



**Table 1.** Effects of chronic dermal application of cypermethrin on enzymes, blood glutathione and lipid peroxidation in Wistar rats

Parameters	Days after dermal application							
	Control	30 days	Control	60 days	Control	90 days	Control	120 days
CAT ( $\mu\text{mol of H}_2\text{O}_2$ $\text{decom. min}^{-1} \text{ mg. Hb}^{-1}$ )	16.23 $\pm$ 2.44 <sup>a</sup>	35.52 $\pm$ 6.18 <sup>b</sup>	14.53 $\pm$ 2.23 <sup>a</sup>	45.25 $\pm$ 7.24 <sup>b</sup>	19.23 $\pm$ 2.64 <sup>a</sup>	59.51 $\pm$ 13.27 <sup>b</sup>	19.42 $\pm$ 2.65 <sup>a</sup>	65.27 $\pm$ 10.45 <sup>b</sup>
SOD ( $\text{Umg. Hb}^{-1}$ )	0.025 $\pm$ 0.005 <sup>a</sup>	0.266 $\pm$ 0.021 <sup>b</sup>	0.035 $\pm$ 0.004 <sup>a</sup>	0.026 $\pm$ 0.009 <sup>c</sup>	0.031 $\pm$ 0.006 <sup>a</sup>	0.015 $\pm$ 0.012 <sup>c</sup>	0.028 $\pm$ 0.004 <sup>a</sup>	0.014 $\pm$ 0.010 <sup>c</sup>
GSH-Px ( $\text{Umg. Hb}^{-1}$ )	7.70 $\pm$ 0.65 <sup>a</sup>	3.35 $\pm$ 0.37 <sup>c</sup>	8.60 $\pm$ 0.55 <sup>a</sup>	2.93 $\pm$ 0.19 <sup>c</sup>	5.50 $\pm$ 0.23 <sup>a</sup>	2.71 $\pm$ 0.11 <sup>c</sup>	8.75 $\pm$ 0.45 <sup>a</sup>	2.59 $\pm$ 0.23 <sup>c</sup>
GST ( $\mu\text{mol of conjugate}$ $\text{of min}^{-1} \text{ mg. Hb}^{-1}$ )	0.0054 $\pm$ 0.001 <sup>a</sup>	0.0057 $\pm$ 0.0032 <sup>a</sup>	0.0051 $\pm$ 0.002 <sup>a</sup>	0.0286 $\pm$ 0.009 <sup>b</sup>	0.0054 $\pm$ 0.003 <sup>a</sup>	0.2207 $\pm$ 0.008 <sup>b</sup>	0.0054 $\pm$ 0.002 <sup>a</sup>	0.2692 $\pm$ 0.0345 <sup>b</sup>
GSH ( $\text{nmol. mL}^{-1}$ )	105.79 $\pm$ 14.74 <sup>a</sup>	27.76 $\pm$ 7.45 <sup>b</sup>	100.56 $\pm$ 15.74 <sup>a</sup>	26.35 $\pm$ 6.59 <sup>c</sup>	112.79 $\pm$ 18.34 <sup>a</sup>	21.57 $\pm$ 5.12 <sup>c</sup>	98.79 $\pm$ 17.77 <sup>a</sup>	18.85 $\pm$ 2.67 <sup>b</sup>
LPO ( $\text{nmol of MDA}$ $\text{gm Hb}^{-1} \text{ h}^{-1}$ )	1.35 $\pm$ 0.31 <sup>a</sup>	3.34 $\pm$ 0.68 <sup>b</sup>	1.65 $\pm$ 0.42 <sup>a</sup>	4.06 $\pm$ 0.96 <sup>b</sup>	1.79 $\pm$ 0.43 <sup>a</sup>	3.93 $\pm$ 0.89 <sup>b</sup>	1.99 $\pm$ 0.42 <sup>a</sup>	5.05 $\pm$ 0.33 <sup>b</sup>

Values are expressed as mean  $\pm$  SE. (n = 6). <sup>a,b,c</sup>Means with different superscripts are significantly different between groups ( $p < 0.05$ ). CAT: catalase, SOD: superoxide dismutase, GSH-Px: glutathione peroxidase, GST: glutathione S-transferase, GSH: reduced glutathione, LPO: lipid peroxidation, MDA: malondialdehyde.

Statistical analyses were done using one-way ANOVA followed by Dunnet's test with  $p < 0.05$  as a limit of significance.

A significant increase ( $p < 0.05$ ) in the catalase activity was observed in all groups (Table 1). Also, a significant increase ( $p < 0.05$ ) in SOD activity was observed in group B, but the activity was reduced significantly ( $p < 0.05$ ) in the other groups compared to control. GSH-Px activity was significantly reduced ( $p < 0.05$ ) in all groups compared to the control group. Similar finding have been reported in other study during oxidative stress [24]. No significant changes in GST activity was seen up to 30 days, but thereafter, a significant increase was noticed up to 120 days. There was significant decrease in the GSH after 30 days and similar pattern followed up to 120 days ( $p < 0.05$ ). Significant increase in lipid peroxidation indicated lipid membrane damage from 30 days onward.

Pyrethroids are metabolized in liver via cytochrome P450 oxidative pathways yielding reactive oxygen species [9,19]. Oxidative stress takes advantage of the available mitochondrial electron to make molecular oxygen, resulting in excess superoxide production in most tissues [2]. These superoxide anions are converted to hydrogen peroxide and water with the help of a group of SOD [10]. A significant drop in erythrocyte SOD levels indicates a decrease in the tissues' ability to handle excessive free radicals [2]. However, an increase in catalase activity enhances the scavenging ability of erythrocytes to handle the hydrogen peroxide to molecular oxygen and water [11,29].

GSH-Pxs catalyze the peroxides and reduce the glutathione to form oxidized glutathione and water [30]. A significant reduction in GSH-Px activity may be due to over production of free radicals [24]. Similarly, GST catalyzes the conjugation of the reduced glutathione to electrophiles and protects cellular components from

oxidative damage [16]. Increased activity of GST was reported in *Drosophila melanogaster* after insecticide exposure [27]. Elevated GSTs were reported in *Nilaparvata lugens*, a pyrethroid insecticide resistant strain of insect [38]. GST levels were also increased significantly after 30 days of exposure to protect RBCs from oxidative damage. Further significant decreases in GSH levels in our study may be due to either the inhibition of GSH synthesis or increased utilization of GSH for detoxification of toxicant induced free radicals [33]. The decrease in SOD, blood GSH and GSH-Px suggests that the dermal exposure of cypermethrin may lead to excessive free radical generation. These free radicals might be attacking the thiol group of cysteine residue and poly-unsaturated fatty acids of biological membranes [6]. Free radical-induced lipid peroxidation resulting in the deterioration of biological membranes [32].

In conclusion, the changes suggest that the accumulation of excess free radicals may be responsible for the increased lipid peroxidation which sensitizes the cells to various degenerative diseases.

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