Journal of Research in Biology

An International Scientific Research Journal

Original Research

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

Authors:
Somaya M. Ismail[1],
Azza A. Said[2],
Samira M. El-Sayad[2].

Institution:
1. Zoology department, Faculty of Science, Cairo university.
2. Zoology department, Faculty of Science, Fayoum university.

Corresponding author:
Somaya M. Ismail

Email:
mragaa11@yahoo.com

Tel:
+201118244212

ABSTRACT:

Evaluating the action of the residues of pesticides on non-target organisms has been of interest to many researchers. The present study aimed to evaluate the pesticides deltamethrin and endosulfan on biochemical toxicity and some neurotransmitter contents in different brain areas of male albino mice. The results showed that the daily oral administration of deltamethrin and endosulfan caused a significant decrease in neurotransmitter contents (NE, DA and GABA) in most of the tested brain areas (cerebellum, striatum, cerebral cortex, hypothalamus, brain stem and hippocampus). On the other hand a gradual significant reduction, ALT, AST and ALP enzyme activities, while the glucose level and acid phosphatase increase were observed in serum of mice treated with deltamethrin and endosulfan for two weeks. Also, this study has a significant inhibition in the activities of enzymes in liver tissues of treated mice including glutathione reductase. Meanwhile, the activity of lipid peroxide, glycolytic (PK, PFK and GPI) and gluconeogenic enzyme activities (F-1, 6-D-Pase) were significantly increased in liver tissues of treated mice in response to treatment. Additionally, total protein and glycogen content showed a significant reduction in liver tissues of mice treated with deltamethrin and endosulfan for two weeks. It was concluded that the pollution of the aquatic environment by deltamethrin and endosulfan pesticides, would adversely affect the metabolism of the mice.

Keywords:
Deltamethrin, Endosulfan pesticide, Laboratory-bred strain Swiss albino male mice, neurotransmitter contents (NE, DA and GABA).

Article Citation:
Somaya M. Ismail, Azza A. Said and Samira M. El-Sayad.
Impact of the residue of Deltamethrin and Endosulfan pesticides on biochemical toxicity and some neurotransmitter contents in different brain areas of male Albino mice.
Journal of Research in Biology (2013) 3(4): 954-966

Dates:
Received: 12 Jan 2013 **Accepted:** 22 Feb 2013 **Published:** 24 May 2013

Web Address:
http://jresearchbiology.com/documents/RA0324.pdf.

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-dimethylcyclopropanecarboxylate] with molecular formula ($C_{22}H_{19}$ Br_2NO_3). Solubility in water is <0.1 mg/L at 25^{o}C. Relative molecular mass of the compound is 505.2 g/mol, and the melting point is 100^{o}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 ($C_9H_6C_{16}O_3S$). 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)

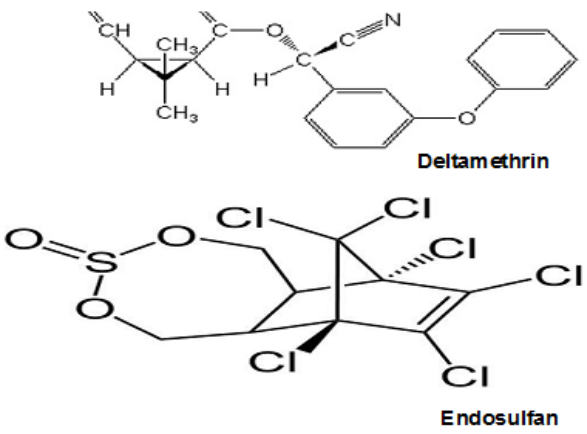

Fig. 1. Chemical structure of the pesticides Deltamethrin and Endosulfan

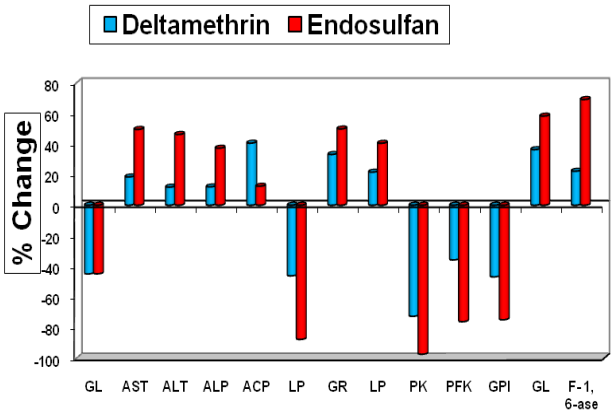

Fig. 2. Changes (%) of activities of glucose level (GL), some enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase (ALP), acid phosphatase (ACP) in serum of male mice,. Lipid peroxide (LP) glutathione (GSH) , pyruvate kinase (PK), phosphofructokinase (PFK), glucose phosphate isomerase (GPI), Fructose -1, 6-diphosphatase (F-1, 6-ase) enzymes, Total protein (TP), glycogen content in tissues of male mice liver exposed to LC25 of Deltamethrin and Endosulfan pesticides for 2 weeks.

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 spectrophometrically by the method of Bucher and pfleiderer (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 l 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 (1): Effect of oral administration of Deltamethrin and Endosulfan on dopamine (DA) content in the different brain areas of male albino rat.

Pesticides		Cerebellum mean ± S.E.	Striatum mean ± S.E.	Cerebral cortex mean ± S.E.	Hypothalamus mean ± S.E.	Brain stem mean ± S.E.	Hippocampus mean ± S.E.
	C	122.7± 0.72	280.5±0.64	52.3±0.084	433 ± 4.2	310.2±0.45	222.1±0.6
Deltamethrin	T	82.3±1.2*	186.6±0.6*	36.5±0.21*	146.3±2.1**	254.5±1.4	160.2±0.62
	%	32.79%	33.69%	30.21%	66.21%	17.69%	-27.87%
	C	122.7± 0.72	280.5±0.64	52.3±0.084	433±4.2	310.2±0.45	222.1±0.6
Endosulfan	T	48.2±2.42**	145.12±2.3**	21.4±0.73**	116.4±2.5***	192.63± 1.5**	112.6±1.6**
	%	60.72%	48.26%	59.1%	73.12%	38.11%	49.30%

- 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**

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.

Pesticide		Cerebellum mean ± S.E.	Striatum mean ± S.E.	Cerebral cortex mean ± S.E.	Hypothalamus mean ± S.E.	Brain stem mean ± S.E.	Hippocampus mean ± S.E.
	C	165.7±0.65	154.21±0.8	44.2±0.62	321.6±0.82	121.2±0.197	204.3±1.6
Deltamethrin	T	102.6±1.3**	92.6±0.428**	35.2±0.8	2925±0.43*	33.3±0.764**	98.8±0.577**
	%	-61.97%	39.82%	18.1%	9%	72.52%	51.64%
	C	165.7±0.65	154.21±0.8	44.2±0.62	321.6±0.82	121.2±0.197	204.3±1.6
Endosulfan	T	60.6±1.2***	72.4±0.87**	28.6±0.83***	252±1.6	23.6±0.82*	88.4±1.6***
	%	63.43%	53.1%	35.29%	21.64%	80.52%	56.73%

- 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.

Pesticide		Cerebellum mean ± S.E.	Striatum mean ± S.E.	Cerebral cortex mean ± S.E.	Hypothalamus mean ± S.E.	Brain stem mean ± S.E.	Hippocampus mean ± S.E.
	C	102.6±1.4	434.2±1.6	64.6±1.54	462.2±2.11	342±0.53	233.1±1.4
Deltamethrin	T	77.5±0.56**	344.23±1.4**	35.2±0.54*	212.2±052**	243.1±0.45**	106.2±0.62***
	%	24.64%	20.72%	48.57%	54.1%	28.95%	45.44%
	C	102.6±1.4	434.2±1.6	64.6±1.54	462.2±2.11	342±0.53	233.1±1.4
Endosulfan	T	48.2±0.62**	223.3±0.61**	22.3±1.4***	210.8±1.1***	168.5±1.4***	86.5±0.83***
	%	53%	48.57%	65.48%	99.45%	50.73%	62.89%

- 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 4: Effect of Deltamethrin and Endosulfan on liver function enzymes in serum of male mice.

	Glucose (GL) mg/g tissue		Liver function enzymes (umole/mg protein/min.)							
			AST		ALT		ALP		Acid phosphatase (ACP)	
		% Change		% Change		% Change		% Change		% Change
Control	22.4 ±1.5		18.21 ±0.432		8.36 ±0.338		3.61 ±0.03		6.44 ±0.23	
Deltamethrin	44.5 ±0.64	49.7%	14.21 ±0.316	44.87%	6.835 ±0.12	18.48%	2.85 ±0.05	11.8%	7.21 ±0.22	11.96%
Endosulfan	15.6 ±1.8	64.9%	10.04 ±0.311	44.8%	4.22 ±0.45	49.52%	1.94 ±0.01	46.26%	8.84 F±0.22	37.27%

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.

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

Table 5: Effect of Deltamethrin and Endosulfan on lipid peroxide, glutathione and total protein in male mice liver.

	Lipid peroxide(LP) (ug/g tissue)		Glutathione(GR) (ug/g tissue)		Total protein(TP) (mg/ml)	
		% change		% Change		% change
Control	0.65 ±0.01		30.22 ±1.22		52.44 ±2.11	
Deltamethrin	0.95 ±0.57	-46.15%	20.20 ±1.12	33.16%	41.11 ±1.15	21.61%
Endosulfan	1.22±0.06	-87.69%	15.16 ±0.85	49.83%	31.22 ±1.65	40.46%

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 6: Effect of Deltamethrin and Endosulfan on some glycolytic enzymes in male mice liver.

	Glycolytic enzmes (umole/mg protein/min.)					
	PK		PFK		GPI	
		% change		% change		% change
Control	4.16 ±0.26		7.44 ±1.16		77.34 ±2.43	
Deltamethrin	7.18 ±1.44	-72.6%	10. 1 ±1.22	-35.75%	113.50 ±3.2	-46.81%
Endosulfan	8.23 ±1.64	-97.36%	13.1 ±1.23	-76.1%	135.22 ±6.4	-74.84%

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.

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

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

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).

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 H_2O_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 gluconeogensis; F,1-6-diphosphtase. 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).

REFERENCES

Abdel-Rahman HM, .El-Shanawani FM, Hassan MM, .Salem M, El-Salhy AM. 1993. Alkaline phosphatise isoenzymes abnormalities in hepatic schitosomiasis. Egypt J. Bilh., 15:41-60.

Ahmed SA and Gad MZ. 1995. Effect of schistosomal infection and its treatment on some key enzymes of glucose metabolism in mice livers. Arzneim Forsch. 45 (12): 1324-1330.

Ahmsd R, Salem NM, Estaitieh H. 2010. Occurrence of organochlorine pesticide residues in eggs,chicken and meat in Jordan.Chemosphere,78(6): 667-671.

Ansorge MS, Morelli E, JA. 2008. Gingrich Inhibition of serotonin but not norepinephrine transport during development produces delayed, persistent perturbations of emotional behaviours in mice J. Neurosci., 28(1) : 199 -207.

Barlow SM, Sullivan FM, Lines J. 2001. Risk assessment of the use of deltamethrin on bednets for the prevention of malaria, Food Chem. Toxicol., 39 (5): 407 – 422.

Baskaran P and Palanichamy S. 1990. Impact of agricultural (ammonium chloride) fertilizer on physiology and biochemistry of fresh water teleost fish, Oreochromis mossambicus, J. Ecobiol., 2 : 97–106.

Bernardi MM and Palermo-Neto J. 1983. Effects of apomorphine administration on locomotor activity of control and experimental rats withdrawn from long-term haloperidol treatment Gen. Pharmacol., 14 (5):545–547.

Belfield A and Goldberg DM. 1971. Hydrolysis of adenosine-monophosphate by acid phosphatase as measured by a continuous spectrophotometric assay. Enzyme. 4(2): 561-566.

Bloom AS, Staaz CG, Dieringer T. 1983. Pyrethroid effects on operant responding and feeding Neurobehav.

Toxicol. Teratol., 5 (3): 321–324.

Botella B, Crespo J, Rivas A, Gerrillo I, Olea-Serrano F and Olea N. 2004. Exposure of women to organochlorine pesticides in souther Spain.Environ.Res., 96(1):34-40.

Botros SS, Mahmoud MR, Moussa MM, Nosseir MM. 2007. Immunohistopathological and biochemical changes in Schistosoma mansoni-infected mice treated with artemether. J. Inf., 55(5):470-477.

Bradford MM. 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal. Biochem.,7 : 248-254.

Broomhall S. 2002. The effects of endosulfan and variable water temperature on survivorship and subsequent vulnerability to predation in Litoria citropa tadpoles. Aquat. Toxical., 61(3-4):243-250.

Buege JA and Aust SD. 1978. Microsomal lipid per oxidation. Meth. Enzymol., 52 : 302-310.

Bucher T and pflrider G. 1975. Pyruvate kinase, In: Methods in Enzymology (SP Colowick , SP Kaplan eds.) Academic Press NY. 435-440.

Buznikov GA, Shmukler YB, Lauder JM. 1996. From oocyte to neuron: do neurotransmitters function in the same way throughout development Cell. Mol. Neurobiol., 16 (5):.533–559

Castagna C and Ball GFJ. 1997. Balthazart Effects of dopamine agonists on appetitive and consummatory male sexual behavior in Japanese quail Pharmacol. Biochem. Behav.,. 58 :403–414.

Chang CC. 1964. Asensitive method for spectrophoto metric assay of catecholamines. Int. J. Neuropharmacol., 19 (3):643-649.

Chiavegatto S, Nasello AG, Bernanrdi MM. 1998. Histamine and spontaneous motor activity: biphasic changes, receptors involved and participation of the striatal dopamine system Life Sci., 62 (20):875–1888

Ciarlone. AE. 1978. Further modification of a fluorometric method for analyzing brain amines .Michrochemical .J., 23:9-12.

Di Pino G, Moessner R, Lesch KP,. Lauder JM,. Persico AM. 2004. Roles for serotonin in neurodevelopment: more than just neural transmission Curr. Neuropharmacol.,2(4): 403–417.

Dinu D, Marinescu D, Munteanu MC, Staicu ACM, Costache A. 2010. Dinischiotu, Modulatory effects of deltamethrin on antioxidant defense mechanisms and lipid peroxidation in Carassius auratusgibelio liver and intestine. Arch. Environ. Contam.Toxicol., 58(3):757-764.

El-Shazly AM, Soliman M, El-Kalla MR, Rezk H, El-Nemr HE, Handousa AE, Helmy MM. 2001. Studies on patients with Schitosomiasis mansoni ; HCVand /or typhoid fever .J. Egypt Soc .Parasitol., 31(2): 583-400.

El-Aasar AA, El-Merzabzni MM, Zakhary NI, Farag HI, Abdeen AM, Abd El-Slam I, Mokhtar NM. 1989. Biochemical and biophysical studies on schistosomal liver of mice .Egypt J. Bilh., 11:19-25.

El-Rigal NS, Aly SA, Rizk MZ, Said AA. 2006. Effect of Ailanthus altissima and Ziziphus spina Christi extracts on some hepatic marker enzymes and antioxidants in Shistosoma mansoni infected mice. Pol. J.Food Nutr. Sci., 15/56(2):199-206.

Glowinski J and Iversen, LL. 1966. Regional studies catecholamines in the rat brain .I. The disposition of [3H] norepinephrine, [3H] dopamine and [3H] dopa in various regions of the brain. J. Neurochem., 13:655-669

Harner T, Pozo K, Gouin T, Macdonald AM, Hung H, .Cainey J and Peters A. 2006. Global pilot dtudy for persistent organic pollutants (POPs) using PUP disk passive air samples Environ. Pollut.,144:445-452.

Insel TR, Zohar J, Benkelf ATC, Murphy DL. 1990. Serotonin in obsessions, compulsions, and the control of aggressive impulses Ann. N. Y. Acad. Sci., 600: 574–585.

Jergentz S, Mugni H, Bonetto C, Schulz R. 2004. Runoffrelated endosulfan contamination and aquatic macroinvertebrate response in rural basins near Buenos aires, Argentina. Arch. Environ.Contam. Toxicol., 46 (3):345-352.

Kaye W. 2008. Neurobiology of anorexia and bulimia nervosa Physiol. Behav., 94, 121–135

King J. 1965. Glucose phosphate isomerase In : practical Clinical Enzymology. London., 1113-1117.

Klover PJ and Mooney RA. 2004. Hepatocytes critical for glucose homeostsis . Int J Biochem. Cell Biol., 36(5): 753-758.

Konkle ATM and McCarthy MM. 2011. Developmental time course of estradiol, testosterone, and dihydrotestosterone levels in discrete regions of male and female rat brain. Neuroendocrinology, 152 (1): 223–235.

Leret ML, Rua C, Garcia-Montojo M, Lecumberri, MJC. 2009. González Influence of metyrapone treatment during pregnancy on the development and maturation of brain monoaminergic systems in the rat Acta Physiol., 197 (4) :333–340

Levitt P, Harvey JA, Friedman EK, Simansky EH. 1997. Murphy New evidence for neurotransmitter influences on brain development Trends Neurosci., 20 (6) :269–274

Mansour MM, Farid ZB, Salah LH, Watten 1982. Serum enzymes tests in hepatosplenic schitosomiasis .Trans. R. Soc. Med. Hyg., 76:109-119.

Metwally AA, Janku I, Komper F, Khayyal MT, .Fbeid FA, Botros SS. 1990. Effect of schistosomiasis infection on the clearance of pheazone in mice . Arzneim Forsc., 40(2 Pt 1):206-220.

Moron MS, Depierre JW, Mannervik B. 1979. Level of glutathione, glutathione reductase and glutathion-s-transferase activities in rat lung and liver. Biochem. Biophys.Acta. 582:67-68.

Mittelstaedt RA, Mei N, Webb PJ, Shaddock JG, .Dobrovolsky VN, .MacGarrity LJ, Morris SM, Chen T, Beland FA, Greenlees KJ, HeXich RH. 2004. Genotoxicity of malachite green and leucomalachite green in female Big Blue B6C3F1 mice. Mut. Res., 561 (1-2): 127–138.

Muneoka K, Kuwagata M, Ogawa T,. Shioda S. 2010. Sex-specific effects of early neonatal progesterone treatment on dopamine and serotonin metabolism in rat striatum and frontal cortex Life Sci., 87(23–26):738–742.

Nakano T and Tomlinson N. 1967. Catecholamine and carbohydrate concentrations in rainbow trout (Salmo gairdneri) in relation to physical disturbance, J. Fish Res. Board Can. 24 : 1707–1715.

Nicotra A and Schatten G. 1990. Propranolol, a beta-adrenergic receptor blocker, affects microfilament organization, but not microtubules, during the first division in sea urchin eggs Cell Motil. Cytoskeleton, 16 (3) :182–189.

Nicholas V, Carroll B, Longley W, Joseph HR. 1956. The determination of glycogen in liver and muscle by the use of anthrone reagent. J. Biol Chem., 220(2): 583-593.

Pappas SS, Tiernan CT, Behrouz B, Jordan CL, Breedlove SM, Goudreau JL, KJ. 2010. Lookingland Neonatal androgen-dependent sex differences in lumbar spinal cord dopamine concentrations and the number of A11 diencephalospinal dopamine neurons J. Comp. Neurol., 518 (13): 2423–2436.

Parasad MR, Popescu LM, .Moraru LI, Liu X, Maity S, Engdoman RM, Das DK. 1991. Role of phospholipase A,and C in myocardial ischemic reperfusion injury.Am. J. Physiol., 29: 877.

Pozo K, Harner K, Wania F, Muir D, Jones K, Barrie L. 2006. Toward aglobal network for persistent organic pollutants in air: Results from the GAPS study.Environ.Sci.Technol.,40(16):4867-4873.

Rand GM, Carriger JF, Gardinali PR and Castro J. 2010. Endosulfan and its metabolite, endosulfan sulfate, in freshwater ecosystems of South Floride: A probabilistic aquatic ecological risk assessment, Ecotoxicology,19 (5): 879-900.

Retiman S and Frankel S. 1957. Colorimetric method for the determination of serum glutamic oxaloacetic acid and glutamic pyruvic tranaminases . Am. J .Clin. Pathol., 28(1):56-65.

Richardson JR, Caudle WM, Wang M, Dean ED, Pennell KD, Miller GW. 2006. Developmental exposure to the pesticide dieldrin alters the dopamine system and increases neurotoxicity in an animal model of Parkinson's disease J. Fed. Am. Soc. Exp. Biol., 20 (10) :1695–1697.

Sambasiva RKRS. 1999. Pesticide Impact on Fish Metabolism, Discovery Publishing House, New Delhi, 129–149 .

Sand O, .Petersen IM and Emmersen BK. 1980. Changes in some carbohydrate metabolizing enzymes and glycogen in liver , glucose and lipid in serum during vitellogensis and after induction by estradiol-17-B in the flounder Platichtys flesusL. Comp .Biochem. Phsiol., 65 : 327.

Simsek S, Koprucu S, Yonar E, Seker E. 2008. Effects of deltamethrin on antioxidant status and oxidative stress biomarker freshwater mussel, Unio elongatulus eucirrus. Bull.Environ.Contam.Toxicol., 81(3): 253–257.

Slikker W and Schwetz BA. 2003. Childhood obesity: the possible role of maternal smoking and impact on public health.J. Children's Health, 1 (1): 29–40

Steel RGD and Torrie JH. 1980. Principles and Procedures of Statistics, 2nd ed., McGraw Hill Book Company, New York

Sutton I and Simmonds MA. 1973. Effects of acute and chronicethanol on the gama-aminobutyric acid system in rat brain.Biochem. Pharmacol., 22:1685- 1692.

Tilson HA. 2000. Neurotoxicology risk assessment guidelines: developmental neurotoxicology Neurotoxicology, 21(1-2):189–194

Trinder P. 1969. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor, Annals of Clinical Biochemistry. 6 : 24–27.

US EPA. Reregistration eligibility decision for endosulfan.EPA 738-R-02-013.Pollution pesticides and toxic substances (7508C), United ststes environmental protection agency Http://www.epa.gov/oppsrrd 1/REDs/ endosulfan_red.pdf.

Usmani KA, Cho TM, Rose RL, Hodgson E. 2006. Inhibition of the human liver microsomal and human cytochrom P450 1A2 and 3A4 metabolism of oestra- diol by deployment-related and other chemicals. Drug Metab. Dispos., 34 (9):1606–1614

Vasanthi RP and Baskaran S. 1990. Palanichamy, Influence of carbofuran on growth and protein

conversion efficiency in some fresh water fishes, J. Ecobiol., 2 (1): 85–88.

Villarini M, Moretti M, Pasquini R, Scassellati Sforzolini G, Fatigoni C, Silvano MM, Monarca AV. 1998. Rodriguez, In vitro genotoxic effects of the insecticide Deltamethrin in human peripheral blood leukocytes: DNA damage („comet assay") in relation to the induction of sister-chromatid exchanges and micronuclei, Toxicology 130 (2-3): 129–139.

Vincent S, Ambrose T, Cyrill L, Selvanaygam M. 1995. Biochemical responses of the Indian major carp, Catla catla (Ham.) to chromium toxicity, Indian J. Environ. Health 37 :192–196.

Volpi E, Lucidi P, Cruciani C, Monacchia F, Reoldi G, Brunetti P, Bolli GB and De Feo P. 1997. Nicotinamide counteracts alcohol induced impairment of hepatic protein metabolism in humans. J. Nut., 127 (11): 2199-2204.

Wattiaux R and De Duve C. 1956. Release of bound hydrolase by mean of Triton X-100. Biochem. J., 63: 606 -608.

Whitaker-Azmitia PM. 1992. Role of serotonin and other neurotransmitter receptors in brain development: basis for developmental pharmacolog Pharm. Rev., 43, 553–561.

Yousef MI, Awad TI, Mohamed EH. 2006. Deltamethrin-induced oxidative damage and biochemical alterations in rat and its attenuation by Vitamin E. Toxicology 227(3): 240–247.

Zammit VA, Beis I, ENewshlome A. 1978. Maximum activities and effects of fructose biophosphate pyruvatekinase from muscle ofvertebrates and invertebrates in relation to the control of glycolysis Biochem. J., 174(3): 989-917.