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ASSESSMENT OF CYPERMETHRIN AND DIMETHOATE TOXICITY IN BARKI SHEEP: BIOCHEMICAL AND HISTOLOGICAL CHANGES, AND TISSUE RESIDUES

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SUMMARY

The effect of two formulated pesticides (6 and 12 mg cypermethrin/kg body wt/day and 1.6 and 3.2 mg dimethoate/kg b.wt/day), on biochemical analysis, histological changes and their tissue residues in male sheep were studied. The tested doses were given orally to sheep for 63 consecutive days. A vehicle-control group of sheep given corn oil (0.1 ml/kg/day) only was used for comparison. Three animals of each group (control and treated groups) were slaughtered 24 h after the 63th daily treatment. No fatality was recorded during the course of this study. Cypermethrin and dimethoate produced significant increase in the weights of liver and spleen, while there is no effects on the weights of brain, kidneys, heart and testes. Histological changes were noticed in the pesticide-treated animals on microscopical examination of spleen, liver, brain and testes. There were an increased number of lymphoid cells in the spleen of sheep treated with cypermethrin and dimethoate. Brain cortex of sheep treated with the high doses of tested pesticides showed a large number of cells, which have darker, smaller and slightly irregular nuclei. A slight increase in mononuclear inflammatory cells and swelling of hepatocytes in the central vein area were noticed in the liver of treated sheep with the high dose of cypermethrin. Testis of sheep treated with the high doses of tested pesticides showed a marked swelling of the tubular seminiferous cells. No histological changes were observed in kidneys and heart of the pesticide-treated animals. A significant increase in liver aspartate amino transaminase (AST) and alanine amino transaminase (ALT) activities and a significant decrease in liver lactate dehydrogenase (LDH) activity were recorded in the pesticide-treated animals. There were no significant changes in acid and alkaline phosphatase activities after treatment. Significant decreases were observed in brain AChE in dimethoate-treated animals and in brain Na^+, K^+-ATPase and Mg^{++}-ATPase in cypermethrin-treated animals. Residue analysis revealed higher levels of

cypermethrin in spleen, kidneys and muscle than liver. On the other hand, the residues of dimethoate were detected at high levels in kidneys compared to the other organs. Residues of tested pesticides were detected in all samples of urine and faeces of treated sheep, and were dose-dependent.

Keywords: Sheep, cypermethrin, dimethoate, histology, enzymes, residue analysis

INTRODUCTION

Pesticides have been recognized as the first generation of environmental chemicals. They create difficult problems from the point of view of environmental protection and pose hazards to human health and animal production. Greater reliance on the use of pesticides to maintain higher agricultural productivity appears inevitable as the demand for food increases with increasing population. More than one billion pounds of pesticides are used each year in the USA alone (Abou Zeid *et al.*, 1993). In Egypt, intensive agriculture requires the import and application of large quantities of pesticides, more than 30,000 metric tons of formulated pesticides are imported and used annually. The long term application of these pesticides has resulted in pesticide residues accumulation in soil, water, and in the general environment, thereby posing a serious threat to public health in Egypt. With the continuous population growth and intensified agriculture, pesticides are expected to be imported and used in Egypt at present and in future (Selim and El-Sebae, 1995). It is believed that numerous undocumented cases of acute poisoning to human, farm animals, honey bees and fish, due to direct dermal contact or ingestion of contaminated food and water occur annually in Egypt (El-Sebae, 1990). Since 1970's a profound shift in agriculture has occurred in which organophosphate, carbamate, and pyrethroid classes of pesticides have largely replaced the organochlorines. This shift has alleviated problems associated with the high environmental persistence and bioaccumulation of organochlorines.

Organophosphorus insecticides are widely used in agriculture. Their presence in water, food and animal feedstuffs presents a potential hazard due to their high mammalian toxicity. Dimethoate is an organophosphorus insecticide. It is widely used as a contact and systematic insecticide against a broad range of insects and mites in agriculture and for the indoor control of houseflies. Also, it is used for control of warble fly larvae and grubs in cattle (Worthing and Walker, 1983). On the other hand, synthetic pyrethroids possess suitable properties such as low toxicity to mammals and higher inscticide activity against a wide range of insects. In spite of claims of low mammalian toxicity of synthetic pyrethroids, evidence is gradually accumulated against it (Shakoori *et al.*, 1988). Cypermethrin is active synthetic pyrethroid insecticide, effective against a wide range of pests in agriculture, public health, and animal husbandry (WHO, 1989). Reports are available on the toxicological effects of various organophosphorus and pyrethroid insecticides in many species of animals (EL-Sebae *et al.*, 1977 and 1979; Soliman *et al.*, 1983; Appleyard *et al.*, 1984; EL-Sebae *et al.*, 1988; Shakoori *et al.*, 1988; Hardeng *et al.*, 1992). The magnitude of toxic effects of pesticides depends mainly on the type and

dose of compound, duration of exposure, species and age of animals and other environmental factors (Dunnick *et al.*, 1984). Farm animals have been contaminated in a variety of ways, thus possibly affecting the animal's growth and production. Therefore, the present work was undertaken to study the effect of cypermethrin and dimethoate on biochemical and histological changes and their tissue residues in male sheep after repeated oral administration.

MATERIALS AND METHODS

Tested pesticides

Two formulated pesticides (cypermethrin and dimethoate) were used in the present study. Cypermethrin 25% E.C (RS)-alpha-cyano-3-phenoxybenzyl (IRS)-cis-, trans-3- (2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylate (Mitchell Cotts Chemicals, Belgium) and dimethoate 40% E.C [O,O-dimethyl S-methyl-carbamoyl-methyl phosphorodithioate] (Protex S. A., Belgium). These insecticides were prepared in corn oil and were administered orally in gelatin capsules to sheep.

Animals and treatment

Thirty male Barki sheep aged eight to ten months of 26.5 ± .78 kg average body weight at the beginning of the experiment were used in this study. The animals were housed in shelter in groups of six, fed on roughage (rice straw) and concentrate supplement according to their actual requirements (NRC, 1985). The concentrate contained at least 61% total digestible nutrients (TDN) and 11.5 % digestible proteins (DP). Feed and water were provided to animals *ad libitum* throughout the experiment. The animals were divided into five groups of six animals each. The first group of sheep was treated orally with corn oil daily at 0.1 ml/kg for 63 days and kept as vehicle control. The second and third groups were orally treated with cypermethrin at the dose rate of 6 and 12 mg/kg body weight/day, respectively, while the fourth and fifth groups received dimethoate at 1.6 and 3.2 mg/kg body weight/day, respectively. The tested compounds were administered daily for 63 successive days. Doses of tested pesticides were formulated weekly to meet the weight changes. The dose for each animal was contained in a gelatin capsule that was inserted orally into the esopharyngeal region with the help of a glass rod. Animals were observed daily for the nature and onset of toxic signs. Body weights were recorded at the beginning of the experiment and every week thereafter. One day after the last treatment, three animals from each group were slaughtered and their liver, kidney, heart, spleen, testis, brain and lung were immediately excised and washed in cold saline. The organs were weighed after blotting them dry. The organ: body weight ratio was calculated.

Histological examination

Specimens of liver, spleen, brain, kidney, heart, and testes from all sacrificed animals (control and treated) were immediately fixed in 10% buffered formalin

solution for at least 24 hours. Fixed specimens were dehydrated in alcohol, then cleared in two changes of chloroform. Thereafter, these specimens were embedded in melted paraffin wax at 60 °C and then blocked. The paraffin blocks were sectioned by a microtome into five micron thick sections, and were stained with Hematoxylin and eosin (Luna, 1968). Prepared sections were evaluated for degenerative lesions by light microscopy.

Biochemical studies

Freshly removed liver and brain were washed using chilled saline solution and homogenized (10% w/v) in 0.25 M ice cold sucrose solution in a Potter-Elvehjem type homogenizer. The homogenates were centrifuged at 700 xg for 10 min. at 4 °C to remove cell debris. The liver supernatant was used for estimation of aspartate amino transaminase (AST) and alanine amino transaminase (ALT), acid phosphatase (AcP), alkaline phosphatase (AlP) and lactate dehydrogenase (LDH) activities according to the methods of Reitman and Frankel (1957); Bergmeyer (1963); Bessey *et al.* (1964) and Cabaud and Wroblewski (1958), respectively, using commercially available kits (Pasteur Lab, USA). The brain supernatant was used for estimation of acetylcholinesterase (AChE) activity according to the method of Ellman *et al.* (1961). Brain tissues of sheep were prepared by the method of Koch (1969) for determination of Na^{+}, K^{+}-ATPase and Mg^{++}-ATPase activities. ATPase activities were assayed according to the method of Cutkomp *et al.* (1971) where inorganic phosphate was determined according to the method of Fiske and Subbarow (1925). Protein in brain ATPase preparations was estimated by the method of Lowry *et al.* (1951).

Residue analysis

Samples of urine (100 ml) and faeces (100 gm) were collected once a week and continued throughout the experimental period (nine weeks). Kidney (50 gm), spleen (25 gm), liver (50 gm) and forequarter muscles (100 gm) were collected from the sacrificed animals (control and treated). Levels of cypermethrin and dimethoate in all samples were analysed according to Braun and Stanek (1982), and AOAC (1984), respectively. Gas chromatograph (GC) Hewlett Packard series 5890 was used. GC equipped with ^{3}H-electron capture detector (ECD) and nitrogen phosphorus detector (NPD) to detect cypermethrin and dimethoate, respectively. Megabore column HP-608 part No. 190955-023; (30 m x 0.53 mm i.d x 0.5 µm film thickness) was used. Split injection (0.8 min. hold) was applied with temperature at 220 °C, helium as carrier gas at 6 ml/min. flow rate. ECD and NPD temperatures were at 270 °C and 225 °C, respectively. Column temperatures for cypermethrin and dimethoate resolution were at 170 °C and 200 °C, respectively. According to these conditions, cypermethrin which contains a third asymmetric center, was resolved into an envelope of three peaks with retention times of 21.93, 22.66 and 23.34 min. Dimethoate was resolved as one peak at retention time of 15.38 min.

For the assessment of the extraction efficiency of cypermethrin and dimethoate; triplicate fortified samples with 100 ng of technical tested pesticides were made directly to urine and the extract of each of feces, kidneys, spleen, liver and muscles samples of control animals. Reported levels of cypermethrin and dimethoate in the collected samples from control and treated animals had not been adjusted on the basis of percent recoveries. This was due to the very high percent of recovery.

Statistical significance between experimental and control values were calculated according to Student's "t" test as described by Fisher (1950).

RESULTS AND DISCUSSION

Organ: body weight ratio

Sheep in all groups survived to the end of the study. A significant increase in relative liver and spleen weights was observed in sheep treated with cypermethrin or dimethoate, and a dose-response relationship was observed for both compounds (Table 1). Weights of brain, heart kidneys and testis were not affected (data not shown). The liver enlargement after cypermethrin and dimethoate exposure was significant and indicated an increase in the functional load of the organ. These findings are in agreement with the results reported by Hend and Butterworth (1977) and US-EPA (1984) in rats treated with cypermethrin. An increase in spleen weight was observed in the present study for sheep being treated with pesticides. A similar enlargement in the spleen was seen in rats dosed with aromatic amines in studies previously reported by Chhabra *et al.* (1990). They suggested that splenic weight increases in dosed rats were due to excessive deposition of damaged erythrocytes as a result of aromatic amine toxicity and thus splenomegaly is a secondary effect of erythrocyte toxicity and sequestration of damaged erythrocytes in splenic sinusoids.

Table 1. Mean body and relative organ weights of slaughtered male sheep after oral daily administration of pesticides for 63 days

Pesticide	Dose (mg/kg/day)	Body weight (kg)	Relative weight (g/g) $\times 10^3$	
			Liver	Spleen
None (control)	0	29.47 ± 4.35	13.54 ± 0.83	5.42 ± 1.35
Cypermethrin	6	29.20 ± 3.86	17.09 ± 1.58*	6.98 ± 2.11*
	12	30.40 ± 2.89	17.54 ± 1.51*	8.99 ± 2.55*
Dimethoate	1.6	29.67 ± 3.39	18.08 ± 1.74*	7.51 ± 2.09*
	3.2	30.33 ± 3.82	19.61 ± 2.04*	8.53 ± 2.20*

Values represent the mean ± SE of three animals.

* Within columns, significantly different from control ($P < 0.05$).

Histologic findings

Histopathology is a sensitive tool not only for the detection of low dose effects but also for providing insight into the onset, site(s), and mechanism(s) of action. Previous studies indicated that treatment of several animal species with different

pesticides induced, not only marked changes in body and organ weights, but also histopathological changes in these organs (Hayes and Laws, 1991). In the present study, histopathological examinations of spleen, brain, liver, testes, kidney and heart of control and sheep given cypermethrin (6 and 12 mg/kg b. wt/day) and dimethoate (1.6 and 3.2 mg/kg b. wt/day) for 63 days were investigated. Spleen, brain, liver and testes of treated animals showed pathological alterations as compared to control group. There were an increased number of lymphoid cells organized in follicles with relatively big germinal centers in the spleen from sheep treated with cypermethrin. There was no recognizable difference between low and high doses of cypermethrin. There was an increase in the number of lymphoid cells and degradation of red blood cells, but here they were organized both in follicles and diffusely, the changes were negligible for the low dose of dimethoate, but marked for the high dose (Data not shown). There were no structural or cellular changes in the different sections of brain cortex, but in the section for high dose-treatment of cypermethrin and dimethoate there was a large number of cells which have darker, smaller and slightly irregular nuclei which may indicate pyknotic changes. Some swelling of the cells can also be seen. Necrosis and myelin degeneration cannot be identified (Data not shown). In the liver sections from the cypermethrin treated sheep there was a slight increase in mononuclear inflammatory cells, especially around the biliary intrahepatic ducts and swelling of hepatocytes in the central vein area. The changes were most obvious in the sections for the high dose of cypermethrin (Fig. 1). However, in the sections from the dimethoate treated sheep there were no significant changes, but a slight swelling of the hepatocytes was seen (Fig. 1). In the testis sections from the cypermethrin and dimethoate treated sheep there were no obvious changes for the low dose treatment (data not shown), but for the high doses of cypermethrin and dimethoate there was a marked swelling of the tubular seminiferous cells and a general more atrophic looking epithelium, respectively (Fig. 2). Microscopic examination of kidney and heart organs did not show any noticeable morphological changes (data not shown).

In the present study histopathological effects of cypermethrin and dimethoate on org-ans revealed morphological changes in the spleen, brain, liver and testes. These findings are in general agreement with the results reported by Shakoori *et al.* (1988) and Afifi *et al.* (1991) in rats treated with cypermethrin and dimethoate, respectively. Similar observations have also been made by Shakoori *et al.* (1992) in rabbits treated with cyhalothrin. Hend and Butterworth (1977) reported that histopathological examinations revealed substantial degeneration in both liver and sciatic nerve at 1500 mg cypermethrin/kg diet in rats, while no lesions were observed in the brain or spinal cord. Carter and Butterworth (1976) found that single oral dose of cypermethrin (400 mg/kg body weight) in rats showed swelling of the myelin sheaths and breaks of some of the axons of the sciatic nerves.

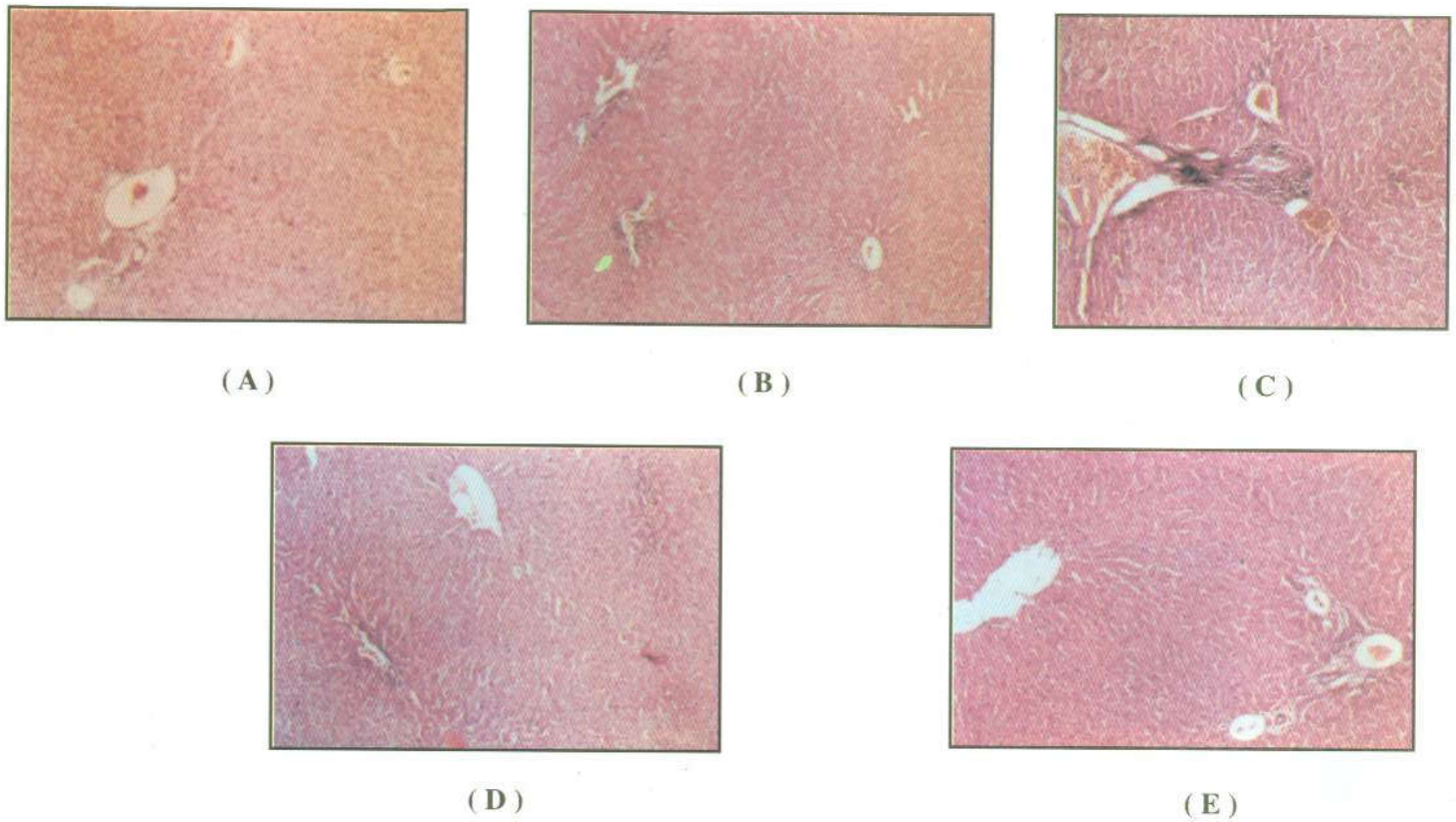

Figure 1. Histological structure of sheep liver of control (A), low dose of cypermethrin (B), high dose of cypermethrin (C), low dose of dimethoate (D) and high dose of dimethoate (E). Hematoxylin and eosin used as stain. Magnification: X100.

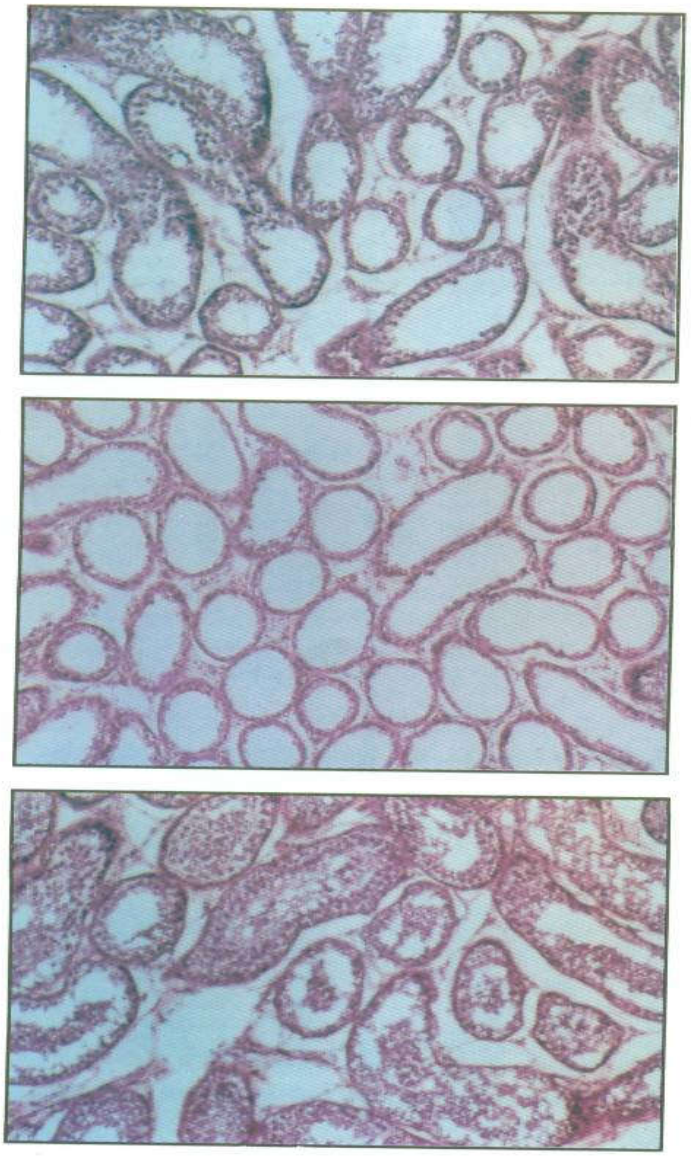

Fig. 2. Histological structure of sheep testis of control (A), high dose of cypermethrin (B) and high dose of dimethoate (C). Hematoxylin and eosin used as stain. Magnification: X100.

Liver and brain biochemistry

The activities of liver AST, ALT, AlP, AcP, and LDH are shown in Table (2). Liver AST and ALT activities in male sheep were significantly increased after treatment with cypermethrin or dimethoate (6, 12 and 1.6, 3.2 mg/kg body weight, respectively).

Table 2. Liver biochemical changes in male sheep after oral administration of pesticides for 63 days

Parameters [(a)]	Control	Treatment (mg/kg/day)			
		Cypermethrin		Dimethoate	
		6	12	1.6	3.2
AST (IU/g)	14.71 ± 1.53	21.2 ± 1.88*	25.9 ± 3.14*	23.8 ± 2.38*	28.4 ± 3.21*
ALT (IU/g)	3.02 ± 0.25	3.66 ± 0.27*	4.24 ± 0.43*	4.12 ± 0.39*	5.08 ± 0.46*
AlP (IU/g)	0.43 ± 0.02	0.44 ± 0.03	0.45 ± 0.04	0.44 ± 0.04	0.44 ± 0.05
AcP (IU/g)	1.96 ± 0.08	1.94 ± 0.06	1.98 ± 0.07	2.01 ± 0.09	1.99 ± 0.02
LDH($\times 10^4$IU/g)	23.12 ± 2.06	16.3 ± 1.14*	14.2 ± 1.21*	13.4 ± 1.33*	11.9 ± 1.31*

Values represent the mean ± SE of three animals.

(a) IU/g = International unit, the amount of the enzyme that under defined assay conditions will catalyze 1 mole of substrate per minute per gram liver tissue.

* Within rows significantly different from control ($P<0.05$).

The elevation of liver AST and ALT activities was dose dependent. No significant alterations in the activities of liver alkaline and acid phosphatases were observed (Table 2). Liver LDH activity was significantly lower than those of the control in sheep treated with either cypermethrin or dimethoate (Table 2). Table (3) shows the effect of oral administration of cypermethrin and dimethoate on the activities of brain enzymes after 63 days of treatment. Animals treated with dimethoate at doses levels of 1.6 and 3.2 mg/kg/day showed a considerably lower activity of AChE as compared to control. Cypermethrin at both doses did not show any significant change in AChE activity. Cypermethrin treated animals at both doses show a significant decrease in Na^+, K^+-ATPase and Mg^{++}-ATPase activities as compared to control. There were no significant changes in the activities of brain ATPases in the group treated with dimethoate at both doses of 1.6 and 3.2 mg/kg/day.

The present study demonstrates biochemical parameter changes in liver and brain. Transaminases (AST and ALT) are important and critical enzymes in the biological processes. These enzymes are involved in the breakdown of amino acids into α keto acid which are routed for complete metabolism through the Kreb's cycle and electron transport chain. Consequently, they are considered as a specific indicator for liver damage (Harper *et al.*, 1979). An increased AST activity was observed by Shakoori *et al.* (1988) in albino rats administrated cypermethrin. Shakoori *et al.* (1992) also reported increased liver transaminases (AST and ALT) activities after cyhalothrin administration in rabbits. The dosages of cypermethrin and dimethoate given for 63 days did not elicit significant changes in the liver

phosphatases, as it is well known that phosphatases are responsible for transport mechanisms involving phosphates. The hepatic LDH activity indicates the switching over of anaerobic glycolysis to aerobic respiration. The decreased hepatic LDH activity may be due to the hepatocellular necrosis leading to leakage of the enzyme and /or enzyme inhibition. The results of this study showed a significant decrease in LDH activity of cypermethrin and dimethoate treated sheep. These results are in agreement with the results reported by Wang and Zhai (1988).

Table 3. Brain biochemical changes in male sheep after oral administration of pesticides for 63 days

Parameters [(a)]	Control	Treatment (mg/kg/day)			
		Cypermethrin		Dimethoate	
		6	12	1.6	3.2
AchE[a]	31.67 ± 1.23	30.58 ± 1.12	31.13 ± 1.08	24.5 ± 0.94*	21.8 ± 1.02*
Na^+, K^+-ATPase[b]	66.21 ± 3.20	47.51 ± 2.83*	41.8 ± 2.24*	66.01 ± 3.11	66.1 ± 3.15
Mg^{++}-ATPase[b]	36.10 ± 2.14	22.71 ± 1.78*	19.3 ± 1.45*	35.87 ± 2.83	36.1 ± 2.23

Values represent the mean ± SE of three animals.

(a) Activity expressed in μmoles substrate hydrolysed/min./g tissue.

b Activity expressed in μmole Pi/g protein/min.

- Within rows significantly different from control ($P < 0.05$).

Brain showed significant decrease in the activity of acetylcholinesterase (AChE) in sheep treated with both doses of dimethoate, but there are no differences in sheep treated with cypermethrin compared with control (Table 3). Inhibition of AChE activity by organophosphorus pesticides has been reported by several investigators (El-Sebae *et al.*, 1977 and 1979; Enan *et al.*, 1982; Soliman *et al.*, 1983; Abou Zeid *et al.*, 1993). Brain ATPase is a key enzyme in cellular water balance and in osmoregulation in the whole animal. Cypermethrin treated animals at both doses show a significant decreases in brain Na^+, K^+-ATPase and Mg^{++}-ATPase activities.. Several classes of pesticides were known to inhibit ATPases activities (Koch, 1969; Cutkomp *et al.*, 1976). Several opinions were expressed for such an inhibition in the ATPase activity in the cellular system. Inhibition indicates an overall disruption in the energy metabolism. Na^+, K^+-ATPase enzyme is associated with lipoprotein in the form of a complex (Nakao *et al.*, 1974). If a lipophilic compound were to come in contact with this lipoprotein and partitioning into the lipid fraction occurred an allosteric change could occur which could alter the activity of the enzyme. Kinter *et al.* (1972) speculated that lipophilic pesticides exert their biologic effects on ATPase system by interacting with the phospholipid-activating component of the enzyme complex. The lipophilic partitioning of ATPase enzyme by cypermethrin may produce allosteric change resulting in decreased ATPase activity. A decrease in Mg^{++}-ATPase and Na^+, K^+-ATPase activities in the rat was reported by La Rocca and Carlson (1979).

Residue analysis

Residues of pesticides were below the detection levels (50 pg/µl of cypermethrin and 100 pg/µl of dimethoate) in all samples collected from control animals. Average recoveries of 100 ng of cypermethrin and dimethoate each from urine, feces, kidneys, spleen, liver and forequarter muscles of control sheep were ranged from 64 to 96%, and the relative standard error for detected levels of pesticides ranged between 2.34 and 5.49% (Table 4).

Table 4. Percentage recovery of 100 ng of cypermethrin and dimethoate in feces, urine, kidney, spleen, liver and muscle of control sheep (mean ± SE)

Pesticides	Feces	Urine	Kidney	Spleen	Liver	Muscle
Cypermethrin	79.54	96.37	90.2	87.0	89.6	74.1
	±2.37	±2.85	±2.34	±2.66	±2.68	±3.89
Dimethoate	74.08	83.90	80.7	73.2	77.7	64.5
	±3.49	±2.89	±4.19	±4.30	±2.40	±5.49

The present study indicated that the main routes for cypermethrin excretion from the body were through both urine and feces (Table 5). Croucher *et al.* (1985) found that the major routes for elimination of oral administration of cypermethrin in cows were via both urine (approximately 50 %) and feces (approximately 40%). The elimination pattern in sheep, given one oral dose of cypermethrin (3.9 mg/kg body weight), showed that 41% of the administered dose excreted in the urine and 20 % was eliminated in feces (Crawford and Hutson, 1977). On the other hand, the obtained results showed that the major route for excretion of dimethoate was via urine.The detected levels of pesticides were dose-dependent. Kaplanis *et al.* (1959) found that about 87-90% of an oral dose of 10 mg dimethoate/kg was eliminated in the urine and 3.7 - 5% in the faeces of cattle at the end of treatment (24 h). Brady and Arthur (1963) found that about 45% of dimethoate administered orally to rats was excreted in the urine and only 5.8% was eliminated in the feces.

Results on the residues of cypermethrin and dimethoate in the tissues of kidneys, spleen, liver and forequarter muscles of treated animals after 63 days are presented in Table (6).

The results indicated that cypermethrin and dimethoate were detected in all tissue samples of treated animals except in liver at low dose of dimethoate. The pesticides residues in tissues of control animals were under detection limits (50 and 100 pg/µl, respectively). The none detection of low dose of dimethoate residues in liver of sheep may be due to the rapid degradation of it in liver, very little occurs in other tissues (lung, muscle, pancreas, brain, blood). The ability of the liver to degrade dimethoate in various species decreased in the order: rabbit > sheep > dog > rat > cattle > hen > guinea-pig > mouse > pig (Uchida *et al.*, 1964). The present results showed that the residue levels of cypermethrin and dimethoate were in the following decreasing order: kidneys > spleen > muscles > liver at levels ranging from 12.2 to 156.1 ng/g for cypermethrin and from 0.23 to 3.49 ng/g for dimethoate (Table 6). Croucher *et al.* (1985) found that the residues of cypermethrin were

detected in milk, blood, liver, kidneys and subcutaneous and renal fat of cows. Crawford and Hutson (1977) also reported that the residues of cypermethrin were detected in muscle, liver, kidneys and renal fat of sheep. Cattle sprayed once with 0.1% and 0.2% of cypermethrin showed that the residues in muscle, liver, and kidneys were ≤ 0.005 mg/kg in tissues and < 0.01 mg/kg in fat. In cattle treated twice with cypermethrin, fat samples contained residues ranging from 0.01 to 0.05 mg/kg tissue (Bosio, 1979).

Table 5. Residue levels in feces (ng/g) and urine (ng/ml) during treatment of male sheep with pesticides (mean ± SE of three animals)

Pesticides	Treatment (weeks)								
	1	2	3	4	5	6	7	8	9
Cypermethrin									
Feces									
6 mg/kg/day	11.31	15.92	16.0	14.43	31.79	53.49	52.31	54.62	50.37
	±1.64	±0.45	±1.71	±1.78	±1.49	±2.90	±1.39	±5.30	±3.34
12 mg/kg/day	14.59	17.65	28.09	23.67	51.09	64.73	66.03	63.51	69.35
	±0.67	±2.19	±0.89	±2.76	±4.34	±4.60	±4.54	±4.34	±2.47
Urine									
6 mg/kg/day	18.64	32.91	41.63	36.41	35.68	37.19	45.75	56.19	72.04
	±1.81	±1.44	±1.88	±2.83	±3.03	±1.65	±3.43	±3.85	±3.66
12 mg/kg/day	23.69	48.89	47.1	57.06	52.83	60.16	72.97	116.0	102.3
	±0.36	±3.25	±2.89	±3.00	±4.60	±3.00	±5.09	±8.16	±6.89
Dimethoate									
Feces									
1.6 mg/kg/day	1.66	3.12	3.82	4.58	5.06	5.05	6.52	6.50	6.56
	±0.19	±0.39	±0.12	±0.45	±0.43	±0.52	±0.17	±0.33	±0.42
3.2 mg/kg/day	4.07	5.39	5.49	6.97	6.36	7.26	7.33	8.37	8.46
	±0.12	±0.31	±0.55	±0.42	±0.46	±0.74	±0.32	±0.64	±0.61
Urine									
1.6 mg/kg/day	26.40	41.27	58.83	76.13	60.70	63.73	75.11	77.13	71.69
	±2.05	±3.78	±3.59	±1.26	±4.45	±2.47	±2.66	±4.06	±1.86
3.2 mg/kg/day	41.15	55.4	73.8	85.2	82.85	124.1	114.9	111.0	105.3
	±0.93	±3.08	±4.84	±4.45	±4.19	±7.70	±6.79	±4.81	±3.15

Table 6. Residues levels (ng/g) of cypermethrin and dimethoate in tissues of male sheep after treatment with pesticides (mean ± SE of three animals)

Treatment	Cypermethrin		Dimethoate	
(mg/kg/day)	6	12	1.6	3.2
Tissues				
Kidney	64.2±3.05	156.1±3.97	2.78±0.05	3.49±0.17
Spleen	69.0±4.04	148.5±2.98	0.62±0.02	0.74±0.01
Liver	12.2±0.20	14.3±0.33	n.d*	0.23±0.01
Muscle	62.4±3.03	84.6±4.25	0.23±0.02	0.32±0.03

* n.d = Not detectable.

The above-mentioned results indicate that cypermethrin and dimethoate produce moderate toxic effects in different animal systems, biochemically and histologically. Therefore, great attention should be taken during its field application to avoid the possible harmful effects in farm animals and occupationally exposed human.

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تقييم سمية مبيدات السيبرمثرين والدايميثويث في أغنام البرقي على التغيرات البيوكيماوية والهستولوجية وتقدير متبقياتها

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تم أستخدام ٣٠ حيوان من ذكور أغنام البرقى لدراسة تأثير مبيدي السيبرمثرين بجرعات ٦، ١٢ والدايميثويث بجرعات ١٦,، ٣٢, مليجرام /كيلوجرام من وزن الجسم/يوم على بعض الخواص البيوكيماوية والهستولوجية لذكور أغنام البرقي. كما تم تقدير متبقيات المبيدات في البول والروث أسبوعياً خلال فترة المعاملة وفى أنسجة الجسم (الكلى والطحال والكبد والعضلات) في نهاية فترة المعاملة بالمبيدات .و تم إعطاء الجرعات عن طريق الفم لمدة ٦٣ يوم على التوالى. وفى نهاية فترة المعاملة تم ذبح ٣ حيوانات من كل مجموعة.

أوضحت النتائج أن هناك اختلافات معنوية في الوزن النسبي لكل من الكبد والطحال بينما لايوجد تأثير على أوزان المخ والكلى والقلب والخصية. وحدثت تغيرات هستولوجية في التركيب التشريحي للطحال والكبد والمخ للحيوانات المعاملة بالمبيدات. كما حدث زيادة في نشاط أنزيمي أسبرتيت أمينو ترانس أمينيز والانين أمينو ترانس أمينيز وانخفاض في نشاط إنزيم اللاكتيك دى هيدروجينيز و لم يحدث أي تغيير في نشاط إنزيمات الفوسفاتيز الحلمضى والقاعدى في كبد الحيوانات المعاملة بالمقارنه بالحيوانات الغير معامله. كما أوضحت النتائج انخفاض نشاط إنزيم الاسيتيل كولين استريز في مخ الحيوانات المعاملة بالدايميثويث بينما لم يحدث تأثير علي نشاط الإنزيم بالمعاملة بالسيبرمثرين. كذلك حدث إنخفاض في نشاط إنزيم الصوديوم و البوتاسيوم ادنيوزين ثالث الفوسفاتيز والماغنسيوم ادنيوزين ثالث الفوسفاتيز في مخ الحيوانات المعاملة بالسيبرمثرين بينما لم يحدث تأثير علي نشاط الإنزيم في مخ

الحيوانات المعاملة بالدايميثويث. أظهرت نتائج تحليل متبقيات المبيدات تواجد مستويات منها في كل من عينات البول والروث المجمعة أسبوعياً من الحيوانات المعاملة وكان اخراج السيبرمثرين بمعدل متقارب عن طريق البول و الروث بينما فى حاله الدايمثويت كان المعدل أعلى فى البول عن الروث. كما أظهرت النتائج تواجد متبقيات المبيدات المختبرة في الكلى والطحال والكبد والعضلات وكان أعلى مستوى لها في الكلى والطحال.

يتضح في ضوء هذه الدراسة أن تعرض حيوانات المزرعة للتلوث بمبيدات السيبرمثرين والدايميثويث يؤدى إلى حدوث تغيرات واضحة في عديد من المعايير البيوكيماوية و الهستولوجية مما ينعكس على إنتاجية الحيوان. وأيضا هذه المبيدات وجد لها متبقيات في الأنسجة لمدة طويلة تحت ظروف هذه الدراسة وعليه يجب تفادى تعرض حيوانات المزرعه للتلوث بالمبيدات عن طريق الغذاء ومياه الشرب.