Impact of the residue of Deltamethrin and Endosulfan pesticides on biochemical toxicity and some neurotransmitter contents in different brain areas of male Albino mice

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INTRODUCTION

Using pesticides is an important procedure for enhancing agriculture yield. However, the great consciousness, brought back upon their deleterious effects on human, animal and environmental health, leading to the shortage of their use by imposing various rules (Ahmsd et al., 2010; Botella et al., 2004).

Among pesticides, Deltamethrin, which is a type II pyrethroids, has a wide acceptability, and is used in agriculture and forestry because of its high activity against a broad spectrum of insect pests (Villarini et al., 1998). The oral route constitutes the main sources of general population exposure to this pesticide which is ingested within food and water (Barlow et al., 2001).

It has been reported that deltamethrin caused an oxidative damage in liver and intestine of Carassius auratus gibelio explained by an increase of LPO level and an enhancement of antioxidative defence parameters (Dinu et al., 2010). Oral absorption of deltamethrin is rapid and is metabolized with microsomal enzyme system in liver and with tissue esterase present in intestinal wall and liver in addition to plasma carboxylesterases (Usmani et al., 2006). According to Simsek et al., (2008), Deltamethrin applied at different concentrations of 25, 50, 100, 200, 400, 800 and 1600 mg /L, for 1,24, 48, 72 and 96 h increased lipid peroxidation which is accompanied by a decrease of reduced glutathione and catalase activity in digestive gland and gill of fresh water mussel.

Endosulfan (6, 7, 8, 9, 10-hexachloro -1,5,5a,6, 9a-hexahydro-6,9-methano -2, 4, 3 benzodioxathiepine-3-oxide) is a broad-spectrum organochlorine pesticide (insecticide and acaricide) first registered for use in the United States in 1954 to control agricultural insect and mite pests on a variety of fruits, vegetables, rice, grains, tea, coffee, cotton and also in animal farm and houses (US EPA). Results from a global monitoring network for persistent organic pollutants revealed that endosulfan is abundant in the environment and its use is increasing (Pozo et al., 2006; Harner et al., 2006). It reaches aquatic systems through direct application, as well as spray drift and runoff from agricultural areas (Broomhall, 2002; Jergentz et al., 2004 and Rand et al., 2010).

It is known that exposure to pesticides during development may interfere with the normal development of neurotransmitter systems and cause their direct damage (Richardson et al., 2006). The central nervous system (CNS) during development is particularly susceptible to the toxic effects of xenobiotics (Tilson, 2000). The mechanism by which these effects occur is not known but currently it is assumed that the monoaminergic neurotransmitters play a role during development, defined as “morphogenetic” (Buznikov et al., 1996; Levitt et al., 1997; Nicotra and Schatten, 1990).

Organophosphate pesticide represent one of the world’s most commonly used agrochemical. Consequently, many of its residues are frequently found in the environment. The aim of this study was to determine the effects of the pesticides, deltamethrin and endosulfan on biochemical toxicity and some neurotransmitter contents in different brain areas of male albino mice.

MATERIALS AND METHODS

Pesticides

Deltamethrin

Deltamethrin is a synthetic pyrethroid pesticide [(S)-acyano-3-phenoxybenzyl(1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate] with molecular formula (C_{23}H_{19} Br_{2}NO_{3}). Solubility in water is <0.1 mg/L at 25°C. Relative molecular mass of the compound is 505.2 g/mol, and the melting point is 100°C (Figure 1).

Endosulfan

Endosulfan is an off-patent organochlorine pesticide and acaricide that is being phased out globally.
[6, 7, 8, 9, 10, 10-Hexachloro-1, 5,5a, 6, 9, 9a-hexahydro-6, 9-methano-2,4,3-benzodioxathiepine-3-oxide]. With the molecular formula of \((\text{C}_9\text{H}_6\text{C}_\text{Cl}_6\text{O}_3\text{S})\). Solubility in water is 0.33 mg/L. Relative molecular mass is found to be 406.93 g mol\(^{-1}\), and the melting point is 70-100°C, 343-373 K, 158-212 °F (Figure 1).

Animals

Swiss albino male mice of 10 weeks old with an average weight of 28.5±2.5 g obtained from the National Research Centre, Cairo, Egypt were used. They were maintained in a well ventilated animal house. They were housed in large polypropylene cages with free access to food and water ad labium during the course of the experiment. Animals were housed in groups (5 animals/group) and maintained under standard conditions of temperature (23°C to 25°C), a relative humidity of 65% to 86% and in a schedule of 12 hours of light and 12 hours of dark.

Animal treatment

The animals were divided into three groups (n=6) of equal number. The control group (1) was orally and daily administered with equivalent amount of the vehicle (distilled water) for two weeks, the second group was given drinking water with 1.28 mg/kg BW of deltamethrin (Yousef et al., 2006) during two weeks of oral and daily administration and the third group was orally and daily administered with endosulfan (1.5 mg/kg BW). At the ends of the experimental period (2 weeks), the mice were sacrificed under diethyl ether anesthesia at fasting state.

Effect of deltamethrin and endosulfan (pesticide) on some neurotransmitter contents in different brain areas of male albino mice

During the experiment six mice of each group were decapitated each week till the end of the 2-week duration times. The mice were killed by sudden decapitation at the designed times. The brain was rapidly and carefully excised and then dissected on dry ice glass plate according to the method of Glowinski and Lversen (1966) into the following regions; cerebellum, striatum cerebral cortex, hypothalamus, brain stem and hippocampus. Brain tissues were wiped dry with filter paper, weighed, wrapped in plastic films and then in aluminum foil and quickly frozen in dry ice. NE and DA were extracted and estimated in the brain tissues.
according to the method of Chang (1964) modified by Ciarlone (1978). GABA were extracted and estimated in the brain tissues according to the method of Sutton and Simmonds (1973). The fluorescence was measured in Jenway 6200 fluorometer.

**Effect of deltamethrin and endosulfan (pesticide) on biochemical toxicity of male albino mice**

Serum samples were obtained by the centrifugation of blood of six rats of each group at 4000 rpm for 15 min at 4°C, and were then divided in to Eppendorf tubes. Isolated sera from each group were stored at -20°C until they were used for the analyses. For preparation of tissue homogenates of mouse liver tissue of six mice of each group, one gram of liver tissues of mouse from each group was homogenized in 5 ml distilled water at pH 7.5. A glass homogenizer was used and the homogenate was centrifuged for 10 minutes at 3000 rpm, fresh supernatant was used.

The levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) were measured according to Reitman and Frankel (1957). Alkaline phosphatase (ALP) was measured according to Belfield and Goldberg (1971) and acid phosphatase (ACP) was measured according to Wattiaux and De Duve (1956) and sera glucose concentrations (GL) were determined according to the glucose oxides method of Trinder (1969). Total protein (TP) content was determined according to Bradford (1976). Determination of tissues glycogen was evaluated according to Nicholas et al., (1956). Lipid peroxide (LP) was measured according to Buege and Aust (1978). Glutathione (GSH) was measured according to Moron et al., (1979). Pyruvate kinase (PK) relative activity was measured spectrophotometrically by the method of Bucher and pfeiderer (1975). phosphofructokinase (PFK) was measured according to Zammit et al., (1978). Glucose phosphate isomerase (GPI) was measured according to King (1965). Fructose-1, 6-diphosphatase (F- 1, 6-ase) was measured according to Sand et al., (1980). All biochemical 1 parameters determined in this study were determined spectrophotometrically, using reagent kits purchased from BioMerieux Company, France. Kits purchased from BioMerieux Company, France.

**Statistical analysis**

The results obtained in the present work are represented as means ± standard deviation (SD), and were analyzed using analysis of variance (ANOVA). The significance of difference between means were calculated using the Duncan Multiple Range Test (Steel and Torrie, 1980).

**RESULTS**

Results in Table 1 showed that the daily oral administration of deltamethrin and endosulfan resulted in

<table>
<thead>
<tr>
<th>Pesticides</th>
<th>Cerebellum mean ± S.E.</th>
<th>Striatum mean ± S.E.</th>
<th>Cerebral cortex mean ± S.E.</th>
<th>Hypothalamus mean ± S.E.</th>
<th>Brain stem mean ± S.E.</th>
<th>Hippocampus mean ± S.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deltamethrin</td>
<td>122.7±0.72</td>
<td>280.5±0.64</td>
<td>52.3±0.084</td>
<td>433±4.2</td>
<td>310.2±0.45</td>
<td>222.1±0.6</td>
</tr>
<tr>
<td>%</td>
<td>82.3±1.2*</td>
<td>186.6±0.6*</td>
<td>36.5±0.21*</td>
<td>146.3±2.1**</td>
<td>254.5±1.4</td>
<td>160.2±0.62</td>
</tr>
<tr>
<td>Endosulfan</td>
<td>122.7±0.72</td>
<td>280.5±0.64</td>
<td>52.3±0.084</td>
<td>433±4.2</td>
<td>310.2±0.45</td>
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<td>36.5±0.21*</td>
<td>146.3±2.1**</td>
<td>254.5±1.4</td>
<td>160.2±0.62</td>
</tr>
</tbody>
</table>

- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired t' test
% : Percentage of change from control  *p< 0.05,**p< 0.01 & ***p< 0.001
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A significant decrease in DA content in all brain area. The maximal decrease (p<0.001) in DA content was found in the hypothalamus of mice treated with deltamethrin and endosulfan at the concentrations of 66.21% and 73.1%, respectively. Also, Table 2 showed that the daily oral administration of deltamethrin and endosulfan caused a significant (p<0.001) decrease in GABA content in all the brain area, the maximal decrease (p< 0.001) in GABA content was found in brain stem of mice treated with deltamethrin and endosulfan at the concentration of 72.52% and 80.52%, respectively.

The results obtained from Table 3 showed that the maximal decrease (p<0.001) in NE content was found in the hypothalamus of mice treated with deltamethrin and endosulfan at the concentrations of 54.1% and 62.89%, respectively.

The results in Table 4 showed that a clear reduction (P<0.001) in liver enzyme activities in serum of mice treated with deltamethrin and endosulfan as compared to the control mice. On the other hand, the glucose concentration and Acid phosphatase in serum of treated mice showed a marked increase (P<0.001) in comparison with the control group. Glycogen content in tissues of treated mice showed a significant (p>0.001) decrease in comparison with the control group. The reduction rates were 36.32% and 58.24% for mice treated with deltamethrin and endosulfan, respectively (Table 7).

Table (2): Effect of oral administration of Deltamethrin and Endosulfan on gama-butyric acid (GABA) content in the different brain areas of male albino rat.

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Cerebellum mean ± S.E.</th>
<th>Striatum mean ± S.E.</th>
<th>Cerebral cortex mean ± S.E.</th>
<th>Hypothalamus mean ± S.E.</th>
<th>Brain stem mean ± S.E.</th>
<th>Hippocampus mean ± S.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deltamethrin C</td>
<td>165.7±0.65</td>
<td>154.21±0.8</td>
<td>44.2±0.62</td>
<td>321.6±0.82</td>
<td>121.2±0.197</td>
<td>204.3±1.6</td>
</tr>
<tr>
<td>T</td>
<td>102.6±1.3**</td>
<td>92.6±0.428**</td>
<td>35.2±0.8</td>
<td>2925±0.43*</td>
<td>33.3±0.764**</td>
<td>98.8±0.577**</td>
</tr>
<tr>
<td>%</td>
<td>-61.97%</td>
<td>39.82%</td>
<td>18.1%</td>
<td>72.52%</td>
<td>72.52%</td>
<td>51.64%</td>
</tr>
<tr>
<td>Endosulfan  C</td>
<td>165.7±0.65</td>
<td>154.21±0.8</td>
<td>44.2±0.62</td>
<td>321.6±0.82</td>
<td>121.2±0.197</td>
<td>204.3±1.6</td>
</tr>
<tr>
<td>T</td>
<td>60.6±1.2***</td>
<td>72.4±0.87**</td>
<td>28.6±0.83***</td>
<td>252±1.6</td>
<td>23.6±0.82*</td>
<td>88.4±1.6***</td>
</tr>
<tr>
<td>%</td>
<td>63.43%</td>
<td>53.1%</td>
<td>35.29%</td>
<td>21.64%</td>
<td>80.52%</td>
<td>56.73%</td>
</tr>
</tbody>
</table>

- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired t' test. % : Percentage of change from control. *p< 0.05,**p< 0.01 & ***p< 0.001

Table (3): Effect of oral administration of Deltamethrin and Endosulfan on norepinephrine (NE) content in the different brain areas of male albino rat.

<table>
<thead>
<tr>
<th>Pesticide</th>
<th>Cerebellum mean ± S.E.</th>
<th>Striatum mean ± S.E.</th>
<th>Cerebral cortex mean ± S.E.</th>
<th>Hypothalamus mean ± S.E.</th>
<th>Brain stem mean ± S.E.</th>
<th>Hippocampus mean ± S.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deltamethrin C</td>
<td>102.6±1.4</td>
<td>434.2±1.6</td>
<td>64.6±1.54</td>
<td>462.2±2.11</td>
<td>342±0.53</td>
<td>233.1±1.4</td>
</tr>
<tr>
<td>T</td>
<td>77.5±0.56**</td>
<td>344.23±1.4**</td>
<td>35.2±0.54*</td>
<td>212.2±0.52**</td>
<td>243.1±0.45**</td>
<td>106.2±0.62***</td>
</tr>
<tr>
<td>%</td>
<td>24.64%</td>
<td>20.72%</td>
<td>48.57%</td>
<td>54.1%</td>
<td>28.95%</td>
<td>45.44%</td>
</tr>
<tr>
<td>Endosulfan  C</td>
<td>102.6±1.4</td>
<td>434.2±1.6</td>
<td>64.6±1.54</td>
<td>462.2±2.11</td>
<td>342±0.53</td>
<td>233.1±1.4</td>
</tr>
<tr>
<td>T</td>
<td>48.2±0.62**</td>
<td>223.3±0.61**</td>
<td>22.3±1.4***</td>
<td>210.8±1.1***</td>
<td>168.5±1.4***</td>
<td>86.5±0.83***</td>
</tr>
<tr>
<td>%</td>
<td>53%</td>
<td>48.57%</td>
<td>65.48%</td>
<td>99.45%</td>
<td>50.73%</td>
<td>62.89%</td>
</tr>
</tbody>
</table>

- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired t' test. % : Percentage of change from control. *p< 0.05,**p< 0.01 & ***p< 0.001
The present result in Table 5 indicated that a significant increase in lipid peroxide accompanied with a significant reduction in glutathione and total protein in liver enzyme activities of mice treated with deltamethrin and endosulfan as compared to the control mice.

The present results in tables (6, 7) demonstrate a significant elevated level of glycolytic (PK, PFK and GPI) and gluconeogenic enzyme activities (F-1,6-D-Pase) in tissue of mice treated with deltamethrin and endosulfan as compared to the control. The elevation rates in the activities of PK, PFK, GPI and F-1,6-D-Pase enzymes were 97.36%, 76.1%, 74.84% and 69.1%, respectively for mice treated with endosulfan.

DISCUSSION

Many monoamine neurotransmitters, including DA, NE and GABA are important in the regulation of brain development prior to assuming their roles as transmitters in the mature brain (Whitaker-Azmitia, 1992; Di Pino, 2004; Ansorge, 2008), thus any circumstance that affects these neurotransmitters in the developing brain can alter the final structure and function of the brain. Developmental neurotoxicity involves alterations in behavior, neurophysiology.

From the present results, it is clear that the daily oral administration of deltamethrin and endosulfan caused reducing side effect in some neurotransmitter tissue in the brain and a significant decrease in neurotransmitter contents (NE, DA and GABA) in most of the tested brain areas. Cerebellum which is responsible for the voluntary movement; pons and medulla oblongata which is responsible of essential reflexive acts; striatum which is a brain region responsible for motor activity; cerebral cortex is responsible for sensation including visual, auditory and olfactory as well as motor coordination and association, also is responsible for higher mental function such as thinking, planning, reasoning, memory and consciousness and hippocampus, this is the key area
concerned with learning (Ansorge, 2008). Brain stem is responsible for integration of coordination of essential reflexive acts such as swallowing, vomiting and respiration (Bloom, 1983).

Our findings support the idea that deltamethrin and endosulfan is neurotoxic in the developing brain. The present result found that these pesticides induced a decrease in DA levels in cerebellum, striatum, cerebral cortex, hypothalamus, brain stem and hippocampus of treated mice. The loss of hippocampus DA levels was higher in treated mice. DA is an important component of the neuroendocrine mechanism that regulates the activation of male sexual behavior in mammalian species (Castagna and Ball, 1997). Moreover, steroidogenesis in the brain may play a critical role in mammalian brain developmental of both sexes (Konkle and McCarthy, 2011). Steroids play a role in the development of catecholamines systems (Leret, 2009; Muneoka et al., 2010; Pappas et al., 2010).

It is known that DA is the major compound involved in the control of the motor system. Bernardi and Palermo-Neto, (1983) showed that locomotion and rearing frequencies observed in an open field might be used to detect drug-induced dopaminergic interference. Locomotors activity as measured in the open field appears to be associated with the dopaminergic system (Chiavegatto et al., 1998). Also, in the present study, we similarly found a loss of the NE and gamma-butyric acid (GABA) content in the cerebellum, striatum, cerebral cortex, hypothalamus, brain stem and hippocampus. The loss of brain stem DA levels and the loss of hippocampus GABA levels were higher in treated mice.

These effects may represent a large number of actions involved in the development of synaptic dysfunction in these neurotransmitter systems that ultimately contribute to behavioral anomalies. Nevertheless further behavioral testing is needed to confirm this suggestion. Moreover, the present findings might indicate that prenatal and postnatal exposure to pesticide altered the program for developmental of DA, NE, and GABA synaptic functions. Given that, the dysfunction in serotonin and dopamine systems is involved such as appetite, affective, locomotion, learning, neurological and neuropsychiatric disorders (Insel et al., 1990; Kaye, 2008), further testing of this function is needed to confirm that alteration of these neurotransmitter systems is the cause of some of these dysfunctions. In general, our results support the

<table>
<thead>
<tr>
<th>Table 5: Effect of Deltamethrin and Endosulfan on lipid peroxide, glutathione and total protein in male mice liver.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid peroxide (LP) (ug/g tissue)</td>
</tr>
<tr>
<td>% change</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Deltamethrin</td>
</tr>
<tr>
<td>Endosulfan</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 6: Effect of Deltamethrin and Endosulfan on some glycolytic enzymes in male mice liver.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolytic enzmes (umole/mg protein/min.)</td>
</tr>
<tr>
<td>PK</td>
</tr>
<tr>
<td>% change</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Deltamethrin</td>
</tr>
<tr>
<td>Endosulfan</td>
</tr>
</tbody>
</table>

Data represent mean values of five replicates. Within columns for dose, time and (dose x time), mean values followed by different letters are statistically significantly different based on LSD at P = 0.05.
suggestion that at least some of the effects of these disorders that are increasing in humans can be caused by exposure to neurotoxin environmental contaminants (Slikker W and Schwetz, 2003).

In conclusion, the results observed in this study reinforce the idea of the use of neurochemical measures, such as the DA, NE and GABA content and its metabolites in brain regions as indicators of neurotoxicity, including developmental neurotoxicity, induced by chemical agents. Because of serotonergic dysfunction is involved in appetite and affective disorders, and the catecholamine DA and NE have been most often linked to the behavioral pathology of a number of neurological and psychiatric disorders, studies of pesticide on DA, NE and GABA. Related behaviors in animal models will be needed to clarify the outcomes of long-term alterations in noradrenergic, serotonergic and dopaminergic systems identified here.

Concerning, ALT, AST and ALP enzyme activities, gradual significant reduction was observed in serum of mice treated with deltamethrin and endosulfan for two week. The reduction observed in AST and ALT attributed to the hepatocellular damage resulting from chemical-toxicity, where the transaminases levels showed an intimate relationship to cell necrosis and/or increased cell membrane permeability which led to the discharge of enzyme to blood stream. The decrease in transaminase levels providing additional support for the side effect of the deltamethrin and endosulfan on mitochondria of the hepatic cells as it is the subcellular localization of transaminases (El–Shazly et al., 2001). This was attributed to the irritation of liver cells by toxins or due to increase loss of intracellular enzyme by diffusion through cell membrane. In the present study, acid phosphatase show significant elevation in serum of treated mice. Higher levels of acid phosphatase in tissue was observed by El-Aasar et al., (1989) and Abdel-Rahman et al., (1993), which was attributed to the irritation of liver cells by toxins or metabolic products of growing schistosomula of adult worms and eggs or due to increase loss of intracellular enzyme by diffusion through cell membrane which appear to act as a stimulus to the synthesis of more enzyme.

Regarding the sources of energy for mice, deltamethrin and endosulfan significantly decreased the glycogen content in liver tissues of treated mice, while the glucose level increased in the serum of treated mice. This may be attributed to the activity of the pesticides that impedes oxygen consumption of mice, thus inducing anaerobic respiration. Under hypoxic conditions, animals derive their energy from anaerobic breakdown of glucose, which is available to the cells by increased glycogenolysis (Vincent et al., 1995; Sambasiva, 1999). Nakano and Tomlinson (1967) have suggested that catecholamine levels rise under stressful environmental conditions, enabling the increased utilization of glycogen for energy production. To restore its energy requirements, the mouse has to increase the rate of glycolysis thus bringing about a reduction of the glycogen content and increase glucose level in the blood (Baskaran and Palanichamy, 1990; Vasanthi and Baskaran, 1990).

### Table 7: Effect of Deltamethrin and Endosulfan on Glycogen and some Gluconeogenic enzymes in male mice liver.

<table>
<thead>
<tr>
<th></th>
<th>Glycogen (mg/g tissue)</th>
<th>% change</th>
<th>Fructose-1,6-diphos-phatase (umole/mg protein/min.)</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.8 ±0.64</td>
<td></td>
<td>12.6±1.22</td>
<td></td>
</tr>
<tr>
<td>Deltamethrin</td>
<td>4.33±0.64</td>
<td>36.32%</td>
<td>15.4 ±1.11</td>
<td>22.22%</td>
</tr>
<tr>
<td>Endosulfan</td>
<td>2.84±1.02</td>
<td>58.24%</td>
<td>21.3 ±1.43</td>
<td>69.1%</td>
</tr>
</tbody>
</table>

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The data obtained in the present study showed that lipid peroxide was elevated in the liver of mice treated with deltamethrin and endosulfan. Lipid peroxidation is known to require the participation of highly reactive oxygen and other reactive metabolites in the chain of biochemical reaction (Botros et al., 2007). At the same time, liver GSH was drastically depleted in the liver. Such depletion is critical, as shown by the increased cytotoxicity of \( \text{H}_2\text{O}_2 \) in endothelial cells, as a result of inhibition of glutathione reductase, which keeps glutathione in its reduced state (El-Rigal et al., 2006).

In a good agreement with the present results Mittelstaedt et al., (2004) suggested that nuclei and mitochondria act as major targets of MG toxic action, probably by increasing the generation of free radicals, lipid peroxidation and DNA adducts formation.

Total protein content showed significant reduction in liver tissue of mice treated with deltamethrin and endosulfan for 2 weeks. This could be attributed to cellular damage caused by toxin (Parasad et al., 1991). The significant decrease in total protein content is mainly due to increase in messenger RNA degradation which is the possible cause for the hypoalbuminemia (Metwally et al., 1990). The depletion of the protein fraction in the liver tissue of mice in this experiment may have been due to interference of active substance of pesticides in protein metabolism by inhibiting protein synthesis (Volpi et al., 1997).

The current investigation revealed significant enhancement of PK, PFK and GPI the rate limiting glycolytic enzymes, in liver tissue of treated mice with two pesticides compared to control group accompanied by a marked increase in the gluconeogenesis; F,1-6-diphosphatase. The increase in gluconeogenic enzymes may be also responsible for the production of glucose during treatment (Klover and Mooney, 2004). Stimulation of PK in pesticide toxicity ascertained the enhancement of glycolytic flux previously reported by Ahmed and Gad (1995).

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