The aim of this study was to investigate the tendency of deltamethrin to induce oxidative stress and changes in biochemical parameters in Anatolian water buffaloes. A pour-on 7.5 g deltamethrin per liter of the ready-to-use solution was applied on dorsal skin in 10 buffaloes. Results showed that malondialdehyde levels significantly increased in whole blood on day 7. The activities of catalase and superoxide dismutase significantly decreased in erythrocytes and glutathione reductase activity increased in plasma. On the other hand, deltamethrin treatment increased nitric oxide level in plasma. The present study revealed that application of deltamethrin caused oxidative damage in Anatolian water buffaloes.

Key words: Anatolian water buffalo, deltamethrin, lipid peroxidation, oxidative stress

INTRODUCTION

Oxidative stress can be defined most simply as the imbalance between the production of free radicals capable of causing peroxidation of the lipid layer of cells and the body's antioxidant defense. Free radicals are defined as atoms or molecules that contain one or more unpaired electrons. Free radicals have various chemical structures, such as hydroxyl, superoxide, nitric oxide and lipid peroxyl radicals (Cochrane, 1991). Under normal conditions, the free radicals generated and detoxified by the antioxidants present in the body and there is equilibrium between the generated free radicals and present antioxidants. However, owing to free radicals overproduction or inadequate antioxidant defense, this equilibrium is hampered favoring the free radicals upsurge that culminates in oxidative stress. The free radicals readily attack and induce oxidative damage to various biomolecules including proteins, lipids, lipoproteins and DNA (Farber, 1994; Kaur *et al*., 2006; Küçükkurt *et al*., 2008).

Synthetic pyrethroids constitute a unique group of insecticides having pyrethrum like structures with better performance characteristics and account for over 30% of insecticides used globally (Prasanthi *et al*., 2005; Schmahl *et al*., 2009). Based on the symptoms produced in animals, pyrethroids fall into two distinct classes: type I and II. Deltamethrin ($C_{22}H_{19}Br_2NO_2$), a synthetic pyrethroid type II, is highly effective against a broad spectrum of insects.

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Many of studies demonstrated that deltamethrin induced oxidative stress in humans, laboratory animals, fish and other aquatic organisms (Haya, 1989; Mittal *et al*., 1994; Yarsan *et al*., 2002; Yousef *et al*., 2006). However, deltamethrin has frequently used as clinical medicine to control ectoparasitic infestation and there have been no published articles investigating the oxidative effects of deltamethrin treatment on Anatolian water buffaloes. In this study, we aimed to short-term effect of pour-on deltamethrin treatment on lipid peroxidation, antioxidative biomarkers and biochemical parameters in Anatolian water buffaloes.

MATERIALS AND METHODS

Animals and Experimental Design

In this study, 10 male Anatolian water buffaloes of about 350 kg b.wt. were treated by pour-on application of 30 mL of the product Butox® 7.5 on dorsal skin of the animals. Butox® 7.5 contains 7.5 g deltamethrin per liter of the ready-to-use solution and is a registered trademark of Intervet, Turkey. Animals were ensured from the Anatolian water buffalo husbandry in region of Afyonkarahisar, Turkey. Blood samples were collected into tubes containing heparin as anticoagulant prior to treatment and following drug administration on day 7. Blood samples were separated to plasma and erythrocytes. Samples stored for analysis at -20°C. The experimental protocols were approved by the Animal Care and Use Ethical Committee at Afyon Kocatepe University (90-09). The experiment was conducted in 2009 at Afyon Kocatepe University-Afyonkarahisar.

Biochemical Analysis

Malondialdehyde (MDA) levels were measured by the double heating method of Draper and Hadley (1990). The method is based on spectrophotometric measurement of the purple color generated by the reaction of thiobarbituric acid with MDA. Blood glutathione (GSH) concentrations were assayed by calorimetric method of Beutler *et al*. (1986) using dithio(bis)nitrobenzoic acid. Erythrocytes were prepared according to Winterbourn *et al*. (1975) and erythrocyte hemoglobin levels were determined as described by Fairbanks and Klee (1987). Cu-Zn Superoxide Dismutase Activity (SOD) in erythrocytes was measured by the previously detailed method of Sun *et al*. (1988). Catalase (CAT) in erythrocytes was measured spectrophotometrically as described by Luck (1955). Glutathione Peroxidase (GP_x) and Glutathione Reductase (GR) measured spectrophotometrically with the use of kits from Cayman Chemical Company, USA (Bio-tek, Turkey). The Total Antioxidant Activity (AOA) was determined using the method described by Koracevic *et al*. (2001). Plasma NO_x concentration was measured by a modified method of Griess assay, described by Miranda *et al*. (2001). Plasma aspartate aminotransferase (AST; EC 2.6.1.1), alkaline phosphatase (ALP; EC 3.1.3.1) and alanine aminotransferase (ALT; EC 2.6.1.2) activities were determined spectrophotometrically with the use of kits from Centronic GmbH, Germany (Bio-tek, Turkey). Shimadzu UV-1601 visible spectrophotometer was used for determination biochemical analysis.

Statistical Analysis of Data

Statistical analysis were performed with the SPSS 11.5 computer program (2003). The results were expressed as Mean±SEM. Significant differences between groups were analyzed by paired t test. The significance of the results was ascertained at $p<0.05$.

RESULTS

The mean levels of whole blood MDA, plasma GR ($p<0.001$) and GP_x ($p<0.01$) were increased and erythrocyte SOD ($p<0.01$) and CAT ($p<0.001$) activity levels were decreased

Table 1: Effects of deltamethrin treatment on levels of MDA and GSH concentration in whole blood and CAT, SOD and GP_x, GR activities in erythrocyte and plasma (Mean±SEM)

Parameters (n:10)	0 day	7 day	p-value
MDA (nmol mL^{-1})	4.05±0.25	5.93±1.24***	0.000
GSH (mg dL^{-1})	33.32±1.13	34.08±1.17	0.548
CAT (k gHb^{-1})	156.93±23.44	141.93±21.77***	0.000
SOD (U $mgHb^{-1}$)	33.91±2.36	23.63±1.77**	0.003
GP_x (nmol/min/mL)	0.96±0.90	2.06±1.05**	0.008
GR (nmol/min/mL)	0.08±0.01	0.19±0.07***	0.000

**p<0.01, ***p<0.001. In the same line values with different stars show statistically significant differences in whole blood MDA, erythrocyte CAT, plasma GR (p<0.001), GP_x and erythrocyte SOD (p<0.01)

Table 2: Effects of deltamethrin treatment on levels of AOA, NO_x, ALT, AST and ALP in plasma (Mean±SEM)

Parameters (n:10)	0 day	7 day	p-value
AOA (mmol L^{-1})	4.42±0.65	4.38±0.83	0.772
NO_x (μmol L^{-1})	43.40±3.39	59.36±5.43*	0.041
ALT (U L^{-1})	68.05±5.92	64.99±4.59	0.501
AST (U L^{-1})	25.23±2.86	38.76±7.04	0.101
ALP (U L^{-1})	27.04±6.86	22.53±3.22	0.064

*p<0.05. In the same line values with show star statistically significant difference in plasma NO_x (p<0.05)

whereas whole blood GSH level was not found to be different in animals on day 7 (Table 1). The mean levels of AOA, AST, ALT and ALP were not found to be different in animals. However, plasma NO_x level was found to be higher (p<0.05) on day 7 in Table 2.

DISCUSSION

Lipid peroxidation is the process of oxidative degradation of polyunsaturated fatty acids and its occurrence in biological membranes causes impaired membrane function, decrease in membrane fluidity and inactivation of a several membrane bound enzymes. Therefore, deltamethrin metabolized with enzymes in liver and may cause injury of liver (Gutteridge and Halliwell, 2000). Yousef *et al.* (2006) reported that oral exposure of deltamethrin (1.28 mg kg^{-1} b.wt.) following a 30 days significantly induced plasma thiobarbituric acid-reactive substances in male rats. Similarly, Yarsan *et al.* (2002) reported that MDA levels increased in deltamethrin groups were given at orally 1.5, 2.5 or 7.5 mg kg^{-1} b.wt., especially for the subchronic and chronic periods in mice. Consequently, in this study, MDA was found to be high level in Anatolian water buffaloes on day 7. The GSH is responsible for the cellular antioxidant defenses and acts as an essential cofactor for antioxidant enzymes including the GSH peroxidases (Cathcart, 1985). In this study, pour-on deltamethrin treatment did not affect GSH activity.

The antioxidant enzymes SOD, CAT, GP_x and GR limit the effects of oxidant molecules on tissues and active in the defense against oxidative cell injury by means of their being free radical scavenger (Kyle *et al.*, 1987). These enzymes work together to scavenger active oxygen species and these concentrations may have a dramatic effect on the resistance of cellular lipids, proteins and DNA to oxidative damage (Mates and Jimenez, 1999). Yarsan *et al.* (2002) reported that GP_x, SOD and CAT activities were decreased at high doses (7.5 mg kg^{-1} b.wt.) of deltamethrin in mice erythrocytes. In this study, SOD and CAT activity were decreased in Anatolian water buffaloes on day 7. These data suggest that low level of SOD and CAT activity might be related to the consumption of these enzymes to cope with this increased oxidative stress. However, GP_x and GR activity were increased in Anatolian water buffaloes on day 7. The increased activities of GP_x and GR suggest that free radical scavenging process in the cell are generally cooperative as reductase and peroxidase combine to metabolize H_2O_2.

Antioxidant capacity is an important factor for all physiological standards in animals (Draper *et al*., 1986; Prior and Cao, 1999). This study showed that deltamethrin treatment unchanged plasma antioxidant capacity in Anatolian water buffaloes on day 7. El-Gohary *et al*. (1999) reported that administration of deltamethrin (1 mg kg^{-1} daily for 21 days) to rats resulted in characteristic DNA migration patterns and the plasma levels of both NO and lipid peroxides measured as MDA were found to be significantly increased in deltamethrin treated animals. They also suggest that deltamethrin induced testicular apoptosis is mediated by NO. In the present study, deltamethrin treatment increased plasma NO_x level in Anatolian water buffaloes.

The increase in the activities of liver enzymes (AST, ALP and ALT) in plasma is indicative for liver damage and thus causes alteration in liver function (Yousef *et al*., 2006). Awad *et al*. (1998) reported that cell damage exhibited good correlation with the enzyme leakage. Hence, cellular damage caused by toxic substances is frequently accompanied by increasing cell membrane permeability. In the present study pour-on deltamethrin treatment did not affect on plasma AST, ALP and ALT levels. This result may indicate that pour-on deltamethrin treatment does not affect plasma AST, ALP and ALT levels in Anatolian water buffaloes.

According to these data, it can be concluded that short period deltamethrin treatment by pour-on route may damage antioxidant status in Anatolian water buffaloes. Moreover, future studies should be carried out to understand the underlying mechanisms involved in a long term effects profile of deltamethrin in Anatolian water buffaloes.

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