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ASSESSMENT OF THE CHANGES IN SOME DIAGNOSTICS ENZYMES AND OTHER PARAMETERS IN *Wistar albino* RATS TREATED WITH PESTICIDES DURING GESTATION

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Résumé

Ce travail a pour but d'étudier l'activité enzymatique du LDH, ALP, AST, ALT, CPK et le taux de cholestérol, glucose, triglycérides, bilirubine, créatinine et des protéines totales chez des rats femelles traitées à différentes doses de chlorpyrifos-éthyl et de phosalone. L'étude porte sur 110 rats adultes femelles. Les rattes gestantes sont divisées en 11 lots de 10. Ces lots sont répartis en 3 groupes. Le premier groupe représente le témoin. Le 2ème groupe traité au chlorpyrifos et le 3ème au phosalone reçoivent par gavage les différentes doses (1/5 ; 1/4 ; 1/3 ; 1/2 ; 2/3 DL50) du 6ème au 15ème jour de la gestation. D'après les résultats, le foie est l'organe cible de l'effet des pesticides. L'étude biochimique comme paramètre de la fonction hépatique montre une augmentation de l'activité des enzymes sériques de LDH, ALP, AST, ALT et une diminution de leur activité hépatique. Ainsi le taux de cholestérol et des triglycérides tend à diminuer. Le poids du foie augmente de manière significative après traitement aux différentes doses des deux pesticides. Ces dernières font diminuer le poids des fœtus. Le degré de modification dépend de la dose.

Mots clés: *pesticides organophosphorés ; hépatotoxicité ; tératogène ; fonction hépatique ; rattes gestantes.*

Abstract

The present work investigates the serum enzymes activities (LDH, ALP, AST, ALT, CPK) and the level of cholesterol, glucose, triglycerides, bilirubin, creatinine, and the total protein in female rats treated with pesticides; Chlorpyrifos-ethyl and Phosalone. Pregnant rats were divided into eleven groups containing 10 individuals each, and classified into three categories were treated orally (from the 6th to the 15th day of gestation) with different doses (1/5, 1/4, 1/3, 1/2, 2/3 LD_{50}) of both pesticides .Animals were dissected in the 19th day of gestation, and then blood samples were collected for biochemical study. The obtained results showed that the liver is the target organ for pesticides toxicities, as indicated by the perturbations in its functions. Thus, a significant elevation in serum AST, ALT and ALP activities has been observed, while their liver activities were highly decreased. Serum cholesterol and triglycerides levels were also decreased significantly. However, after treatment with different doses of both pesticides, the liver wet weights were highly increased, whereas, the foetus weights were significantly decreased. Generally, the degrees of observed variations were found to be dose dependent.

Keywords: *organophosphorus pesticides, hepatotoxicity, teratogenic, liver function, pregnant rates.*

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ملخص

تهدف هاته الدراسة الي تقييم نشاط مصل الأنزيمات الناقلة لمجموعة الأمين,الفوسفاتاز القاعدي, الكرياتنين فوسفوكيناز واللاكتات دي هيدروجيناز, و كذلك مستوى الجلوكوز, الكوليسترول, الجليسريدات الثلاثية, الكرياتين, البليريبين و البر وتينات الكلية لدى إناث الجرذان المعاملة بالجرعات المختلفة لكل من الكلوروبيريفوس ايثيل والفوزالون. أجريتالدراسة على 110 إناث الجرذان الحوامل. قسمت إناث الجرذان الحوامل إلى 11 مجموعة, تحتوي كل واحدة على 10 حيوانات. صنفت تلك المجموعات إلي ثلاثة أقسام حيث استعملالقسم الأول والمحتوي علي مجموعة واحدة كشاهد, في حين عوملت مجموعات القسم الثانيبالجرعات 1/5, 1/4, 1/3 , 1/2 , 3/2 من الجرعة القاتلة ل 50 من حيوانات التجارب منمبيد الكلوروبيريفوس-اتيل.كما عوملت مجموعات القسم الثالث بنفس الجرعات من مبيد الفوزالون. تمت المعاملة عن طريق الفم ابتداءا من اليوم السادس إلى غاية اليوم الخامس عشر من الحمل.أثبتت النتائج بأن الكبد هو العضو المستهدف تحت تأثير المبيدات. فالدراسة البيوكيميائيةكمؤشر لوظائف الكبد أظهرت ارتفاع نشاط أنزيمات المصل (الأنزيمات الناقلة لمجموعةالأمين, الفوسفاتاز القاعدي, و اللاكتات دي هيدروجيناز), في حين سجل انخفاض نشاطها فيالكبد, وكذلك انخفاض مستوى الكوليسترول والجليسريدات الثلاثية في المصل. أيضا سجلتزيادة معنوية في وزن الكبد بعد المعاملة بمختلف جرعات المبيدين, بالإضافة إلى نقص فيوزن الأجنة. ولقد وجد بأن درجة التغير تتوافق و الجرعة المستعملة.

الكلمات المفتاحية: *مبيدات فوسفوعضوية, السمية الكبدية, تشوهات جنينية, الوظيفة الكبدية, حرذان حوامل.*

Pesticides have been found to affect the mammalian reproductive system inducing changes in the neuroendocrine organ and target tissues **[1].** The mode of action of organophosphorus insecticides (OPIs) is mainly through the inhibition of the enzyme acetyl cholinesterase (Ach E), an effect which has been observed in mammals **[2].** The acute toxicity of organophosphorus (OP) compounds in mammals is believed to be due their irreversible inhibition of (Ach E), an enzyme that terminates the action of acetylcholine (Ach) in the nervous system. Although the inhibition of Ach E produces a variety of physiological and behavioral effects by increasing Ach at cholinergic synaps **[3],** it appears that all neurons, rather than some particular neurotransmitter or Neurotransmission system, are affected **[4]**. The mechanism initiating organ phosphorus-induced delayed polyneuropathy (OPIDP) is associated with the phosphorylation and specific modification of the so-called neuropathy target esterase (NTE) **[5].** Considerable evidence exists suggesting that the so-called (NTE) is involved in the mechanism responsible for (OPIDP) **[6].**

One of the ways in which (OP) compounds are detoxified is by their enzymatic hydrolysis. The enzymes capable of hydrolyzing these compounds are usually called A-esterase organophosphate acid anhydrase (OPA) **[7, 8, 9]**. Birds are known to be more sensitive to (OP) than most mammalian species for a low or non-existence of these enzymes **[9]**. These enzymes are calcium-dependent and become active by the addition of micro molar concentration of Ca^{++} **[10].** It is now well established that sub acute or chronic exposure (even to low doses) of laboratory animals to (OPIs) may disturb several physiological function including hepatic dysfunction **[11]** nephrotoxicity **[12]** embryotoxicity **[13]** and genotoxicity **[14, 15, 16, 17**]. Many reports also indicate that the most commonly used OPIs induce a teratogenic effect in animals **[18, 19].** The aim of this study is to investigate the toxicity of Phosalone and Chlopyrifos-ethyl in pregnant Wistar albino rats. These pesticides were chosen for the study because of their wide use in agricultural crops and livestock. Their extensive use in the fields treatment led to a possible presence in the mammalian organism. Human exposure to these pesticides may occur with agricultural workers as well as with those involved in their manufacture.

MATERIALS AND METHODS

Animals and experimental protocol

Female *Wistar albino* rats initially 12 weeks of age, weighing (150g-180g) were used in this study. These animals were housed in cages and had free access to food and tap water. Pregnant rats were divided into eleven groups. The first group was used as a control group and received only the solvent (corn oil). The other ten groups were treated with (1/5 , 1/4 , 1/3 , 1/2 , and 2/3 LD_{50}) of both pesticides (phosalone and chlorpyrifos-ethyl).

A daily dose from the 6^{th} to15^{th} day of gestation was administered by gavage. On the day 19^{th}, the animals were dissected, blood samples were collected from the hepatic portal vein , plasma and serum were immediately separated and used for biochemical analyses (Alanine amino transferase (ALT); Aspartate amino transferase(AST); Alkaline phosphatase (ALP) Lactate dehydrogenase (LDH); creatinine phosphokinase (CPK) and the level of cholesterol, glucose, triglycerides and total protein. Residual blood was flushed from the liver with cold physiological saline by perfusion via the portal vein. Different organs were removed and immersed in ice cold physiological saline. Then, after gentle blotting on filter paper, organs were weighed. The liver of different groups was homogenized in 0,25M sucrose-TKM buffer (0,61 % tris-Hcl; 0,19 % potassium chloride ; 0,1% magnesium chloride and 8,6% sucrose) pH 7,5 in Potter ELVejhem homogenizer with a Teflon pestle to give 20% (w/v) tissue suspension. The homogenate was centrifuged at 700 x g for 10 min.

Then, the supernatant was used for the activity estimation of (AST; ALT and ALP) following the procedure of wootton **[20]**. Protein was assayed using the method of Lowry **[21].** Livers homogenate were used for the extraction of total lipid using the method of Bligh and Dayer **[22]** flowed by evaporation of the chloroform extract. This latter was used to determine triglycerides by the method of Van Handel and Silversmith **[23]** as modified by Rice **[24].** Assays of different serum enzymes activities and other biochemical parameters were determined using commercial Kits of Bio-Mérieux.

Statistical evaluation

Data for each group of animals were subjected to analysis of variance (ANOVA). Values are given as mean ±SD. Statistical significances of differences were calculated with either one-way analysis of variance followed by Student-Newman-Keul's multiple range test or by student's t-test as appropriate (SPSS 8.0 for windows). Values with non-identical superscripts are considered significantly different at $P<0.05$.

RESULTS AND DISCUSSION

The effect of different doses of pesticides on the weights.

Body weight.

Rats treated with different doses of both pesticides showed a persisting significant decrease ($P \leq 0.01$, $P \leq 0.001$) in body weight (Table 01) till it exhibited body weight loss at the end of the treatment. The loss of body weight was due to the reduction in both fœtus weights and fœtus numbers. The results of the present work are in agreement with that of **[25, 26]**. Similar findings were found by Gupta et al.,(1992) Esia Amel and Selium, (1992) and Kadota et al., (1976); **[8, 27, 28].**

Liver weight

The analysis of data in Table (01) representing the liver weight for all experimental animals showed a significant increase ($P \leq 0.01$, $P \leq 0.001$) compared to control. The increase in liver weight may be attributed to the increased circulation as a result of increased demands for the detoxification of toxic compounds **[28]**. Also, it denotes to the increase in cell mass or cell density **[29].** While, other reported that liver enlargement may be related to the maintenance of the liver normal functional capacity **[30]**. In contrast, another study **[31]** stated that liver enlargement is not necessarily considered toxic lesions, since this effect is observed in a large number of compounds. Furthermore, Young et al., (1986) **[32]** illustrated that DFB treatment caused an increase in the density of endoplasmic reticulum by two folds.

Liver effects by methidathion were seen in dogs and mice. In the mouse, the liver pathology included biliary stasis, bile duct hyperplasia, and cholangiofibrosisand chronic hepatitis. In addition, increased liver weights and liver tumors were seen in male mice **[33, 34].**

Fetus weight

The obtained results presented in Table (01) indicated that different doses of both pesticides affected the fetus

weight. The present data showed a significant decrease in fetus weight ($p \leq 0.001$) of animals treated with the four high doses of both pesticides; but no effect was observed with the low doses (1/5 LD_{50} was observed. Moreover; the significant decrease in fetus weight of treated animals may be caused principally by the decrease in fetus numbers.

Biochemical studies

Serum biochemical changes

The results in Table (02) show that the treatment with the five doses of the two pesticides increase the serum enzymes activities (ALT, AST, ALP, CPK and LDH). The data show a significant increase ($p \leq 0.001$) in all enzymes of treated animals with the four high doses of both pesticides; while the low dose of chlorpyrifos shows a significant increase ($p \leq 0.001$) in ALP, LDH and no effect on CPK and AST was seen. Furthermore; the same dose of phosalone indicates a significant increase in AST, ALP, LDH ($p \leq 0.001$) and ALT ($p \leq 0.01$) and has no effect on CPK.

The significant increase in the activities of serum AST and ALT in treated rats may be explained by the hepatic potency of (OPIs) resulting in destructive changes in the hepatic cells. The insecticides were administered orally and hence, they reached the liver first through the portal vein. The effect of the (OP) on the liver is in accordance with Kiran et al., (1988) **[35]** who reported that carbamate as a single dose or a daily repeated treatment of female rats stimulated AST and ALT of the liver in vivo and *in vitro*. They added that the observed stimulation of ALT activity came from carbamate interaction with the enzyme molecule rather than with the tissue. It also, shows its hepatotoxic effect on the liver and other extra-hepatic tissues.

The transaminase enzymes are considered as indicator for tissue damage, especially in serum, that is explained by the degree of exposure and the severity of toxic symptoms **[36].** In the present study, the results have confirmed those recorded by many authors working on different insecticides. Accordingly, similar alterations in ALT, AST and ALP activities were induced by chronic administration of several compounds **[25, 26, 27, 37, 3 8 39, 40**and **41].** Also, the increase in the level of AST, ALT and billirubin in the serum could be resulted from the pathological changes such as necrosis of hepatocytes which causes an increase in the permeability of the hepatic cell membrane, resulting in the release of transaminases in the blood stream **[31].**

On the other hand, the data show a significant increase ($P \leq 0.001$) in serum levels of triglyceride, cholesterol, creatinine and bilirubin in rat treated with different doses of both pesticides compared to control Table (03). Similar findings were found by Terada *et al*., (1998) **[42]** where the ingestion of mepanipyrim induced fatty liver in rats. The latter is commonly assumed to be induced by the following two major mechanisms solely or by their combination; the first type is associated with raised levels of plasma fatty acids resulting from the mobilization of fat from adipose tissue and the second type is usually due to a metabolic blockade in the production of plasma lipoprotein which come from :

- A blockade in apoprotein synthesis.
- A blockade in synthesis of the lipoprotein from lipid and apoprotein .
- A failure in provision of phospholipids found in lipoprotein.
- A failure in the secretory mechanism itself. **[43].**

Table 01: the effect of different doses of both pesticides on body weight; liver weight and foetus weight in pregnant *Wistar albino* rats. Each value presents the mean ± SD; n = 10. a: $p< 0.05$; b : $p< 0.01$; c : $p< 0.001$ and n : non significant compared to control..

		Body weight	Liver weight	Foetus weight
Control		217±13,72	7,953±0,47	5,08±0,33
phosalon	1/5	197,2±7,51 ^{c}	9,043±0,63 ^{b}	4,565±0,60 ^{n}
	1/4	191,8±7,10 ^{c}	6,593±0,37 ^{c}	3,279±0,41 ^{c}
	1/3	191,7±6,20 ^{c}	9,470±0,41 ^{c}	3,244±0,29 ^{c}
	1/2	188,2±4,83 ^{c}	9,938±0,34 ^{c}	2,75±0,31 ^{c}
	2/3	173,4±7,76 ^{c}	10,511±0,39 ^{c}	2,029±0,22 ^{c}
Chlorperifos -ethyl	1/5	198,1±6,05 ^{b}	8,920 ±0,27 ^{c}	4,88±0,18 ^{n}
	1/4	196,3±6,34 ^{c}	9,635±0,23 ^{c}	3,494±0,24 ^{c}
	1/3	194,3±6,82 ^{c}	9,598±0,28 ^{c}	3,542±0,70 ^{c}
	1/2	193,6±4,86 ^{c}	9,855±0,20 ^{c}	2,831±0,18 ^{c}
	2/3	171±5,48 ^{c}	9,948±0,13 ^{c}	2,168±0,23 ^{c}

Table 02 : The effect of different doses of both pesticides on serum enzymes (ALT; AST; ALP; LDH and CPK) in pregnant *Wistar albino* rats. Each value presents the mean ± SD; n = 10. a: $p< 0.05$; b: $p< 0.01$; c: $p< 0.001$ and n: non significant compared to control.

		ALT (UI/l)	AST (UI/l)	ALP (UI/l)	LDH (UI/l)	CPK (UI/l)
Control		22,522 ± 1,35	64,82 ± 2,82	93,99 ± 1,97	90,54 ± 1,29	6,329 ± 0,43
Phosalon	1/5	24,28 ± 1,12^{b}	69,45 ± 0,65^{c}	98,01 ± 1,79^{c}	90,61 ± 3,61^{c}	7,152 ± 0,34^{n}
	1/4	26,48 ±1,26^{c}	77,06 ± 2,32^{c}	104,05 ± 2,24^{c}	100,24 ± 1,32^{c}	10,58 ± ,51^{c}
	1/3	32,04 ±1,07^{c}	86,78 ± 3,09^{c}	116,5 ±1,94^{c}	107,16 ±1,44^{c}	12,21 ±0,30^{c}
	1/2	52,86 ±1,39^{c}	103,11 ± 1,93^{c}	135,82 ±2,95^{c}	138,40 ± 0,98^{c}	14,34 ± 0,57^{c}
	2/3	78,89 ±1,10^{c}	135,70 ± 3,43^{c}	178,16 ± 1,67^{c}	149,68 ± 0,89^{c}	18,871 ± 0,63^{c}
Chlorperifos-ethyl	1/5	22,59 ±0,59^{c}	73,34 ±1,61^{a}	95,84 ± 1,27^{c}	92,92 ± 1,50^{c}	7,98 ± 0,41^{n}
	1/4	27,3 ±1,12^{n}	82,44 ±1,44^{c}	113,04 ± 4,42^{c}	104,65 ± 3,53^{c}	7,25 ± 0,17^{c}
	1/3	36,90 ±1,37^{c}	99,65 ±2,69^{c}	127,93 ± 2,82^{c}	121,18 ± 1,80^{c}	9,96 ± 0,40^{c}
	1/2	65,76 ±2,91^{c}	130,11 ±2,83c	143,23 ± 2,81^{c}	142,26 ± 2,23^{c}	12,45 ± 0,65^{c}
	2/3	86,93 ±2,35^{c}	159,25 ±4,00^{c}	182,02 ± 2,87^{c}	167,34 ± 3,73	18,14 ± 0,70^{c}

These findings suggest that mepanipyrim-induced fatty liver results from the blockade of triglyceride release from the liver either by the inhibition of the synthesis of hepatic very low density lipoprotein (VLDL) or by its secretion into the blood **[42].** It has been found that fatty liver induced by mepanipyrim results mainly from the inhibition of the transport of hepatic (VLDL) from Golgi apparatus to the cell surface. The inhibition of the transport of hepatic (VLDL) appears to result from qualitative changes in (VLDL) such as alteration of the apoprotein composition and or insufficient lipidation of VLDL itself **[44].**

Table 03: The effect of different doses of both pesticides on serum (glucose, cholesterol, triglyceride, Creatinin, bilirubine and total protein) in pregnant *Wistar albino* rats. Each value presents the mean ± SD ; n = 10. a : p< 0.05; b : p< 0.01 ; c : p< 0.001 and n : non significant compared to control.

		Glucose (Mmol/l)	Cholesterol (Mmol/l)	Triglyceride (Mmol/l)	Creatinine (Mmol/l)	Bilirubine (Mmol/l)	Total protein (Mmol/l)
Control		5,091 ± 0,12	0,404 ± 0,02	0,544 ± 0,04	43,398 ± 2,01	4,467 ± 0,33	75,227 ± 3,23
phosalon	1/5	4,679 ± 0,31^{c}	0,768 ± 0,04^{c}	0,577 ± 0,03^{n}	53,51 ±2,24 °	4,799 ±0,31 °	70,47 ±1,55^{a}
	1/4	4,016 ±0,07^{c}	0,871 ±0,03^{c}	0,692 ±0,02^{c}	65,83 ±3,40 °	6,070 ±0,15 °	64,46 ±2,42°
	1/3	3,493 ±0,29^{c}	0,987 ± 0,04^{c}	0,884 ±0,28^{c}	62,49 ±3,86 °	7,720 ±0,53 °	56,17 ±2,91°
	1/2	2,650 ±0,17^{c}	1,392 ±0,14^{c}	1,297 ± 0,04^{c}	84,55 ±3,84 °	7,187 ±0,20 °	45,62 ±3,44°
	2/3	1,991 ±0,05^{c}	1,870 ±0,17^{c}	0,951 ± 0,43^{c}	87,68 ±4,74 °	9,396 ±0,30 °	35,97 ±3,09°
Chlorperifos-ethyl	1/5	5,157 ±0,19^{c}	0,763 ± 0,03^{c}	0,596 ± 0,02^{b}	61,96 ±6,98 °	6,118 ±0,14 °	74,62 ±3,54^{n}
	1/4	4,495 ±0,31^{c}	0,888 0,04^{c}	0,876 ±0,01^{c}	72,47 ±2,28 °	8,210 ±0,29 °	53,58 ±3,28°
	1/3	4,476 ±0,33^{c}	1,429 ±0,07^{c}	1,158 ±0,07^{c}	72,49 ±4,04 °	10,15 ±0,15 °	48,26 ±3,70°
	1/2	3,588 ±0,23^{c}	1,918 ±0,05^{c}	1,324 ± 0,01^{c}	80,53 ±2,14 °	11,06 ±0,16 °	44,74 ±2,98°
	2/3	2,946 ±0,06^{c}	2,096 ±0,02^{c}	1,897 ± 0,06^{c}	84,99 ±3,60°	13,12 ±0,14°	38,9 ±2,53°

In contrast, animals treated by both pesticides had a severe hypoglycemia accompanied by a decrease in serum total protein .Table (03).The obtained results which coincide with the general fact, stated by Baron (1984) **[45],** that total protein decreased as a result of chronic disease when large number of parenchyma liver cells have been destroyed. Furthermore; the decrease of total serum protein may caused by the reduction of serum globulin level which markedly declined at the same time. It supports the previously mentioned disturbances of a delayed depressing effect of the OPIs on immunoglobulin production. This was accompanied by a decrease in body weight gain which led to body weight loss at the end of the experiment **[45]**.

Biochemical changes in liver tissues

The data in Table (04) show that the activity of ALT, AST and ALP in liver tissues was decreased in all treatments. This decrease in liver enzyme activity was accompanied by a decrease in glucose and total protein Table (05).

The decrease of glucose and total proteins may be due to an increase in glucose conception by the tissue and an increase in gluconeogenesis. The significant decline in cholesterol accompanied by a significant decrease of serum glucose could be originated from an increase in endogenous insulin release due to a damage of pancreatic tissue. Such decrease could results from a deleterious effect of OPIs on carbohydrate metabolism. It may also be, due to the stimulation of catecholamines that stimulates lipolysis which leads to an increase in fatty acid production.

Table 04: The effect of different doses of both pesticides on liver enzymes (ALT, AST and ALP) in pregnant *Wistar albino* rats. Each value presents the mean ± SD; n = 10. a: p< 0.05; b : p< 0.01 ; c : p< 0.001 and n : non significant compared to control.

		ALT (µmol Pyruvate release/g tissues)	AST (µmol Pyruvate release/g tissues)	ALP (µmol Pyruvate release/g tissues)
Control		22,337 ± 0,54	8,33 ± 0,29	0,893 ± 0,05
phosalon	1/5	22,122 ± 0,41^{n}	8,102 ± 0,35^{n}	0,849 ± 0,03^{a}
	1/4	20,998 ±0,48^{c}	7,528 ±0,37^{c}	0,576 ±0,02^{c}
	1/3	18,024 ±1,01^{c}	6,981 ± 0,10^{c}	0,479 ±0,02^{c}
	1/2	15,437 ±0,83^{c}	5,8 ±0,15^{c}	0,444 ± 0,03^{c}
	2/3	11,529 ±0,89^{c}	4,878 ±0,08^{c}	0,323 ± 0,02^{c}
Chlorperifos-ethyl	1/5	22,518 ±0,60^{b}	8,644 ± 0,14^{c}	0,846 ± 0,02^{b}
	1/4	21,209 ±0,57^{c}	7,911 0,10^{c}	0,751 ±0,03^{c}
	1/3	19,065 ±0,72^{c}	6,917 ±0,11^{c}	0,642 ±0,03^{c}
	1/2	14,048 ±0,64^{c}	5,892 ±0,10^{c}	0,464 ± 0,02^{c}
	2/3	10,478 ±0,64^{c}	3,978 ±0,11^{c}	0,356 ± 0,03^{c}

Table 05 : The effect of different doses of both pesticides on liver (glucose, triglyceride, total lipid and total protein) in pregnant *Wistar albino* rats. Each value presents the mean ± SD ; n = 10. a : p< 0.05 ; b : p< 0.01 ; c : p< 0.001 and n : non significant compared to control.

		Glucose (mg/g wet.tissue)	Triglyceride (mg/g wet.tissue)	Total lipid (mg/g wet.tissue)	Total protein (mg/g wet.tissue)
Control		2,800 ± 0,15	25,722 ± 1,23	64,24 ± 1,58	289,41 ± 7,72
phosalon	1/5	2,605 ± 0,29^{a}	32,67 ± 1,83^{c}	68,83 ± 5,69^{a}	242,15 ± 6,33
	1/4	2,089 ± 0,34^{c}	47,48 ± 1,93^{c}	84,43 ± 3,56^{c}	207,15 ± 4,37
	1/3	1,620 ± 0,22^{c}	68,105 ± 2,10^{c}	108,69 ± 5,23^{c}	192,92 ± 4,27
	1/2	1,345 ± 0,10^{c}	95,79 ± 3,12^{c}	125,27 ± 3,36^{c}	156,89 ± 4,83
	2/3	0,996 ± 0,14^{c}	126,25 ± 2,90^{c}	178,09 ± 7,76^{c}	100,24 ± 7,44
Chlorperifos-ethyl	1/5	2,545 ± 0,12^{c}	36,98 ± 2,48^{c}	85,03 ± 2,79^{c}	253,04 ± 5,06
	1/4	2,374 ± 0,08^{c}	45,33 ± 2,97^{c}	97,49 ± 1,61^{c}	223,21 ± 5,53
	1/3	1,959 ± 0,09^{c}	75,19 ±2,70^{c}	115,75 ± 2,82^{c}	205,81 ± 5,37
	1/2	1,359 ± 0,10^{c}	113,46 ± 4,90^{c}	154,42 ± 4,33^{c}	144,51 ± 7,92
	2/3	1,067 ± 0,10^{c}	84,26 ± 5,76^{c}	215,4 ± 3,13^{c}	90,00 ± 6,51

Additionally, the results found by Urmila and Arvind, (1988) **[46]** indicated that Monocrophos (10ppm) decreased the level of hepatic proteins and RNA as early as 2-5 days of exposure. Such changes were accompanied by increased levels of 5'-nucleotidase in liver indicating degenerative changes.

In contrast, Pradeep and Nirmala, (1986) **[47]** found that hepatic proteins increased after two month of phosphamidon intoxication. This interference might be resulted from autolysis of the hepatic cells; or from hepatic detoxification activities which can involve an increase in protein metabolism. Previous investigations **[47]** indicated that the continuous exposure to even low dose (35ppm) of phosphamidon can cause a hepatic damage.

CONCLUSION

The results show a significant increase in all serum enzymes in animals treated with different doses of both pesticides, with an increase in serum levels of triglyceride, cholesterol, creatinine and bilirubin .In contrast, the same treatment caused a severe hypoglycemia accompanied by a decrease in total protein.

Also, the data show a decrease in liver enzymes activities accompanied by a decrease in glucose and total protein. The decrease of glucose and total protein may be due to an increase in conception of glucose by the tissue and an increase in gluconeogenesis. This decrease may be due to a deleterious effect of OPIs on carbohydrate metabolism. It may also be due to the stimulation of catecholamines which stimulate lipolysis that leads to an increase in fatty acid production.

Generally, the biochemical findings on liver female rats caused by chlorpyrifos-ethyl and phosalone indicated the importance of protecting the animals and humans from the exposure to such compounds. In the light of the results reported here, and those of some previously reported investigations Kniewald et al.,(1987) **[48]** more attention should be paid to the possible effects of various toxic substances found in the environment; particularly those with low toxicity that are present in food and water, as they could induce marked changes at the cellular level**[4].**

The present study has showed the manner of response and the induction of toxicological effects in females rats after exposure of (chlorpyrifos-ethyl and phosalone) by daily doses. It is of importance to note here that the animals were exposed to these doses for a period to disturb the liver function. This study was undertaken to simulate a situation where workers would be exposed to different pesticides during applications and transportation of agrochemicals **[49].**

As a conclusion, it could be recommended that the use of OPIs must be controlled to avoid any hazards to the livings especially humans.

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