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ABSTRACT

To investigate the toxic effects of fenitrothion and lead acetate on dams and their pups during lactation period. Twenty four female pregnant albino rats were divided into four groups, first group as control, second group received orally (80 mg/kg B.wt fenitrothion), third group received orally(60 mg/kg B.wt lead acetate), fourth group received orally (80 mg/kg fenitrothion B.wt plus 60 mg/kg B.wt lead acetate). The results indicated that decrease in body weight of pups for all treated groups compared to control group. The activity of ALT, AST and GGT increased in mothers serum, increased levels of creatinine and urea in mothers serum. Increased in oxidative stress, indicated by increased the level of MDA of liver homogenate for mothers and their pups, and decrease in the antioxidant enzymes, activities (GSH, GST and SOD) in liver homogenate for mothers and pups. Decrease ChE activity in mothers serum and its brain homogenate for mothers and pups. This result consistent histopathological changes were found in the liver, kidney, spleen, pancreas and brain of mothers and liver, kidney, spleen and brain of pups. The results suggested that the transfer of fenitrothion and lead acetate through the mother milk has resulted in oxidative stress and biochemical and histopathological alterations in the suckling pups. Also the combination between lead acetate and fenitrothion consider synergistic effects either on dams or pups.

INTRODUCTION

Fenitrothion is one of the organophosphorus compound which inhibited cholinesterase (ChE) used as insecticide. Fenitrothion used at present in Egypt on cereals, cotton, orchard fruits, rice, vegetables, controlling a wide range of insects and other pests, affecting both invertebrate and vertebrate organisms, including humans. **(Zahran et al. 2005).** Teratogenic effects and postnatal effect was recorded in chicken exposed to fenitrothion before hatching. This effects include reduction in body weight and length, leg weakness and abnormal gait , flaccid paralysis and inhibition of activity ChE enzyme **(Paul and Vadlamudi 1976, Elawar and Francis 1988 and Russ 2005).** Deleterious effects were recorded in rat dams and its fetuses where mothers exposure to fenitrothion during pregnancy and after parturition. This effects include decrease body weight of pups and inhibition of activity ChE enzyme ,

increase of MDA and ALT, AST in both pups and mothers in addition to hisopathologic changes in liver (**Turner et al.2002, Struve et al.2007** and **Sefi et al. 2011).**

Lead (pb) one of the oldest known metal, are harmful to both animal and humans . The metal freely moved in the environment such as water, soil and air or in industrialized compounds. **(Sanin et al. 1998).** Lead affects the postpartum development. Fundamentally through lactation. **(O'Halloran and Spickett 1992).** Deleterious effects were recorded in dams and its foetus when rats, mice and rabbit exposed to lead acetate during gestation and lactation periods. This effects include decrease body weight of pups, poor fur growth, patchy skin. Decrease of SOD and GST, increase of MDA and ALT, AST in both pups and mothers in addition to histopathologic changes in liver, kidney, stomach and brain **(Masso and Antonio 2009, Dhir and Dhand 2010, Taiwo et al. 2010, Moreira et al. 2001, Chang et al. 2012, Sharma and Mogra 2013, Sharma et al. 2013, Hassan and Jassim 2010** and **Schneider et al. 2016).**There are rare or no researches dealing with the deleterious (hazards) effects of co- administration of fenitrothion and lead acetate. So this study was aimed to detect the toxic effects of fenitrothion and lead acetate alone and in combination on the mothers and its foetuses during lactation period.

MATERIAL AND METHODS

Tested compounds:

Sumithion 50%EC (fenitrothion 50%EC). Was purchased from Egychem .Co.for insecticides, Egypt and lead acetate 98% (trihydrate) Powder, was purchased from NATCO Egypt.

Experimental Animals and design :

Twenty four (24) adult female albino rats weight 180± 20 gm aged about 4 months old, and ten (10) adult male albino rats weighing 250 -300 gm aged about 5 months, were obtained from Animals Experimental Unit , Department of Anatomy , Faculty of Medicine, Mansoura University. The animals were apparently clinically healthy. The animals were housed in plastic cages with wood shavings as bedding and kept under controlled condition (23± 1℃ ,12 h light and 12 h dark cycle). Rats were fed on standard laboratory pelleted diet and water ad libitum. The animals were accommodated for our laboratory condition for 2 weeks before starting the experiment. The pregnant rats were divided into 4 groups (6 for each).The first group used as control and received orally 0.5 ml distilled water from parturition till weaning (21 days) post parturition. The second group received 80 mg/kg B.wt orally of fenitrothion from day of parturition till weaning. The third group received 60 mg/kg B.wt orally of lead acetate from day of parturition till weaning. The fourth group received orally both fenitrothion and lead acetate by the previous dose and time over mentioned . On the day of parturition, dams were observed during labour. The number of viable and dead neonates were recorded. The neonates were examined for any gross external malformations and the body weight of the neonates were recoded. Neonates were kept under daily observation and the growth rate and weight was recorded every week through the end of suckling period (21 days). At the end of experimental period, 21 day old rats and their mother were sacrificed, blood was immediately collected from retro – orbital plexus **(Britten et al. 1971).** Clear serum were separated carefully and stored in eppendorf tubes at − 20℃ until estimation of biochemical parameters. For Preparation of tissue homogenate Liver and brain from rats and their neonates were removed washed with saline solution, one gm

of tissue were homogenized in 9 ml ice cold phosphate puffer (PBS) PH 7.4 centrifuged at 3000 rpm for 15 minutes at 4°C , and the supernatant were separated carefully, collected and stored at −20°C until estimation biochemical parameters. **(Ferdandez-botran et al. 2002).**

Serum biochemical analysis:

Serum samples were analysis for alanine aminotransferase (ALT) and aspartate aminotransferase (AST), **Reitman and frankel (1957).** Gamma- glutamyltransferase (GGT), **Dufour (2010).** Urea, **Numann et al. (1977).** Creatinine, **Henry et al. (1974)**.

Antioxidant and oxidative stress analysis:

Liver homogenate samples were analyzed for Malondialdehyde (MDA), **Satoh (1978)**. Glutathione reduced (GSH), **Beutler et al. (1963)**. Glutathione – s – transferase (GST), **Habig and pabst (1974).** Superoxide dismutase (SOD), **Nishikimi et al. (1972)**. Serum and brain homogenate sample were analyzed for Cholinesterase (ChE), **Henry et al. (1974)**.

Histopathological examination:

Specimens from liver, kidney, spleen, pancreas and brain from rat dams and liver, kidney, spleen and brain from foeti, were collected and kept in 10% neutral buffered formalin. Section of 5 micron thickness were prepared from all specimens, stained by hematoxyline and eosin (H&E) and examined microscopically, **Bancrofft et al. (1990).**

All data were subjected to statistical analysis using statistical software program (SPSS for Windows, version 20, USA).

RESULTS

- Effects of fenitrothion, lead acetate and its combination on rat dams:

1.*Serum biochemical parameters:*

A significant increase in the activity of ALT enzyme from all treated groups compared to control. A significant increase in the activity of ALT enzyme from co- treated group (fenitrothion & lead acetate) compared to group treated with 80 mg/kg B.wt fenitrothion and group treated with 60 mg/kg B.wt lead acetate alone. Alanine aminotransferase is significantly elevated in lead acetate group (60mg/kg B.wt) than fenitrothion group (80 mg/kg B.wt). Result showed in table (1) and fig (1). A significant increase in the activity of AST enzyme from all treated groups compared to control. A significant increase in the activity of AST enzyme in both groups, group received 60 mg/kg B.wt lead acetate and group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated only with 80 mg/kg B.wt fenitrothion. Result showed in table (1) and fig (2). A significant increase in the activity of GGT enzyme from all treated groups compared to control. A significant increase in the activity of GGT enzyme in both groups, group received 60 mg/kg B.wt lead acetate and co-treated group 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated only with 80 mg/kg B.wt fenitrothion. Result showed in table (1) and fig (3). A significant increase in the level of creatinine from all treated groups compared to control. A significant increase in the level of creatinine in both groups, group received 60 mg/kg B.wt lead acetate and group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated only with 80 mg/kg B.wt fenitrothion. Result showed in table (1) and fig (4). A significant increase in the level

of urea from all treated groups compared to control group. Result showed in table (1) and fig (5).

2.Antioxidant and oxidative stress Analysis:

A significant decrease in the activity of GSH enzyme from all treated groups compared to control. A significant decrease in the activity GSH enzyme in co-treated group 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to other treated groups. Result showed in table (2) and fig (6). A significant decrease in the activity of GST enzyme from all treated groups compared to control. A significant decrease in the activity GST enzyme in both groups, group received 80 mg/kg B.wt fenitrothion and group received 60 mg/kg B.wt lead acetate compared to co-treated group. Result showed in table (2) and fig (7). A significant decrease in the activity SOD enzyme from all treated groups compared to control. Result showed in table (2) and fig (8). A significant increase in the level of MDA from all treated groups compared to control. A significant increase in the level of MDA in co-treated group (80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate) compared to group treated with 60 mg/kg B.wt lead acetate and group treated with 80 mg/kg B.wt fenitrothion. A significant increase in the level of MDA from group received 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion. Result showed in table (2) and fig (9).

1. Effects on cholinesterase enzyme:

A significant decrease in the activity serum ChE enzyme from all treated groups compared to control. Result showed in table (3) and fig (10).

A significant decrease in the activity brain ChE enzyme from all treated groups compared to control. Result showed in table (3) and fig (11).

- Effects of fenitrothion, lead acetate and combined on suckling foet:

1. Effect on body weight :

There was a significant decrease in the body weight of foeti from all treated groups during 1st , 2nd and 3rd week compared to control. A significant decrease in the body weight between group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead compared to other treated groups in the 1st week.

A significant decrease in the body weight between group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion and group treated with 60 mg/kg B.wt lead acetate in the 2nd week. A significant decrease in the body weight between group received 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion in the 2nd week.

A significant decrease in the body weight between group received both 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared group treated with fenitrothion 80 mg/kg B.wt plus 60 mg/kg B.wt lead acetate in the 3rd week . A significant decrease in the body weight between group received 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion in the 3nd week. Result showed in table (4) and fig (12).

2. *Biochemical parameters* :

A significant decrease in the activity GSH enzyme of foeti from all treated groups compared to control. Result showed in table (5) and fig (13). A significant decrease in the activity GST enzyme of foeti from all treated groups compared to control. A significant decrease in the activity GST enzyme of foeti between group received 80 mg/kg B.wt

fenitrothion plus 60 mg/kg B.wt lead acetate compared to other treated groups. Result showed in table (5) and fig (14). A significant decrease in the activity SOD enzyme of foeti from all treated groups compared to control . A significant decrease in the activity SOD enzyme of foeti between group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion and group treated with 60 mg/kg B.wt lead acetate. A significant decrease in the activity SOD enzyme of foeti between group received 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion . Result showed in table (5) and fig (15). A significant increase in the level MDA of foeti from all treated groups compared to control . A significant increase in the level MDA of foeti between group received 80 mg/kg B.wt fenitrothion plus 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion and group treated with 60 mg/kg B.wt lead acetate. A significant increase in the level MDA of foeti between group received 60 mg/kg B.wt lead acetate compared to group treated with 80 mg/kg B.wt fenitrothion. Result showed in table (5) and fig 16).

3. Cholinesterase (ChE) :

A significant decrease in the activity ChE enzyme of foeti from all treated groups compared to control. Result showed in table (6) and fig (17).

Table (1): serum liver and kidney function tests from rat dams treated postnatally with fenitrothion, lead acetate and its combination (Mean ± SE) :

Groups	ALT U/L	AST U/L	GGT U/L	Creatinin mg/dl	Urea mg/dl
Control	$21.96^{d} \pm 0.527$	$65.00^{c} \pm 0.969$	$7.78^{c} \pm 0.327$	$0.57^{c} \pm 0.015$	$51.62^{b} \pm 2.610$
Fenitrothion 80 mg/kg B.wt	$27.68^{c} \pm 0.912$	$78.60^{b} \pm 2.731$	$12.02^{b} \pm 0.384$	$0.81^{b} \pm 0.028$	$91.08^{a} \pm 2.176$
Lead acetate 60 mg/kg B.wt	$32.10^{b} \pm 1.523$	$97.89^{a} \pm 2.711$	$15.06^{a} \pm 0.797$	$0.90^{a} \pm 0.027$	$96.63^{a} \pm 1.556$
Fenitrothion+ lead acetate 80+60 mg/kg B.wt	$40.05^{a} \pm 0.421$	$98.22^{a} \pm 1.920$	$15.54^{a} \pm 0.523$	$0.97^{a} \pm 0.034$	$94.45^{a} \pm 2.415$

The means in the same column having the same superscript not significantly different ($P \leq 0.05$).

Table (2): Oxidative enzymes of liver homogenate from rat dams treated postnatally with fenitrothion, lead acetate and its combination (Mean ± SE) :

Groups	GSH mg/g. tissue	GST mg/g. tissue	SOD U/g. tissue	MDA nmol/g. tissue
Control	$10.21^{a} \pm 0.579$	$11.07^{a} \pm 0.408$	$76.14^{a} \pm 2.948$	$6.11^{d} \pm 0.344$
Fenitrothion 80 mg/kg B.wt	$6.02^{b} \pm 0.495$	$0.68^{c} \pm 0.050$	$49.48^{b} \pm 1.057$	$21.11^{c} \pm 1.225$
Lead acetate 60 mg/kg B.wt	$5.82^{b} \pm 0.344$	$0.53^{c} \pm 0.042$	$49.82^{b} \pm 3.052$	$33.10^{b} \pm 2.133$
Fenitrothion+ lead acetate 80+60 mg/kg B.wt	$3.68^{c} \pm 0.260$	$3.01^{b} \pm 0.253$	$55.00^{b} \pm 1.159$	$45.03^{a} \pm 2.078$

The means in the same column having the same superscript not significantly different ($P \leq 0.05$).

Table (3): Serum and brain cholinesterase enzyme activities from rat dams treated postnatally with different doses of fenitrothion and its combination with lead acetate (Mean ± SE) :

Groups	ChE serum U/L	ChE brain U/L
Control	3.09^{a} ± 0.074	1.34^{a} ± 0.081
Fenitrothion 80 mg/kg B.wt	1.13^{b} ± 0.077	0.83^{b} ± 0.009
Fenitrothion + lead acetate 80+60 mg/kg B.wt	0.92^{b} ± 0.090	0.84^{b} ± 0.018

The means in the same column having the same superscript not significantly different ($P \leq 0.05$).

Table (4): Postnatal weight (g) of foeti from dam rats orally administered fenitrothion, lead acetate and its combined postnatally (Mean ± SE) :

Groups	Initial weight	1st week	2nd week	3rd week
Control	5.48 ± 0.060	11.43^{a} ± 0.161	18.90^{a} ± 0.226	29.23^{a} ± 0.323
Fenitrothion 80 mg/kg B.wt	5.41 ± 0.084	9.03^{b} ± 0.245	14.40^{b} ± 0.581	17.56^{b} ± 0.814
Lead acetate 60 mg/kg B.wt	5.51 ± 0.072	8.58^{b} ± 0.321	12.56^{c} ± 0.322	15.98^{c} ± 0.599
Fenitrothion+ lead acetate 80+60 mg/kg B.wt	5.39 ± 0.076	7.06^{c} ± 0.263	8.45^{d} ± 0.216	12.17^{d} ± 0.405

The means in the same column having the same superscript not significantly different ($P \leq 0.05$).

Table (5): Oxidative enzymes of foeti liver homogenate from dams treated postnatally with fenitrothion, lead acetate and its combination (mean± SE):

Groups	GSH mg/g. tissue	GST mg/g. tissue	SOD U/g. tissue	MDA nmol/g. tissue
Control	8.14^{a} ± 0.146	5.52^{a} ± 0.391	69.99^{a} ± 1.080	10.99^{d} ± 0.395
Fenitrothion 80 mg/kg B.wt	3.86^{b} ± 0.242	4.11^{b} ± 0.404	51.59^{b} ± 3.155	23.46^{c} ± 1.370
Lead acetate 60 mg/kg B.wt	4.19^{b} ± 0.219	3.66^{b} ± 0.189	44.43^{c} ± 1.506	29.34^{b} ± 1.563
Fenitrothion+ lead acetate 80+60 mg/kg B.wt	3.66^{b} ± 0.126	1.76^{c} ± 0.123	37.00^{d} ± 0.516	33.18^{a} ± 1.146

The means in the same column having the same superscript not significantly different ($P \leq 0.05$).

Table (6): Cholinesterase enzyme of foeti brain homogenate from dams treated postnatally with different doses of fenitrothion and its combination with lead acetate (mean± SE):

Groups	ChE U/L
Control	1.05^{a} ± 0.033
Fenitrothion 80 mg/kg B.wt	0.91^{b} ± 0.057
Fenitrothion + lead acetate 80+60 mg/kg B.wt	0.94^{b} ± 0.017

The means in the same column having the same superscript not significantly different (P< 0.05).

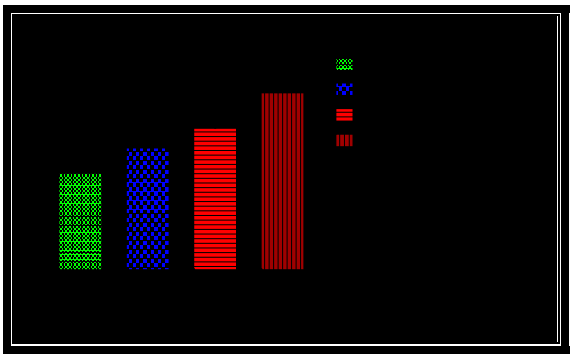

Fig.(1): ALT activity of rat dams orally administered Fenitrothion, lead acetate and combination postnatally

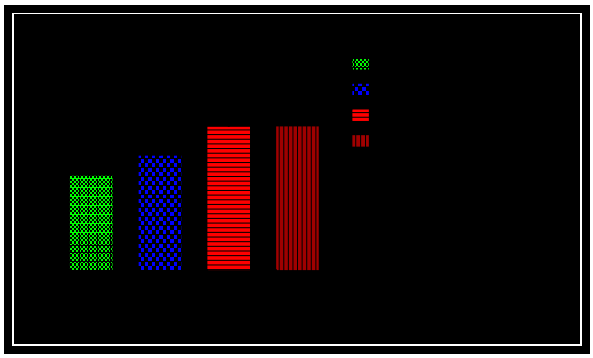

Fig.(2):AST activity of rat dams orally administered Fenitrothion, lead acetate and combination postnatally

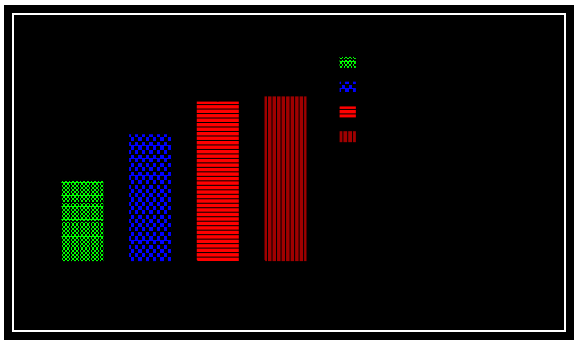

Fig.(3): GGT activity of rat dams orally administered Fenitrothion, lead acetate and combination postnatally

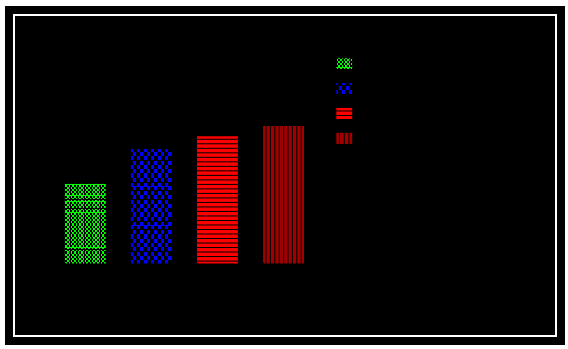

Fig.(4): Creatinine values of rat dams orally administered Fenitrothion, lead acetate and combination postnatolly

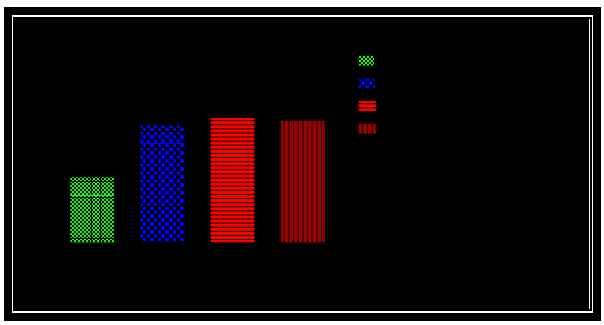

Fig.(5): Urea values of rat dams orally administered fenitrothion, lead acetate and combination postnatally

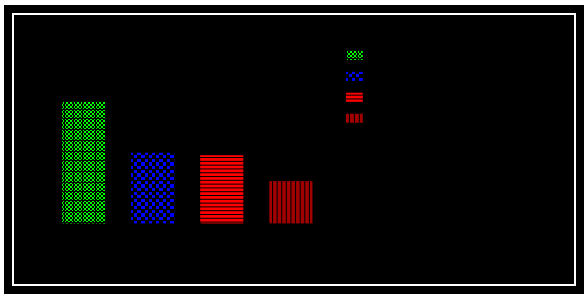

Fig.(6): GSH activity of rat dams orally administered fenitrothion , lead acetate and combination postnatally

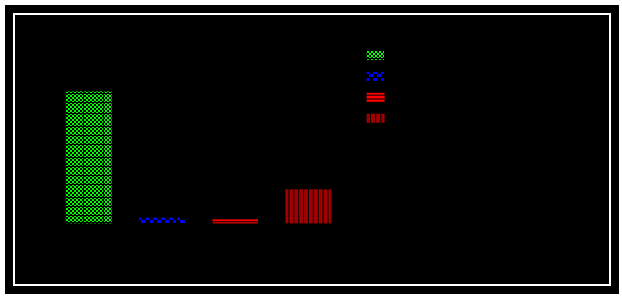

Fig.(7): GST activity of rat dams orally administered fenitrothion , lead acetate and combination postnatally

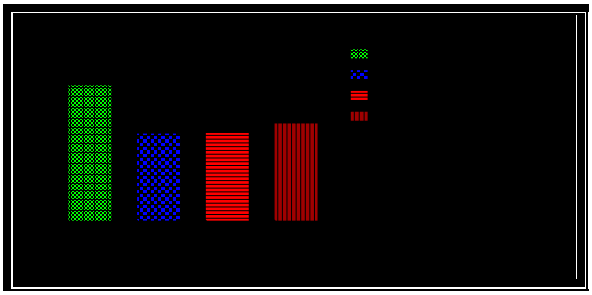

Fig.(8): SOD activity of rat dams orally administered fenitrothion , lead acetate and combination postnatally

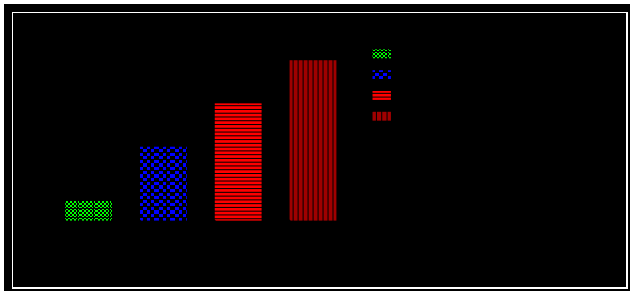

Fig.(9): MDA values of rat dams orally administered fenitrothion , lead acetate and combination postnatally

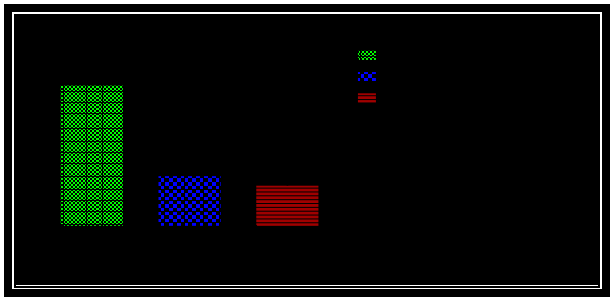

Fig.(10): ChE serum of rat dams orally administered fenitrothion and combination with lead acetate Postnatally

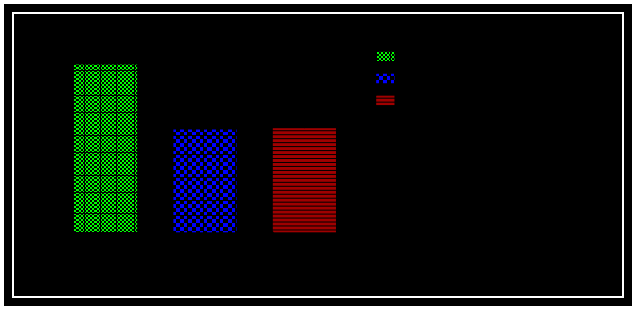

Fig.(11): ChE brain of rat dams orally administered fenitrothion and combination with lead acetate Postnatally.

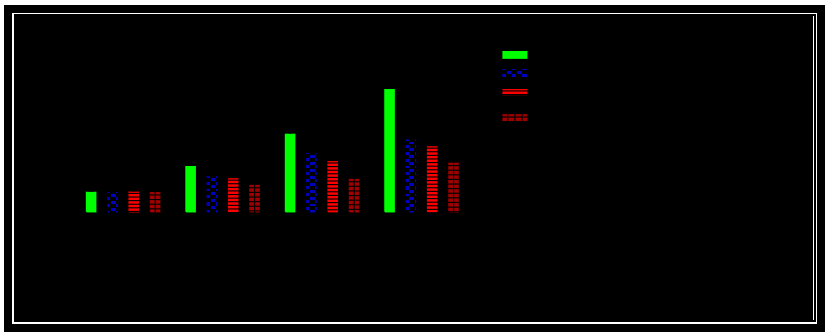

Fig.(12): Postnatal weight of neonates from dam rats orally administered fenitrothion, lead acetate and combined postnatally.

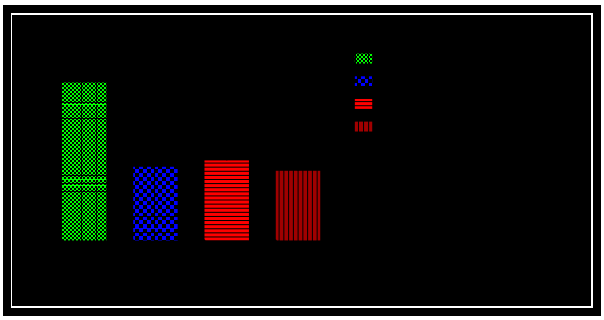

Fig.(14): GST activity of foeti from dams administered orally fenitrothio , lead acetate and combination postnatally.

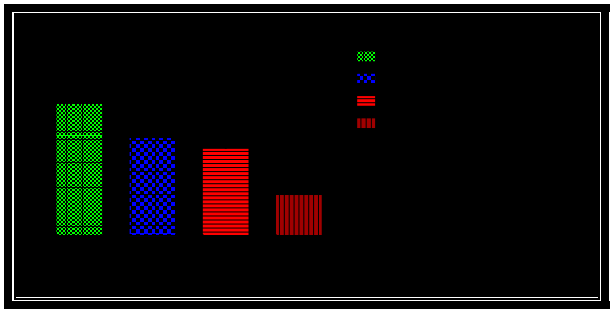

Fig.(13): GSH activity of foeti from dams administered orally fenitrothion , lead acetate and combination postnatally.

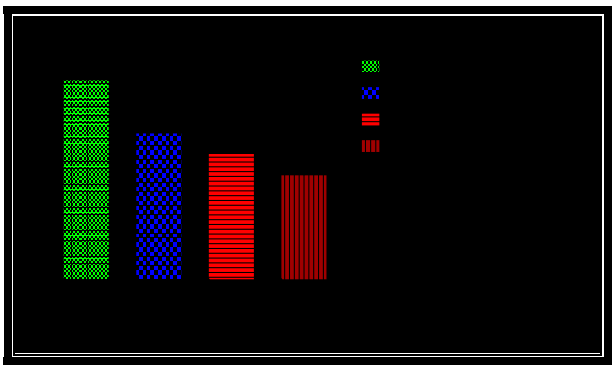

Fig.(15): SOD activity of foeti from dams administered orally fenitrothio , lead acetate and combination postnatally.

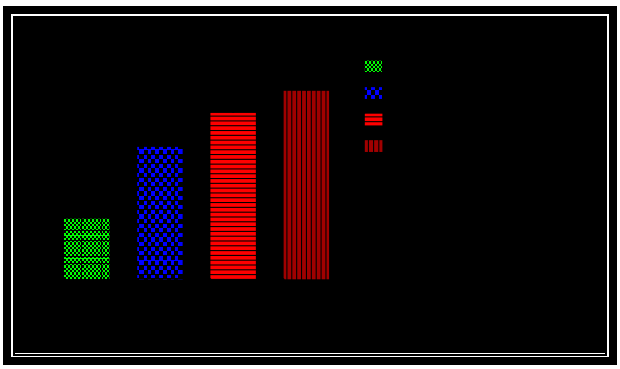

Fig.(16):MDA values of foeti from dams administered orally fenitrothio , lead acetate and combination Postnatally.

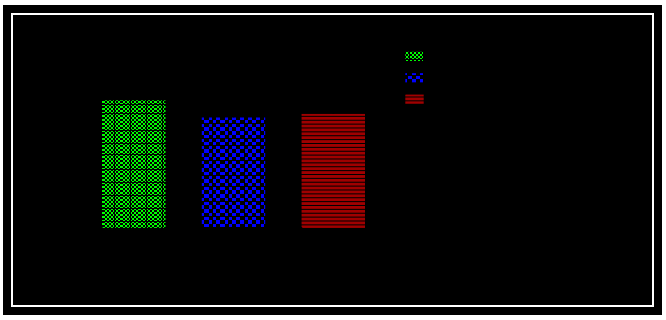

Fig.(17): ChE brain of foeti from dams administered orally fenitrothion and combination with lead acetate postnatall

Histopathologic changes in different organs of dams and its fetuses showed in **Fig 18, 19.**

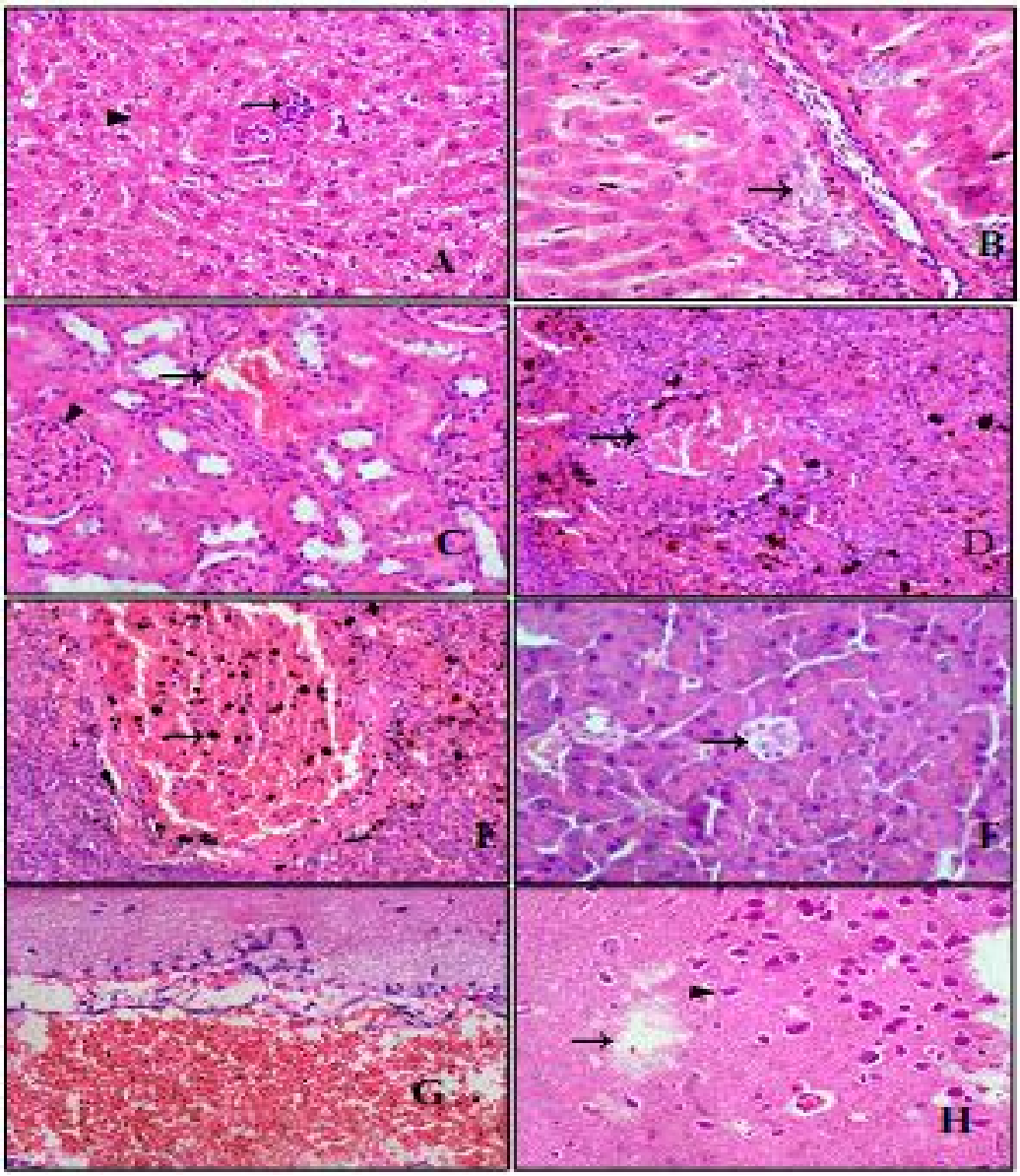

Fig. (18): A. Section from liver of dam received 60 mg/kg B.wt of lead acetate for 21 days post parturition, showing scattered necrosis of hepatocytes allover hepatic tissue (arrow head) and mononuclear cell aggregation in hepatic parenchyma (arrow).(HE, 400X). **B**. Section from liver of dam received 80+ 60 mg/kg B.wt of fenitrothion + lead acetate for 21 days post parturition, showing histiocytic infiltration (arrow) in hepatic tissue. (HE, 400X). **C**. Section from kidney of dam received 80 mg/kg B.wt of fenitrothion for 21 days post parturition, showing epithelial crescent in glomeruli (head arrow) and hemorrhage in interstitial capillaries (arrow).(HE, 400X). **D**. Section from spleen of dam received 80 mg/kg B.wt of fenitrothion for 21 days post parturition, showing congestion (arrow) and marked hemosiderosis. (HE, 400X). **E**. Section from spleen of dam received 60 mg/kg B.wt of lead acetate for 21 days post parturition, showing severe congestion and marked hemosiderosis (arrow). (HE, 400X). F. Section from pancreas of dam received 60 mg/kg B.wt of lead acetate for 21 days post parturition, showing atrophy of islet of Langerhans (arrow). (HE, 400X). **G**. Section from brain of dam received 80 mg/kg B.wt of fenitrothion for 21 days post parturition, showing massive hemorrhage and congestion in meningeal capillaries. (HE, 400X). **H**. Section from brain of dam received 80+ 60 mg/kg B.wt of fenitrothion + lead acetate for 21 days of parturition, showing degenerated neuron (arrow head) and loss of brain parenchyma (encephalomalacia) (arrow). (HE, 400X).

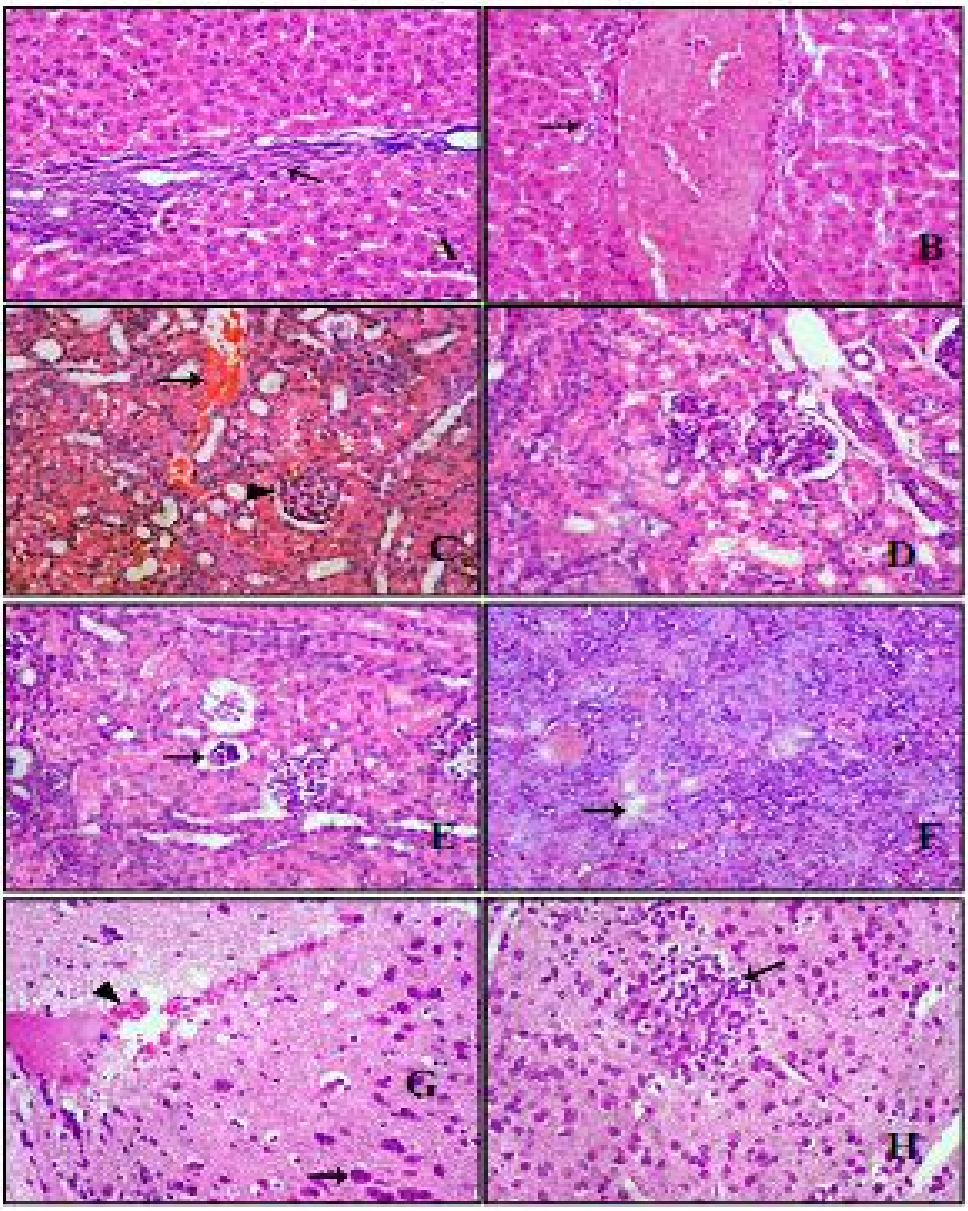

Fig. (19): A. Section from liver of fetus at 21st day postnatal, suckling dam received 80 mg/kg B.wt of fenitrothion, showing intralobular fibroblastic proliferation forming fibrous septa (arrow). (HE, 400X).**B.** Section from liver of fetus at 21st day postnatal, suckling dam received 80+60 mg/kg B.wt of fenitrothion + lead acetate, showing mild histiocytic infiltrates into the hepatic parenchyma (arrow). (HE, 400X).**C.** Section from kidney of fetus at 21st day postnatal, suckling dam received 80 mg/kg B.wt of fenitrothion, showing hemorrhage in interstitial tissue (arrow) and proliferation of mesangial cells in glomeruli (arrow head). (HE, 400X). **D.** Section from kidney of fetus at 21st day postnatal, suckling dam received 60 mg/kg B.wt of lead acetate, showing proliferation of mesangial cells in glomeruli and mild degeneration of renal tubular epithelium. (HE, 400X). **E.** Section from kidney of fetus at 21st day postnatal, suckling dam received 80+ 60 mg/kg B.wt of fenitrothion + lead acetate, showing necrosis and dissolution of glomeruli (arrow). (HE, 400X). **F.):** Section from spleen of fetus at 21st day postnatal, suckling dam received 80 mg/kg B.wt of fenitrothion, showing necrosis of lymphoid tissue (arrow) . (HE, 400X). **G.** Section from brain of fetus at 21st day postnatal, suckling dam received 60 mg/kg B.wt of lead acetate, showing edema and hemorrhage (arrow head) and proliferation of astrocytes (arrow) . (HE, 400X). **H.** Section from brain of fetus at 21st day postnatal, suckling dam received 80+ 60 mg/kg B.wt of fenitrothion + lead acetate, showing microgliosis (arrow) and proliferation of astrocytes. (HE, 400X).

DISCUSSION

The results indicated that fenitrothion and lead acetate caused decreased in the body weight of pups from dams received fenitrothion and lead acetate during lactation period, these result determined previously in fenitrothion **(Turner et al. 2002)**, in lead acetate **(Sharma and Mogra 2013** and **Chang et al. 2012** and **Masso and Antonio 2009).** The decrease in the body weight in pups may be due to decrease in amount of milk production by mother or due to transfer in the milk (Chemical enter breast milk by passive transfer from plasma, and their concentration in milk is proportional to their solubility and lipophilicity) which may be affected the body weight. This proposed was confirmed by inhibition of ChE in the foetus. These results indicate that a significant increase in the activity of ALT, AST and GGT of dams received fenitrothion and lead acetate during lactation period, may be due to the damage of hepatocytes, these results determined previously in fenitrothion **(Kerem et al. 2007, Farag et al. 2010** and **Ogutcu et al. 2008)** in lead actate **(Serrani et al. 1997, Abdou et al.2007, Dhir and Dhand 2010** and **Lee et al. 2004)** These increased in liver enzymes in serum may be due to tissue damage or alterations in the permeability of cell membrane, which releasing of hepatic enzymes into blood circulation is associated with hepatocyte congestion or hepatocellular necrosis. In addition, the lead causes cell lysis by affecting the K+ -Ca2+ channels(**Lakshmi et al. 2013).** GGT is an enzyme mainly present in cell membranes and is susceptible to damage due to the presence of insecticides**(Michelangeli et al. 1990).** The significant increase of malondialdehyde (MDA) levels in mother and pups of dams received fenitrothion and lead acetate during lactation period, these results determined previously in fenitrothion **(Sefi et al. 2011)** in lead acetate **(EL-sokkary et al. 2002** and **Saxena and Flora 2004** and **Masso and Antonio 2009)** MDA the major product of lipid peroxidation(LPO), free radicals might be generated during the metabolism of fenitrothion or lead acetate by the cytochrome P450 oxidase flavin monooxygenases enzymes, present in microsomal membrane of liver and induced consequently lipid peroxidation **(Sefi et al.2011).** Oxidative damage may be due to the generation of reactive oxygen species (ROS) without commensurate increases in the level of antioxidant defences **(Adhami et al. 2000)**. Therefore the increase in the lipid peroxidation potential was accompanied by histological changes including marked congestion in hepatic sinusoids and scattered necrosis of hepatocytes allover hepatic tissue and mononuclear cell aggregation in hepatic parenchyma in dams, while intralobular fibroblastic proliferation forming fibrous septa and congestion in portal vein and proliferation of astrocytes into hepatic parenchyma in pups. The present study demonstrates a significant decrease in the activity of SOD, GST and GSH in mothers and their pups exposed to fenitrothion and lead acetate during lactation period, these result determined previously in fenitrothion **(Hayes and Pulford 1995, Budin et al 2013** and **El-Shenawy 2010)** in lead acetate **(EL-sokkary et al. 2002** and **Moreira e al. 2001** and **Soltaninejadet al. 2003** and **Gurer and Ercan 2000)**. The decrease in the activity of SOD in fenitrothion or lead acetate intoxicated animals may be due to the consumption of this enzyme in converting the O2– to H2O, which is catalyzed by SOD. Considering that GST is a detoxifying enzyme that catalyes the conjugation of a variety of electrophilic substrates to the thiol group of GSH, producing less toxic forms, the decreased activity of GST may be indicate insufficient detoxification of fenitrothion or lead acetate in rats. This finding also confirmed by

histopthologic alterations in spleens of congestion and marked hemosiderosis in dams, and necrosis of lymphoid tissue and depletion of lymphoid tissue and marked hemosiderosis in pups. This histopathological findings may due to the decrease in T lymphocytes determined by flow cytometry **(Li et al., 2010).** Effects of pancreas determined previously in fenitrothion**(Budin et al., 2012)** in lead acetate **(Andrzejewska et al., 1994)** this change of pancreas of dams dilatation of capillaries in islets of langerhans and atrophy of islet of Langerhans. change in the brain for dams showed congestion in cerebral capillaries and degeneration of neurons, in pups showed edema and hemorrhage and proliferation of astrocytes, this effect of lead because their brains are still developing and blood brain barrier is incomplete **(US 1999).** The increased levels of creatinine and urea in serum of dams received fenitrothion and lead acetate during lactation period, these results determined previously in fenitrothion **(Budin et al. 2013** and **Hakim et al. 2014)** in lead acetate **(Taiwo et al. 2010, Lakshmi et al. 2013**and **Ashour et al. 2007)** These increased of creatinine and urea in blood circulation by fenitrothion or lead acetate, may be due to the decrease in glomerular filtration of kidney or tubular dysfunction. Increased of creatinine and urea in serum are biomarkers used to evaluate kidney function. This also is confirmed by the obtained histopatholgical changes in the kidneys, showed epithelial crescent in glomeruli, hemorrhage in interstitial capillaries and necrosis and atrophy of glomeruli. The results indicated that fenitrothion caused inhibition in the ChE enzyme in serum and brain of dams and brain of pups through mothers milk, these result determined previously **(Russ 2005** and **Okahashi et al. 2004).** Inhibited ChE brain mothers and pups suggest that fenitrothion exposure has a greater effect on maternal ChE activities compared to the ChE activities in nursing neonatal animals **(Okahashi et al. 2004).** This may be due to small amount of fenitrothion which transfer through mother milk although the blood brain barrier in the foeti little develop. The results of this study indicate that lead acetate and fenitrothion combination have more serious effects than separately in most parameters. So combination between lead acetate and fenitrothion consider synergistic effects either on dams or pups, but this effect not detected on ChE. The combination between lead as environmental pollutants and insecticides need further studies.

CONCLUSION

The main conclusion of this study that fenitrothion and/or lead acetate could cause evoked some adverse, has been distributed in pups tissue through the milk of lactation mothers and effects on some biochemical parameters and tissue damage as liver, kidney, spleen and brain in pups, in addition effects on generalized growth as well as body weight. We can also conclude that combination between fenitrothion and lead acetate more serious effects than separately in most parameters.

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