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Toxic Impact of Sub-Chronic Oral Exposure of Cyfluthrin on Antioxidant Status in Buffalo Calves

Research Article

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ABSTRACT

Cyfluthrin [cyano[4-fluoro-3-phenoxyphenyl]-methyl-3-[2,2-dichloroethenyl]-2,2-dimethyl-cyclo propane carboxylate] is a synthetic pyrethroid insecticide, that has both contact and stomach poison action. The present study evaluated the long-term toxic effects of cyfluthrin on antioxidant status in buffalo calves. Oral administration of cyfluthrin at a dose rate of 10 and 20 mg/kg/d for 11 consecutive weeks did not produce any marked toxic symptoms in the buffalo calves. However, the oral administration of cyfluthrin resulted in a significant increase in the extent of lipid peroxidation. This increase was dose dependent with an elevation to the extent of 48.5% in low dose group and 64.4% in the high dose group. Similarly there was also an increase in the enzymic activity of glutathione peroxidase to the extent of 16.9% and 18.8%, in low-dose and high-dose groups respectively. The repeated administration of cyfluthrin produced a significant depletion of the blood glutathione levels as well as the enzymic activity of catalase and superoxide dismutase. Thus on the basis of the present investigation it can be concluded that cyfluthrin is a moderately toxic pesticide.

KEY WORDS antioxidant status, buffalo calves, Cyfluthrin, oxidative stress.

INTRODUCTION

An increase in global food demand has resulted in a significant increase in the use of pesticides in agriculture and animal husbandry. Pyrethroid pesticides have gained popularity over other conventional pesticides due to their high efficacy against target species, their relatively low mammalian toxicity and rapid biodegradability. Synthetic pyrethroid pesticides account for over 30% of the global pesticide use and these are preferentially used in place of organophosphates and organochlorines (El-Tawil and Abdel-Rahman 2001). Cyfluthrin is a synthetic type-2 pyrethroid insecticide, which was originally isolated from the flower of chrysanthemum. Due to its versatility it has become a useful ingredient of various formulations used for the control of a wide range of insects including cutworms, cockroaches, ants, termites, grain-beetle, weevil, fleas, flies and mosquitoes (Ecobichon, 2001). Cyfluthrin produces its action through membrane depolarization and loss of electrical excitability in the central and the peripheral nervous system because of its interaction with sodium-ion-gated channels. Cyfluthrin has been reported to exhibit selective toxicity to insects and a sparingly low toxicity in mammals due to rapid liver metabolism and urinary excretion of both the metabolized and intact compound. However, laboratory animals exposed to relatively high doses of cyfluthrin have shown similar toxic effects as those observed in insects; including convulsions, salivation, ataxia, weakness and apathy (Laskowski, 2002). Due to the central role played by the liver in the detoxification of cyfluthrin, there is a ten-

dency for its accumulation and subsequent toxicity to the liver, disrupting the normal hepatic functioning. In addition, certain pyrethroids have been known to produce oxidative stress in animals, but no such data is available regarding cyfluthrin. Low level of chronic exposure to agricultural chemicals may not have clinically recognizable symptoms but could produce subtle cumulative effects that eventually affect the health of organism (Bebe and Panemanglore 2003). The potential hazard due to pesticide residues on the health of livestock is a growing concern. Although some work on the toxicity of cyfluthrin has been done in different animals, there is limited information available regarding its toxic mechanisms in buffalo species. In order to better understand the mechanism of toxicity of cyfluthrin, it was thought pertinent to investigate the ability of cyfluthrin to modulate the activities or concentrations of endogenous antioxidants in buffalo calves.

MATERIALS AND METHODS

Twelve male buffalo calves (6-12 months), weighing between 70-120 kg, were randomly divided into three groups of four animals. These animals were dewormed and acclimatized to uniform environmental conditions and were provided fodder of season and water *ad libidum.* Group I served as control whereas group II and III animals were orally administered cyfluthrin at the rate of 10 and 20 mg/kg/d for 11 consecutive weeks. Blood samples were collected at weekly intervals via jugular venipuncture in heparinized vials during the period of treatment and two weeks after cyfluthrin withdrawal. Erythrocyte lysate was prepared for analyzing various biochemical parameters. Haemoglobin content was estimated by the method of Benjamin (1985). Lipid peroxidation was estimated by determining the malonyl dialdehyde (MDA) produced using thiobarbituric acid (TBA) (Behne, 2001).

The glutathione peroxidase (GPx) activity was measured by the method of Hafeman *et al*. (1974). Glutathione reductase was assayed spectrophotometrically by measuring change in absorbance at 340 nm due to NADPH utilization (Carlberg and Mannervik, 1985). Glutathione-S-transferase activity was analyzed by measuring the amount of glutathione conjugate formed with CDNB (Habig *et al*. 1974). Glucose-6-phosphate dehydrogenase (G6PD) was estimated on the basis of its ability to catalyze the conversion of glucose-6-phosphate and NADP to 6-phosphogluconolactone and NADPH (Deutsch, 1978).

Superoxide dismutase activity was assayed by the ability of the enzyme to inhibit auto-oxidation of pyrogallol (Marklund and Marklund, 1974). Catalase activity was analyzed by the decomposition of hydrogen peroxide (Aebi, 1983). Glutathione levels were determined by the method of Beutler *et al*. (1963). Significance of differences was determined with the help of student's t-test (Snedecor and Cochran, 1967). The permission to conduct the experiment was obtained from the Institutional Animal Ethics Committee prior to the commencement of the study.

RESULTS AND DISCUSSION

Oral administration of cyfluthrin at a dose rate of 10 and 20 mg/kg/d for 11 consecutive weeks produced very mild signs of toxicity in buffalo calves. These included a lenitived egree of inappetance, listlessness, anorexia and diarrhoea. The symptoms were more apparent in the animals of the higher dose group.

In blood, the normal erythrocytic functioning depends on the intactness of the erythrocyte membrane, which is the target for many toxic xenobiotic factors, including cyfluthrin. Lipid peroxidation has been used as a measure of this xenobiotic-induced oxidative stress, which may be defined as the disequilibrium between the peroxidants and antioxidants in biological system (Kelly *et al*. 1998). In the present investigation, there was a dose dependent increase in the extent of lipid peroxidation (Figure 1). The elevation was degreeof 48.5% in low dose group and 64.4% in the high dose group. The enzymic activity of catalase showed a significant decline to the extent of 29.2% and 31.8% in the low-dose and high-dose groups, respectively (Figure 2). A similar trend was observed in the activity of superoxide dismutase (Figure 3). After the withdrawal of cyfluthrin the activity of superoxide dismutase returned to normal within two weeks of the post-treatment period whereas that of catalase remained significantly higher even after two weeks of cyfluthrin withdrawal. Lipid peroxidation is considered to be the main factor for establishing the oxidative stress produced by a particular compound and generally plays a major role in the development and severity of toxicity syndromes.

The corresponding elevation in the activities of antioxidant enzymes especially superoxide dismutase which dismutases the superoxides produced and results in the generation of hydrogen peroxide, which is further decomposed by catalase, however, this increase was not sufficient to overcome the oxidative stress caused to the animals, as is evident by the incline in lipid peroxidation. A similar increase in the erythrocyte fragility has also been observed *in vitro* by Sadowska *et al*. (2010) in humans.

Glutathione plays a pivotal role in the maintenance of intracellular redox status and antioxidant enzyme functions. It acts as a reducing agent and a vital substance in detoxification in the aqueous phase of cellular systems. Its antioxidant activity is through the thiol group of its cysteine residue (Rana *et al*. 2002). The blood glutathione levels showed progressive decline with the incremental dosing of cyfluthrin.

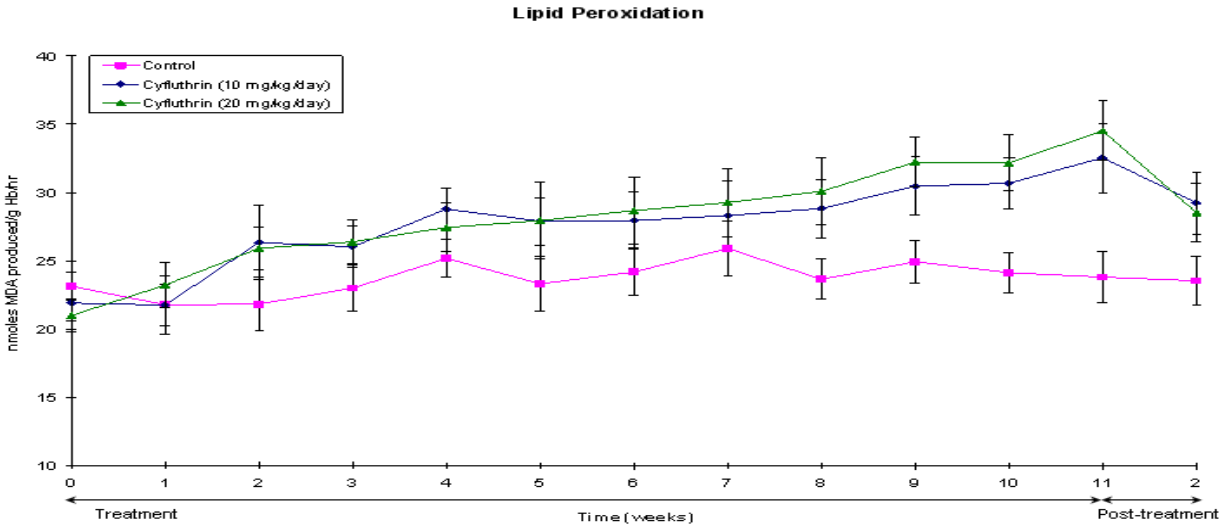

Figure 1 Effect of repeated oral administration of cyfluthrin on lipid peroxidation in buffalo calves

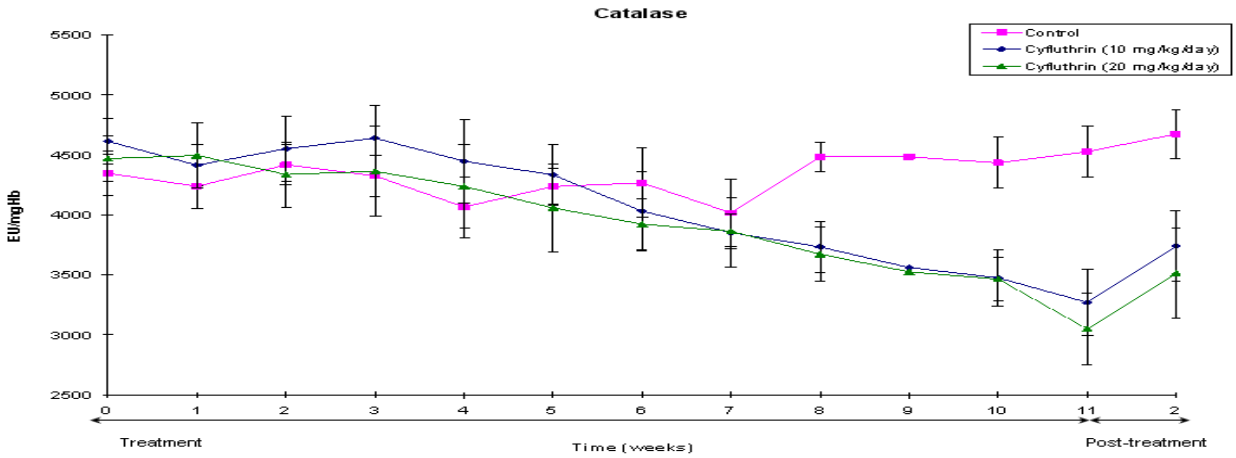

Figure 2 Effect of repeated oral administration of cyfluthrin on catalase activity in buffalo calves

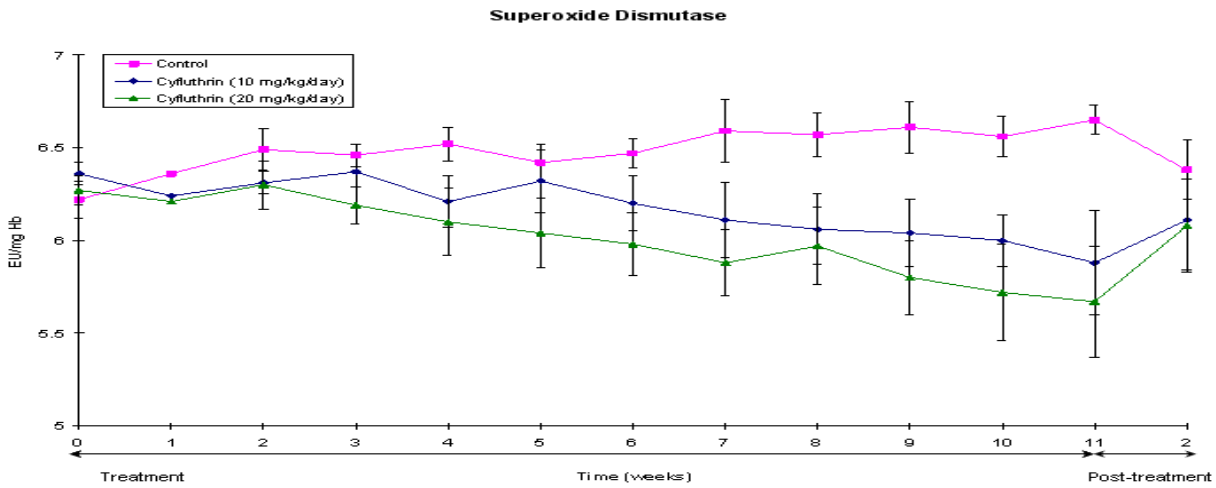

Figure 3 Effect of repeated oral administration of cyfluthrin on superoxide dismutase activity in buffalo calves

The levels were reduced by 22.2% and 27.9% in the low-dose and high-dose groups, respectively, by the 11th week of pesticide treatment (Figure 4). A significant inverse relationship exists between the extent of lipid peroxidation and glutathione status.

In contrast to the decline in the activities of catalase and superoxide dismutase, there was a significant elevation in GPx activity in cyfluthrin treated animals (Figure 5). This increase was to the extent of 16.9 % and 18.8%, in low-dose and high-dose groups, respectively.

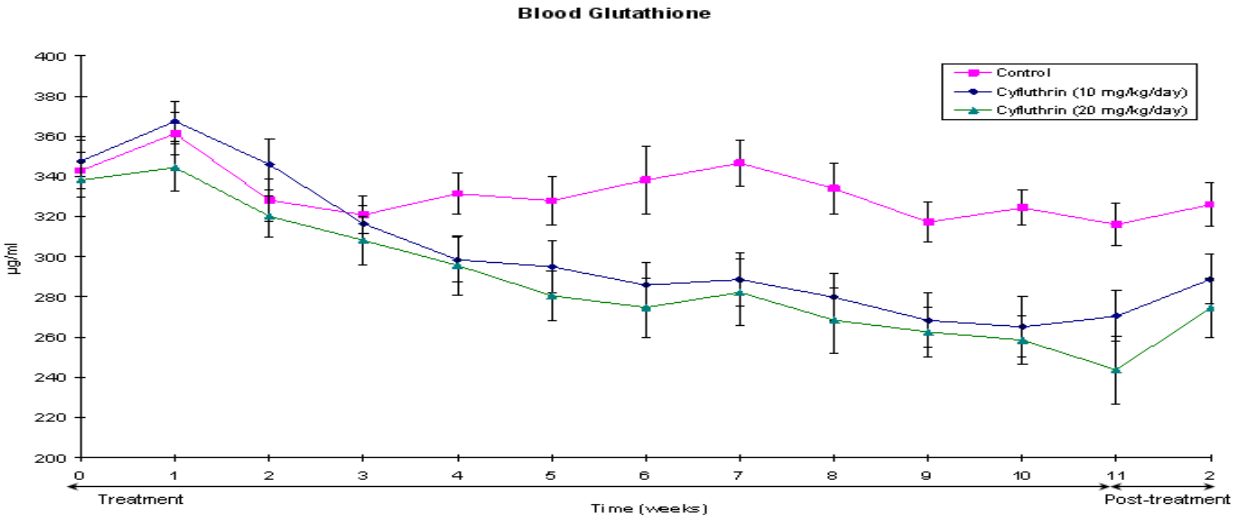

Figure 4 Effect of repeated oral administration of cyfluthrin on blood glutathione levels in buffalo calves

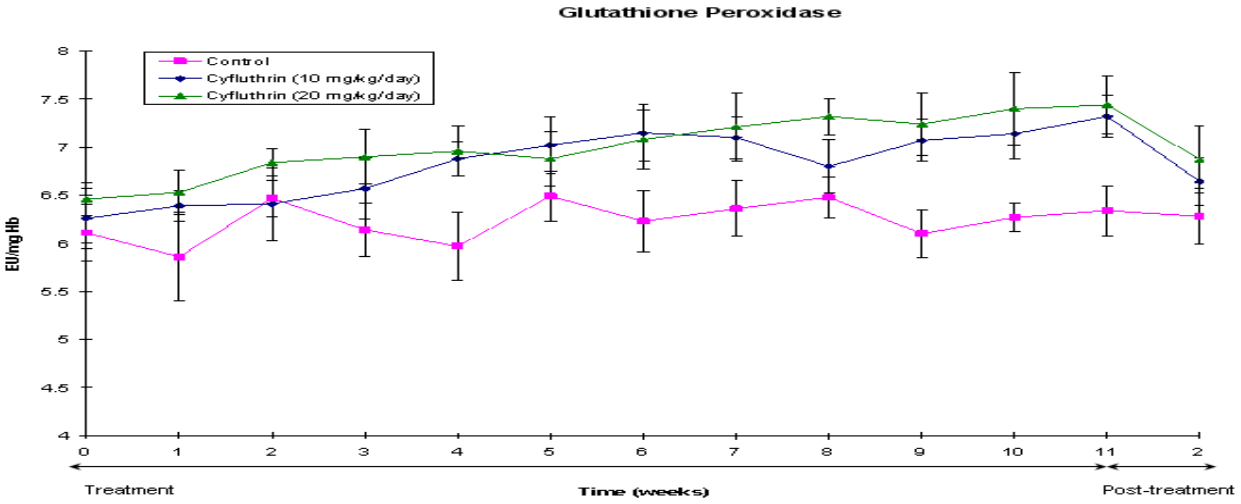

Figure 5 Effect of repeated oral administration of cyfluthrin on glutathione peroxidase activity in buffalo calves

The activity of GPx returned to normal during the post-treatment period in both the treatment groups. In the present investigation, the progressive increase in the extent of lipid peroxidation with time, in animals experimentally induced with cyfluthrin toxicity, is suggestive of peroxidative changes imposed by this pesticide on the erythrocytes. The cell has several mechanisms to alleviate the effects of oxidative stress, either by repairing the damage or by directly diminishing the occurrence of oxidative damage by means of enzymatic and nonenzymatic antioxidants. Reduced glutathione is a powerful and known antioxidant in the cells and plays a vital role in protecting cells against radical and oxyradical damage (Verma and Srivastava, 2000). The corresponding elevation in the activity of glutathione peroxidase and the inhibition of enzymes superoxide dismutase and catalase, which are vital in intra-cellular antioxidant defense, were not able to sufficiently neutralize the oxidative stress in terms of increased lipid peroxidation and decreased glutathione content in animals treated with cyfluthrin.

However, the almost normalization of the enzymic system within two weeks of the withdrawal period is sugestive

that cyfluthrin is a moderately toxic insecticide when used in the recommended concentrations.

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