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BIOCHEMICAL AND PATHOLOGICAL COMPARATIVE STUDIES OF FENITROTHION AND CARBOFURAN PESTICIDES AND THEIR RESIDUES IN FAT AND MEAT OF POULTRY.

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SUMMARY

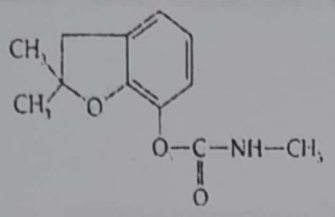
Two hundred and fifty (250) one day old chickens (domestic fowl) (Gallus domesticus) treated with 1/20 of LD_{50} of fenitrothion and carbofuran insecticides for 30 days. Serum, liver and muscle samples were selected for biochemical analysis at 7, 15 and 30 days. While samples for histopathological evaluation was taken at 30 days post treatment with the two insecticides. Samples for residue determination were taken at 7, 15 and 30 days post treatment.

Biochemical findings revealed decrease in serum cholinesterase associated with increase in ALT, AST and triacylglycerol level in both fenitrothion and carbofuran administered chicks. There was decrease in serum cholesterol, total lipid, HDL, LDL and total protein levels. Contrasting of fenitrothion that decreased serum glucose level, carbofuran increased it. There was increased total lipid and decreased total protein in livers of both treated groups. Fenitrothion and carbofuran had adverse effect on liver glycogen content and muscular total lipid. Both treatments decreased total protein content in muscle. The carbofuran decreased muscle glycogen content more pronounced than fenitrothion.

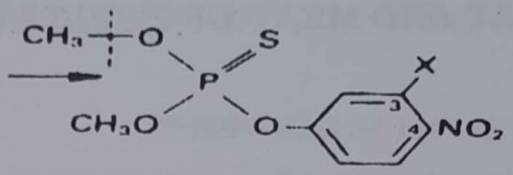
Histopathologically, in fenitrothion treated chicks, there were generalized hyperemia, congestion and degenerative changes in all parenchymatus organs, meanwhile in carbofuran treated chicks, there were congestion, multiple heamorrhages and necrotic changes in parenchymatus organs.

The present report revealed effects of fenitrothion and carbofuran on biochemical and pathological aspects of broiler chicks. Its recommended those birds slaughter at least 10-15 days after fenitrothion and carbofuran contamination.

CARBOFURAN



2,3 dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate



(c) Fenitrothion (X = CH_3)

Nowadays the "Pesticides problem" has been the focus of public interest. The application of pesticides is still the most effective and accepted means for the protection of plants from the pests and to the increase in agricultural productivity. On the other hand, they are dangerous for the environment, nature and for the animals and human beings. The wide spread use of pesticides is usually connected with serious problems of pollution and health hazards.

In Egypt, Fenitrothion (O, P-dimethyl, o- (3-methyl - 4 nitrophenyl) phosphorothionate) (Sumithion) and Carbofuran (2,3 - dihydro-2, 2-dimethyl- 7 - benzofuranyl - N- methylcarbamate). (Furadan) are commonly used in agriculture and forestry as a broad-spectrum insecticides, nematicide, acaricide and pesticide. Zeman, (1987)[50] and Gupta et al., (1994)a[15].

Fenitrothion is an Organo-phosphorus compound. It is an effective agent on a wide range of pests and household insects. Sumithion is considered to be one of the main sources of contamination in grains used in livestock feeds. (Barneveld et al., 1999)[51]. Moreover, Veen et al., (1999)[52] recorded that fenitrothion intoxication is responsible for 16.4% moralities in broiler chicks. Nag and Ghosh, (1985)[32] observed that in pigeons treated with Sumithion at a daily dose of one-tenth of the LD_{50} ,the total protein decreased 40.8% and the cholesterol myelin spinal cord increased 30% which not observed in rat.

Owing to the wide spread use of carbofuran in agriculture purposes, Gupta, (1994)[14] stated that the carbofuran is considered as the main contamination source to water, food and air in when using it in agriculture purposes. Yunigshi et al., (1985)[49] reported that (51%) of deaths in duck herds occurred due to rearing on recently carbofuran sprayed-rice field. Schuh and Blakley, (1988)[43], Ferguson et al, (1997)[10] and Smith and Lewis (1988)[54] reported carbofuran poisoning in cattle and in birds, respectively.

Segal and Fedoroff, (1989)[44] demonstrated that, there were an antagonistic interaction in between

mixtures of fenitrothion and carbofuran. There was a lake of document information about the effect of both insecticides on lipid, carbohydrate and protein parameters in chicks. The improper use of both fenitrothion and carbofuran result in a contamination of the environment and consequently in deleterious health effects to animals and birds.

The aim of the present work is to identify and compare both the biochemical and pathological changes in chicks treated with the two-insecticide fenitrothion and carbofuran.

MATERIALS AND METHODS

1. **Materials:** Fenitrothion (Sumithion) (50%) (weight/volume) (concentrate solution can be emulsified in water) (1 liter), (Soumittomo chemicals Co., ltd., Ozaka, Japan) and carbofuran (Furadan) (10%) (weight/weight) (10% granules) (1kg) (FMC corporation, agriculture production group, Philadelphia, PA19103, USA).
2. **Chicks:** Two hundred and fifty (250) white leghorn chicks were housed in free laboratory yard under strict hygienic conditions in the Animal health research institute, Dokki. Reared on balanced ration and fresh water ad libitum.
3. **Expermintal design:** The chicks were divided into three groups.

Group one: Fenitrothion group (Sumithion): consists of 100 chicks received an oral administration of 10 mg/Kg body weight daily (1/20 of LD_{50}) (5 days/week) for 30days.

Group two: Carbofuran group (Furadan): consists of 100 chicks and received an oral administration 315 µg mg/Kg body weight daily (1/20 of LD_{50}) (5 days/week) fro 30 days.

Group three: Control gorup: 50 chicks were kept untreated.

4- **Biochemical studies:** At 7, 15 and 30 days, 15 chicks from gorup 1,2 and 10 chicks from gorup 3 were slaughtered and blood samples were let to clot. A clear, non-hemolyised specimen was centrifuged for 10 minutes at 3500 r.p.p. and stored in -20°C for further biochemical analysis. In addition, samples from liver and breast muscle were stored at -20°C for biochemical analysis.

The following biochemical analysis were estimated in:

1.Serum: the following parameter as: Cholinesterase, Ellman et al, (1961)[6]; ALT and AST, Reitman & Frankel, (1957)[42]; Total Lipid, Chabrol & Charonnat, (1984)[54]; Total cholesterol, Trinder, (1969)[48] ; HDL, Fruchart, (1982)[53]; LDL, Steinberg, (1981)[46]; triacylglycerol, Eggstein & Kreutz, (1966)[5] ; glucose, Trinder, (1969)[48] and total protein, Peter et al., (1982)[16].

2. **Liver and muscle:** the following parameters were estimated: Total lipid, Girard et al,

(1970)[12] ,total protein, Henery, (1964)[20] and glycogen, Handel, (1965)[18].

7, 15 and 30 days after cessation of fenitrothion and carbofuran administration (post-treatment), 5 chicks from all groups were slaughtered and residues measure for both fenitrothion (dimethyl fenitrothion) and carbofuran (3-hydroxy-carbofuran, a significant metabolites of carbofuran) were estimated in liver, breast muscle by method descried by Ali et al., (1993)[1], Faragea et al., (1988)[8] and Kumar et al., (1993)[29], respectively.

5. **Histopathological studies:** The representative specimens from the liver, lung, heart, kidney, spleen, brain, bursa and thymus glands were selected from the sacrificed chick at 30 days post treatment. The specimens were immersed in 10% neutral buffered formalin solution, routinely processed, embedded in paraffin wax, sectioned at 3 microns and stained with Hematoxylin and eosin.(Bancroft et al, 1994)[2]
6. **Statistical analysis:** The statistical analysis of the results was preformed using T-test, ANOVA test (two way Analysis of variance). (Farver, 1989)[9].

RESULTS

1. The biochemical studies:

The biochemical analysis was measured and tabulated in table 1, 2 and 3. The initial observation was the significant decrease in body weight, food and water intakes over the period of the experiment in the two pesticide treated groups compare with to the control group which reached 10% and 30% in Sumithion and carbofuran respectively. This agree with the observation of Pande et al., (1995)[35] and in contrast to the observation of Kanoh et al., (1982)[26] and FAO -WHO, (1997)[7] on long term Sumithion and carbofuran administration, respectively. The difference may be originated from the difference in the animal species used. The second observation was the absence of any commutative action to either insecticide, or significant difference (within insecticide group itself) which was observed between groups.

Table 1: Biochemical changes in serum of Fenitrothion, Carbofuran administered chicks and control once.

	Day	Carb. ad. Chicks	Feni. ad. Chicks	Control chicks
Serum Choline-esterase (IU/L)	7	840.45±58.83***	900.96±27.03 ***	1200±63
	15	815.54±20.38 ***	757.25±26.50 ***	1165±95.25
	30	835.25±39.08 ***	796.47±29.38***	1285±52.46
ALT (U/L)	7	68.57±2.06 ***	73.62±2.21 ***	50.48 ± 2.52
	15	63.36±1.90 ***	76.64±2.03 ***	52.80 ±2.64
	30	67.64±2.03 ***	72.61±5.27 ***	49.70 ±2.49
AST(U/L)	7	132.95±3.98 ***	168.22±5.05 ***	120.87± 3.63
	15	170.49±5.12 ***	230.63±8.23 ***	150.45± 7.52
	30	185.13±4.62 ***	235.62±7.42 ***	158.30± 5.05
Cholesterol (total) (mg/dL)	7	93.18±3.72 ***	120.34±3.01***	150.43±8.12
	15	91.98±4.67 ***	131.45±3.68 ***	164.25±9.86
	30	96.89±4.85***	141.24±8.19***	190.87±6.03
Total lipid (mg/dL)	7	246.45±1.76**	334.67±1.43***	265.90±1.85
	15	202.26±2.26**	240.73±1.95***	282.82±2.43
	30	119.74±2.38***	261.59±2.52***	323.78±2.91
HDL (mg/dL)	7	45.58±1.59***	49.58±1.72*	51.08±1.78
	15	46.35±1.61***	47.89±1.67**	50.87±1.77
	30	45.89±1.60 ***	47.89±1.67 ***	55.47±1.93
LDL (mg/dL)	7	9.47±0.43*	12.88±0.58*	10.88±0.49
	15	8.54±0.38*	13.87±0.63**	11.05±1.49
	30	9.87±0.57**	12.58±0.72*	12.58±0.73
Triacylglcerol (mg/dL)	7	8.38±0.42***	9.03±0.45***	6.45±0.32
	15	10.73±0.54***	9.68±0.49***	7.23±0.62
	30	10.12±0.50***	9.85±0.54***	6.89±0.34
Total protein (gm/dL)	7	4.52±0.17***	4.85±0.18***	5.64±0.23
	15	4.69±0.18***	4.98±0.19***	6.87±0.28
	30	4.70±0.19***	4.98±0.18***	6.45±0.24
Glucose (mg/dL)	7	117.51±8.93***	198.24±15.06***	167.88±12.75
	15	112.32±8.53***	192.54±4.63***	160.47±12.19
	30	116.59±6.86***	183.23±8.54***	166.57±9.93

*, **, *** Significant difference at 0.5, 0.1 and 0.01 level of probability.
Fenitrothion administered chicks: Feni. ad. Chicks.
Carbofuran administered chicks: Carb. ad. Chicks.

There was 20% -30%, 10%-40% increase in ALT AST level in fenitrothion and carbofuran ad. Chicks respectively; 30% -40%, decrease in cholinesterase level in fenitrothion and carbofuran ad. Chicks respectively. There was decrease in serum cholesterol, total lipid, HDL, LDL and total protein levels. There was significant increase triaglycerol level. While fenitrothion decreases serum glucose level, carbofuran has adverse effect, increases serum glucose level.

Table 2: Biochemical changes in organs of Fenitrothion, Carbofuran treated chicks and control chicks

Organ	Day	Feni. ad. Chicks	Carb. Ad. Chicks	Control chicks
LiverTotal Lipid (gm/100 gm tissue)	7	5.65±0.27***	6.09±0.29***	4.35±0.65
	15	5.32±0.78***	5.81±0.28***	4.15±0.28
	30	5.44±0.26***	6.54±0.89***	3.89±0.19
Total protein (gm/100 gm tissue)	7	1.12±0.38***	1.22±0.42***	1.88±0.06
	15	1.66±0.06***	1.81±0.06***	2.78±0.09
	30	1.73±0.04***	1.87±0.04***	2.88±0.08
Glycogen (gm/ 100 tissue)	7	2.69±0.15**	4.35±0.24**	3.78±0.21
	15	2.88±0.16***	3.98±0.22*	3.45±0.19
	30	2.89±0.18**	4.02±0.29**	3.65±0.25
MuscleTotal Lipid (gm/100 gm tissue)	7	2.64±0.77***	4.15±0.39***	3.35±0.75
	15	2.73±0.58**	4.88±0.78***	3.15±0.88
	30	2.22±0.28**	5.54±0.88***	2.89±0.79
Total protein (gm/100 gm tissue)	7	2.12±0.48***	2.32±0.42***	4.48±0.16
	15	2.66±0.16***	2.71±0.06***	4.58±0.19
	30	2.73±0.14***	2.97±0.04***	4.88±0.18
Glycogen (gm/ 100 gm tissue)	7	3.32±0.15***	2.35±0.24***	5.78±0.21
	15	3.28±0.16***	1.98±0.22***	4.45±0.19
	30	3.29±0.18***	2.02±0.29***	5.65±0.25

*, **, *** Significant difference at 0.5, 0.1 and 0.01 level of probability.
Fenitrothion administered chicks: Feni. ad. Chicks.
Carbofuran administered chicks: Carb. ad. Chicks.

There was increased total lipid and decrease in total protein in liver of both fenitrothion and carbofuran administered chicks. Moreover, fenitrothion decreased liver glycogen content while carbofuran increased liver glycogen content. There was decreased total lipid in fenitrothion ad. Chicks and increase in muscular total lipid in carbofuran ad. Chicks. Both fenitrothion and carbofuran decreased total protein content in muscle of both treated groups. The decreased muscle glycogen content was more pronounced in carbofuran ad chicks than fenitrothion ad.chicks.

Table 3: Residues of Fenitrothion, Carbofuran in organs of treated chick.

Organ	Day	Feni. ad. Chicks	Carb. Ad. Chicks
Liver	7	3±0.06 ppb	5± 0.13 ppm
	15	1±0.003 ppb	2±0.02 ppm
	30	N.D.	N.D.
Muscle	7	1±0.03 ppb	2±0.07 ppb
	15	ND	1.5±0.04 ppb
	30	ND	N.D.

N.D. non-detected residue. The residue of both fenitrothion and carbofuran was mainly in liver followed by muscle. The residue is not detected in 30 days.

Pathological findings:

Fenitrothion:

1.1. Macroscopic findings: The liver was enlarged, congested with the presence of minute petechial haemorrhages on its surface, congestion of the lung, pericardium, kidneys, meningeal blood vessels and mild congestion of the thymus lobes.

Microscopic finding:

Liver: revealed congestion of the hepatic blood vessels and small areas of haemorrhages in between hepatic cords. There were activation of the Kupffer cells and granular degenerative changes of the hepatocytes with few individual cell necrosis. Moreover, necrosis of the epithelial lining of the intrahepatic bile ductuoles was also observed.

Lung: revealed congestion, multiple small scattered areas of haemorrhages in the pulmonary interstitial tissue and emphysema of the air alveoli. Sometimes thickening of the interalveolar walls was also detected.

Heart: Small haemorrhages were detected in between cardiac muscles. Degeneration and necrosis in some of the cardiac muscles, which manifested by loss of striations, swollen dark eosinophilic sarcoplasm and karyolysis of the nuclei meanwhile other cardiac muscles revealed marked fragmentation of the myofibrils. (Fig 1) Intermuscular and perivascular oedema was also seen in between degenerative muscles and admixed with mononuclear cell infiltrate.

Kidney: There were congestion of renal blood vessels. Various degenerative and necrotic changes of the tubular epithelium or even may be destructed and sheded into the lumina. Epithelial castes were detected inside the lumen of some renal tubules and cystic dilatation of the others was also observed.

Spleen: revealed mild depletion of lymphoid cells in the white pulp. (Fig 2).

Brain: showed congestion of the meningeal blood vessels and marked pericellular and perivascular oedema. Multi-focal malacic areas were detected in the cerebellar cortex. Diffuse proliferation of the microglia cells in both cerebrum and cerebellum (diffuse gliosis) was also detected (Fig 3) and congestion of the choroid pleuxsus.

Thymus gland: revealed dilatation of the blood vessels with the presence of intra-vascular thrombi.

Carbofuran:

2.1. Macroscopice findings: the liver was enlarged and congested with the presence of minute sub-capsular petechial haemorrhages on its surface. The lung revealed congestion with presence of multiple irregular areas of haemorrhages on its pleural surface. The Kidney was congested with the presence of minute haemorrhages on cut section. Congestion of the meningeal and thymic blood vessels were also observed.

Microscopic finding:

Liver: there were distortion and disorganization of hepatic cords with individulization of the hepatic cells. The hepatocytes revealed necrotic changes emphasized microscopically by granular, and vacuolar degenerative change meanwhile focal areas of coagulation necrosis were also detected. (Fig 4) some hepatic blood vessels showed recent thrombi represented by fibrin network infiltrated with leukocytes. Few mononuclear cells were dispersed in the fibrous tissue of the portal traids.

Lung: revealed congestion of the pulmonary blood vessels and multiple extensive areas of haemorrhages in the pulmonary interstitial tissue and in the lumina of some air alveoli. (Fig 5) The wall of some air alveoli appeared to be thickened and mononuclear inflammatory cells were dispersed in the pulmonary tissue. Emphysema of the air alveoli and oedema around some of the pulmonary blood vessels were observed meanwhile some pulmonary blood vessels revealed presence of recent thrombi.

Heart: revealed haemorrhages, inter-muscular and perivascular oedema. Some of cardiac muscles exhibited degenerative and necrotic changes. (Fig 6).

Kidney: There were congestion of the renal blood vessels and haemorrhage in the renal interstitial tissue. Necrotic changes of the tubular epithelium which emphasized by granular, vacuolar degeneration and necrosis of the tubular epithelium or even may be distructed and sloughed into the lumina. Erythrocytic renal casts were detected in the lumen of some renal tubules (Fig 7) and eosinophilic hyaline renal castes and/or epithelial casts in the others (Fig 8).

Spleen: showed hyperplasia of lymphoid cells in the white pulp of the spleen.

Brain: showed sever pericellular and perivascular oedema (Fig 9). Necrosis of the neurons which emphasized by chromatolysis, karyolysis of the nuclei and presence of focal (Fig 10) and diffuse malacic areas in the cerebeller cortex.

Thymus gland: congestion of the thymic blood vessles.

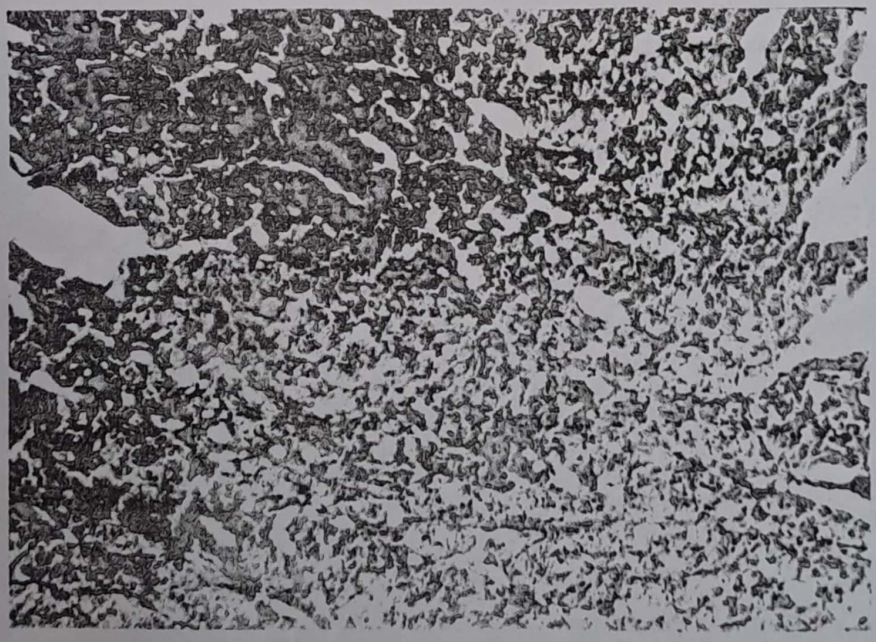


Fig 1: Heart of chicken 30 days post treatment with fenitrothion insecticide revealed marked degeneration and fragmentation of the cardiac muscles. (H & E X 160).

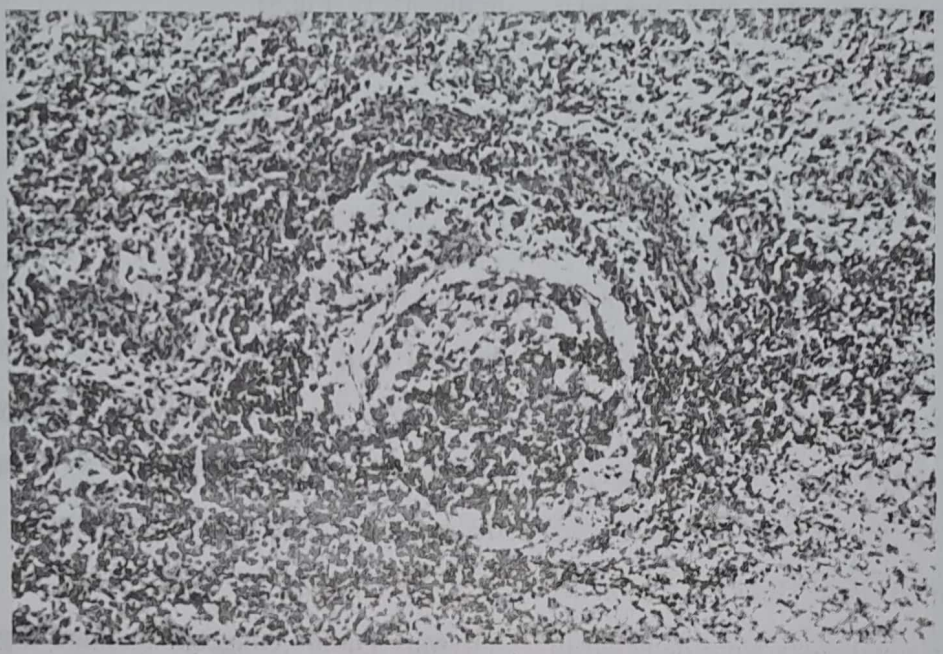


Fig 2: spleen of a chicken 30 days post treatment with fenitrothion insecticide revealed mild depletion of lymphoid cells in the white pulp. (H & E X 160).

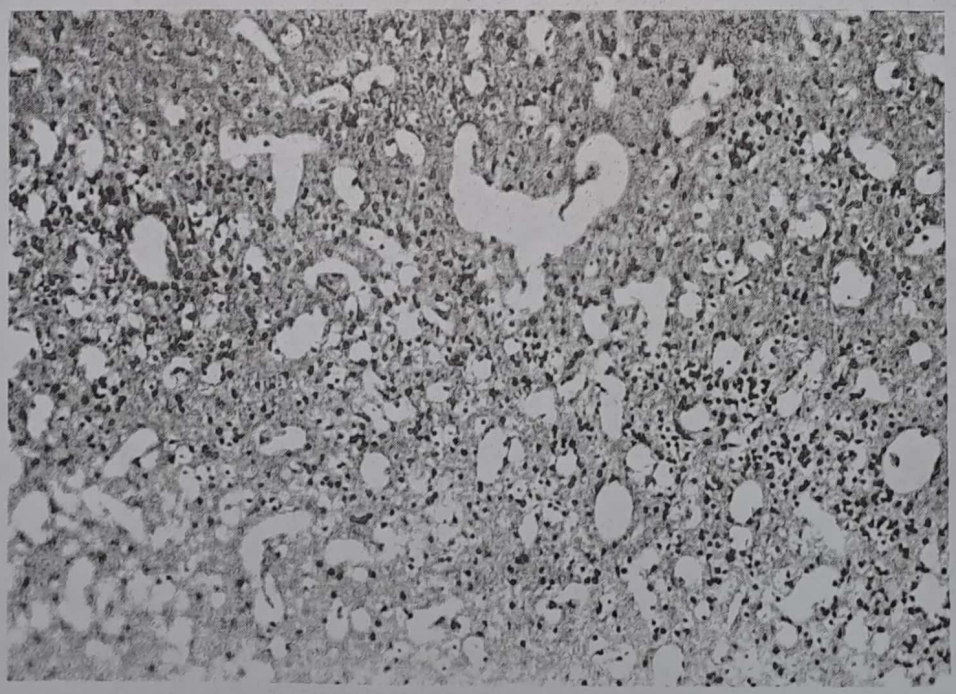


Fig 3: brain of a chicken 30 days post treatment with fenitrothion pesticide illustrating diffuse gliosis. (H & E X 160).

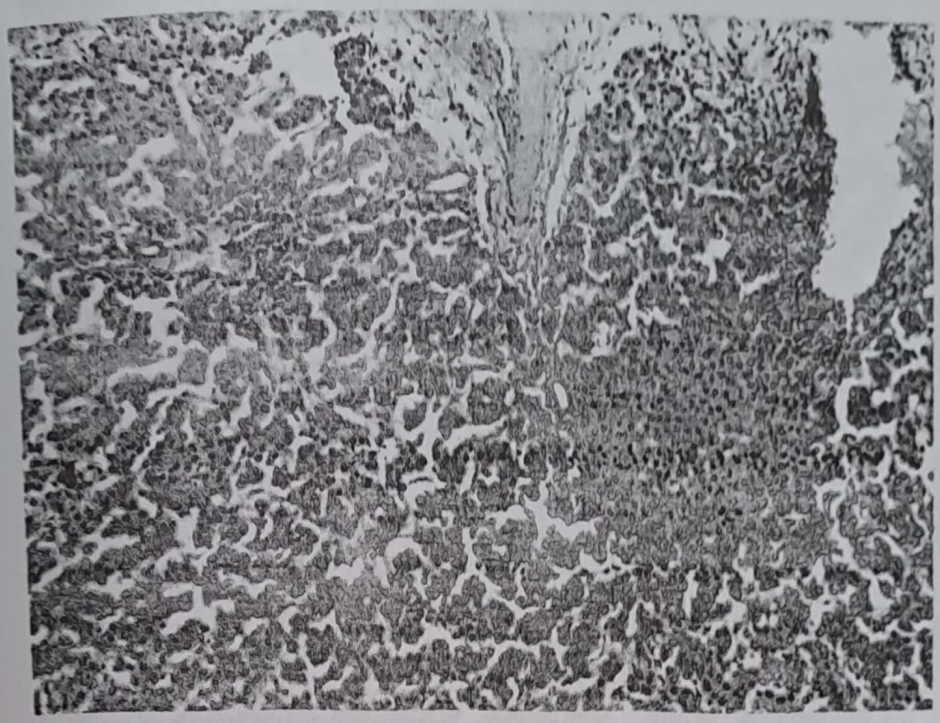


Fig 4: Liver of a chicken 30 days post treatment with carbofuran insecticide illustrating focal coagulation necrosis. (H & E X 160).

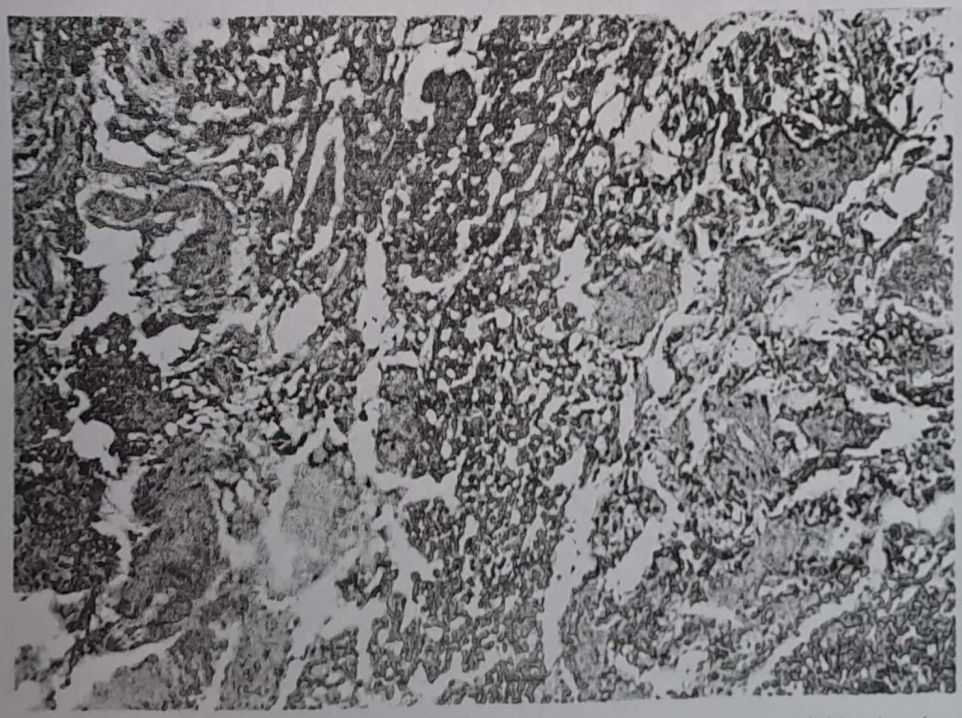


Fig 5: lung of a chicken 30 days post treatment with carbofuran insecticide showing hemorrhages in the alveolar spaces. (H & E X 160).

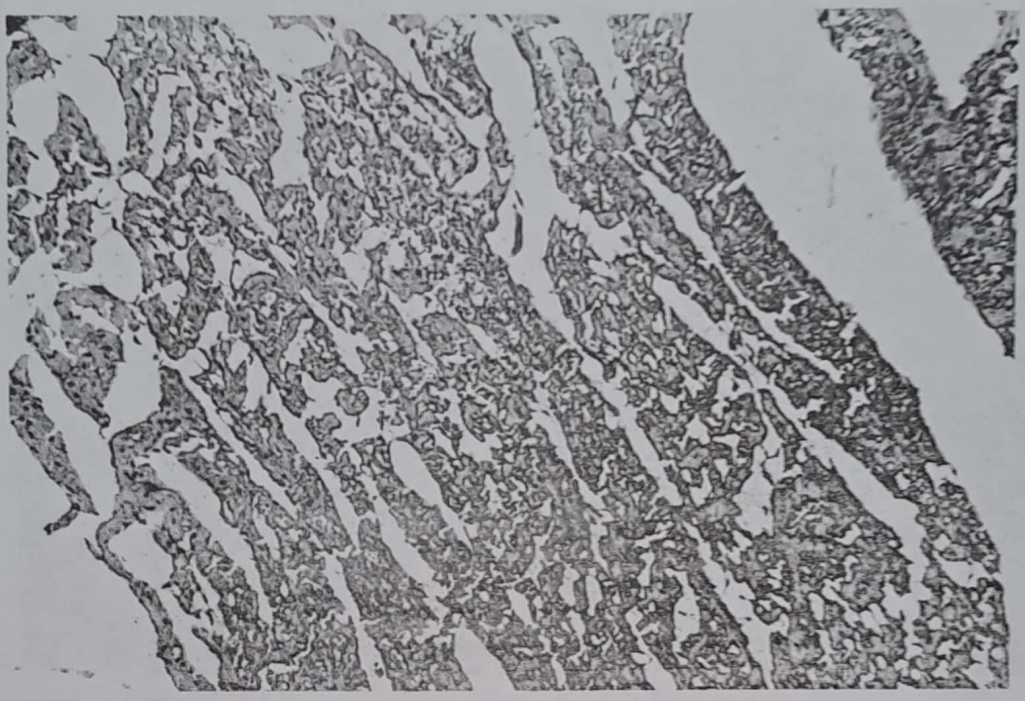


Fig 6: heart of a chicken 30 days post treatment with carbofuran insecticide illustrating necrosis of the cardiac muscles. (H & E X 160).

Fig 7: Kidney of a chicken 30 days post treatment with carbofuran insecticide revealed necrobiotic changes of the tubular epithelium and erythrocytic renal castes in the others. (H & E X 160).

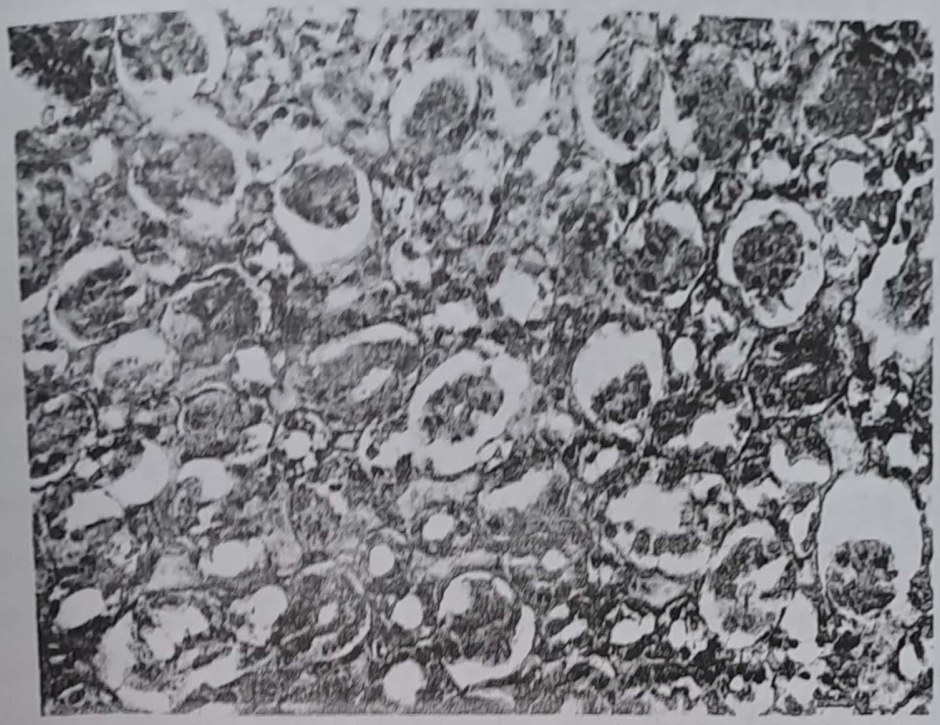


Fig 8: Kidney of a chicken 30 days post treatment with carbofuran insecticide showing congestion of intertubular blood vessel and epithelial casts in the lumen of renal tubules. (H & E X 160).

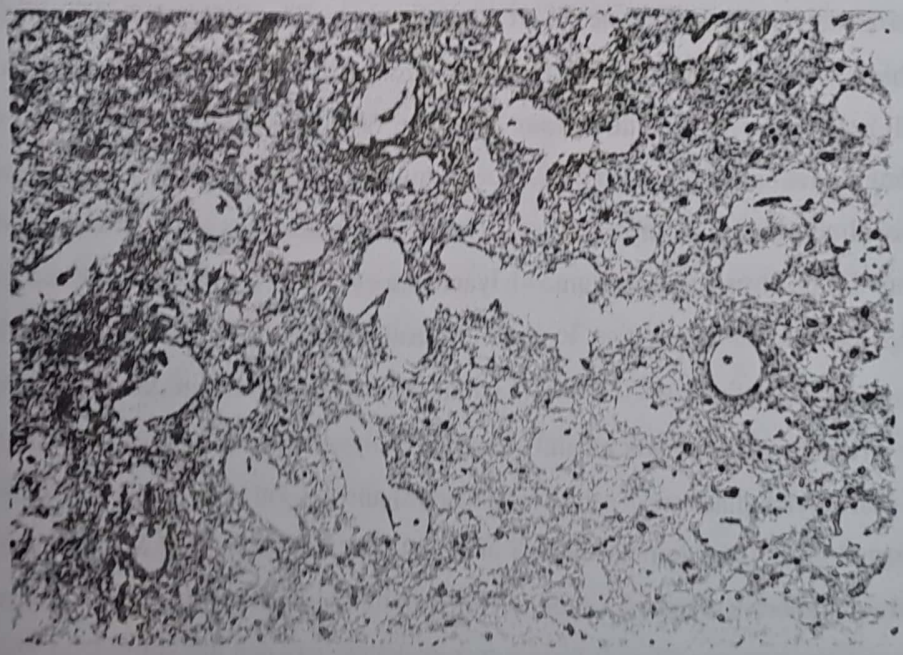


Fig 9: Brain of a chicken 30 days post treatment with carbofuran insecticide showing severe pericellular and preivascular oedema. (H & E X 160).

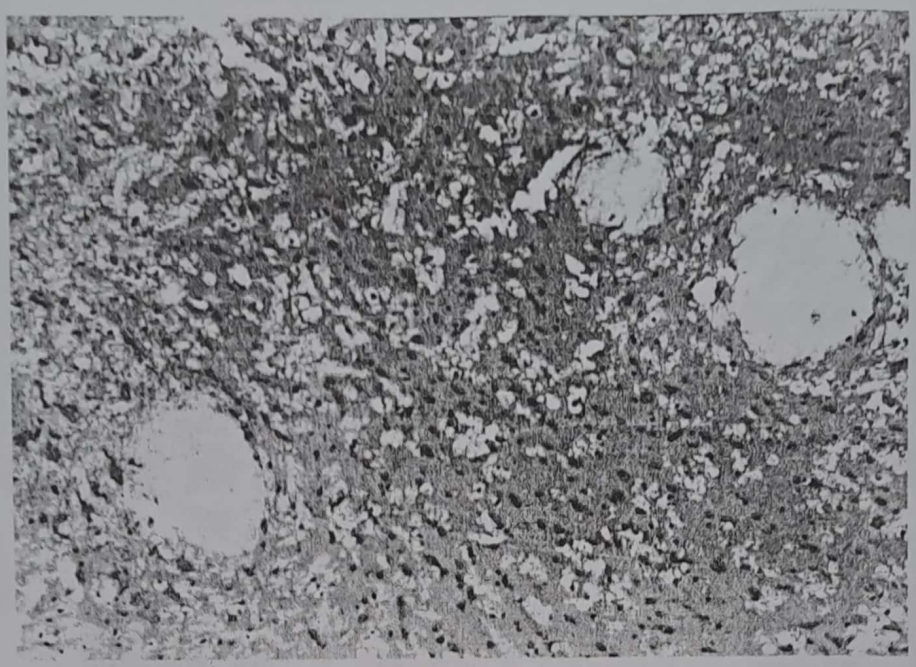


Fig 10: brain of a chicken 30 days post treatment with carbofuran insecticide showing focal areas of encephala malacia. (H & E X 160).

DISCUSSION

Although serum cholinesterase was inhibited in both fenitrothion and carbofuran treated chicks, (there was 30% -40%, decrease in cholinesterase level in fenitrothion and carbofuran treated chicks, respectively). It is not like erythrocyte cholinesterase in determination in long stand poisoning but serum cholinesterase -activity is also depressed during abnormal liver function Rama and Jaga, (1991)[38].

In contrary to the present result, Kanoh et al., (1982)[26] observed that actylcholinesterase activity recovered in normal level unit after the first month till the end of experiment (year), after chronic Sumithion administration. The difference may be originated from the difference of dose and animal used. It indicated also the sensitivity of chickens to fenitrothion administration. Fenitrothion are oxidized by mono-oxygenases in animals and thereby changed to derivatives containing the P=O groups which are more powerful inhibitor of cholinesterase than was the original thionphosphate. The P-O- phenyl linkage is ruptured through hydrolytic process and fenitrothion by action of glutathione-S-alkayltransferase into demethyl fenitrothion and fenitrooxon. Hassal, (1990)[19]. Carbofuran is also, anti-cholinesterase. Iyaniwura, (1991)[22] observed that carbofuran was greatly inhabited the serum and erythrocytes cholinesterase. Carbofuran shares other carbamate family as anti-cholinestrase activity in chicks, studies of Faragea et al., (1988)[8] by both aldicarb and Carbaryl and Moregaonkar et al (1993)[30] by butocarboxim. There was no difference in action between the sumithion and carbofuran on serum cholinesterase activity but the pronounced inhibitory effect to carbofuran.

There was 20%-30%, 10%-40% increase in ALT, AST level in fenitrothion and carbofuran ad Chicks respectively. The effect of fenitrothion and carbofuran was also reported by Kiran et al., (1989)[28], Kadyrova et al (1990)[25] and Mostafa et al., (1992)[31] . It can be attributed to: 1. Intoxication processes and formation of demethylfenitrothion and 3-hydroxycarfuran and 3-ketocarfuran which are more toxic to the liver cells. 2. The domestic fowel is able to maintain the blood glucose concentration during starvation. On the other hand, although alanine and aspartate, is poorly used as gluconeogenic precurser for glucose production, Freeman, (1983)[11]. The intracellular distribution and activity of alanine aminotranssferase indicated the selective stimulatory effect of carbofuran on ALT and AST activity. This explained observation that carbofuran has pronounced effects on transaminases than fenitrothion.

There was decrease in serum cholesterol, total lipid, HDL, LDL. There was significant increase in triacylglycerol level in both fenitrothion and carbofuran treated chicks. The present results were different from those reported by Gupta et al, (1986)[13] who observed that, in both liver and serum but not brain, furadan (0.125,0.25 and 0.50 mg/kg) elevated significantly total lipid, cholesterol, triacylglycerol, in treated mice. Also, Gupta et al., (1994)a[15] who reported that rats intoxicated with carbofuran (1.5mg/Kg sc) produced significant increase in triacylglycrol and cholesterol in liver and serum. Meanwhile, the present result share Gupta et al., (1994)b[17] that in both liver and serum, the levels of low-density lipoprotein cholesterol were reduced.

The explanations of this difference arise from that 1. Despite the facts that blood glucose concentration is greater in birds and the liver glycogen content is lower in chicken. Gluconeogenesis from lactate and glycerol were better utilized, Freeman, (1983)[11] for glucose production than other precursors (alanine, aspartate..etc) . Also, β-hydroxyputarate stimulate the conversion of lactate to glucose. Lipolysis gives rise a mixture of free fatty acids, 2- monoglycrides and glycerol with 1, 2-diglycrides as intermediate products reflecting formation of triacylglycrol. Also, it may be the reason why increase of serum triacylglycerol? It may be due to that the hydrolysis of triacylglycerol in lipoproteins is an essential steps in the transfer of triacylglycerol fatty acids to extrahepatic tissues. Besides, Jurez, (1995)[24] observed that fenitrothion inhibit the incorporation of {1-14C} propionate and {1-14C} acetate as a precursor of methyl-branched hydrocarbons (lipid biosynthesis). It also altered both body fat and cystolic fatty acid synthesis

There was decrease in serum total protein levels in both fenitrothion and carbofuran treated chicks which was unexpected. While Kadyrova et al (1990)[25] observed that total protein contents in blood serum increased by 3rd day the of

administration of Deltamethrin, Pande et al, (1995)[35] observed no significant change in serum protein levels after the administration of Oncol (benfuracarb) (20 and 40 mg/Kg, carbamate insecticides to white leg horn chickens (9 month old). Khurana et al., (1997)[27] observed a significant decrease in total serum protein in carbofuran treated lambs. The changes in serum protein level may be due to 1. Inhibition of protein synthesis in the liver Ramaswamy, (1987)[39] 2. Increase of protein degradation, Moregaonkar et al (1993)[30] observed increased serum urea nitrogen level in butocarboxim, a new carbamate insecticides in day-old to 75 day old chicks. 3. Increase protein synthesis for intoxicated proteins on account the secretary proteins (albumin, globulin).

While fenitrothion decreases serum glucose level, carbofuran has adverse effect, increases serum glucose level. Although, Pande et al, (1995)[35] observed no significant change in blood glucose when administration of Oncol (benfuracarb) (20 and 40 mg/Kg, carbamate insecticides to white leg horn chickens (9 month old). Rahman et al., (1990)[37] observed an increase in glucose at aldicarb (75, 112.5 and 150 mg / Kg daily for 21 days in male and female chicks (white leg horns).

The present work declared that carbofuran has pronounced action on carbohydrate metabolism more than fenitrothion. In parallel with our observation, Gupta, et al., (1994)b[17] mentioned that in liver, carbofuran caused marked depletion of ATP and phosphocreatine (38%-22% of controls, respectively) resulting in increased cell membrane permeability, thereby allowing leakage of cell constituent.

There was increased total lipid and decrease in total protein in liver of both fenitrothion and carbofuran administered chicks. First, these changes associated with the changes arise from the necrotic effect of the toxic agent. Palanichamy et al., (1989)[34] mentioned that compared with controls, protein content of muscle, liver, gill and intestine least gain with carabyl (1.4 p. p .m.) intermediate with malathion (3.0 p.p.m.). Singh and Sharma, (1998)[53] observed that carbofuran (an organocarbamate pesticide) showed a drastic decrease effect in the protein content in different body organs of teleost fish, *Clarias Barachus*. second, change in the liver lipid and protein metabolism. Barneveld et al., (1994)[51] suggested that cytochrome P-450 2E1 is enzyme responsible for 3-hydroxy carbofuran formation this enzyme was found in much greater in the liver than other tissues. These carbofuran metabolites are more powerful protein inhibitor factor.

Moreover, fenitrothion decreased liver glycogen content while carbofuran increased liver glycogen content. Besides the low glycogen content of liver in chicks compared to other animals. Gupta et al., (1991)[16] observed characteristic changes in LDH and it's isoenzymes, indicating organ-specific tissue damage of the rat tissues. Segal and Fedoroff

989)[44] observed increased activity of LDH (terinal glycolytic enzymes). Reddy and Bhagyalaushmi (1995)[41] reported that Sumithion was ound to inhibit the activity levels of NADependant dehydrogenases and NADP-dependant hydrogenases in the hepato-pancreas and muscle. The final step lead to pyruvate is converted to actate. Freeman, (1983)[11] reported that the availbility of reduced NAD is a limiting factor in the tilization of pyruvate in chicks liver. Nivedhitha t al (1998)[33] observed adaptive utilization of tored liver glycogen and adaptive accumulation of liver glycogen in muscle and heart tissues probably by glyconeogenesis to meet the stress to sub-lethal exposure in the fresh water edible fish (Orechromis mossambicus) exposed to Ziram (Carbamate fungicide).

There was decreased total lipid in fenitrothion group and increased total lipid in carbofuran group in muscle. Both fenitrothion and carbofuran decreased total protein content in muscle. The carbofuran decreased muscle glycogen content more pronounced than fenitrothion on muscular glycogen content. Our data was agree with, Reddy & Rao (1991)[40] who observed a decrease in glycogen and pyruvic acid with increase in lactic acid levels in muscle tissues of penaeid prawn (*Metapenaeus Monoceros*). This were indicative of reduced mobilization of pyruvate into citric acid cycle resulting enhanced glycolysis and shift of metabolic emphasis from aerobiosis to anaerobiosis. Gupta et al., (1994)a[15] observed that carbofuran as an anticholineesterase insecticides induced increased muscle activity produces characteristic changes in CK/LDH isoenzymes pattern with leakage of these enzymes into serum due to depletion of ATP and PCr which are required to maintain the cell membrane permeability. The change in liver and muscle protein indicated the selective effect of fenitrothion and carbofuran on this parameter.

The residue of both fenitrothion and carbofuran mainly accumulated in liver followed by muscle. The residue is not detected in 30 days. The carbofuran residues restricted mainly in liver. It may be due to first, Carbofuran was converted by deamination to a new metabolite in the serum, liver, kidney and brain 6-h after administration of insecticides. Second, extensive and rapid metabolism of carbofuran, to (3-hydroxycarbofuran and 3-ketocarboufuran) levels not expect to persist in tissue or fluid for prolonged periods after exposure. (Huang et al, 1989)[21]. Mostafa et al (1992)[31] observed that faba-bean residues of carbofuran were fed to rats 46% was eliminated via CO2 and urine, while tissue contained 25%. Yunigshi et al., (1985)[49] measured the carbofuran residues in dead duck liver ranged from 1.5 to 5.5 ppm. There seem to be minimal or no health risks to bird meat consumer, since the birds exposed to fenitrothion and carbofuran largely excreted it and its metabolites in the urine, thereby leaving very little residue in the tissues.

Concerning the gross and histopathological changes detected in chickes treated with fenitrothion and those treated with carbofuran insecticides, It was found that in fenitrothion treated chicks revealed marked generalized hyperemia and congestion as those mentioned by Carlton and McGavin, (1995)[3]. Since fenitrothion is one of the Organo-phosphorus compounds, it was activated to fenitro-oxon by biotransformation and a liposoluble compound diffuse readily into tissue and organs (muscle, brain and lung) Veen et al, (1999)[52]. On the other side, Thompson et al., (1995)[47] pointed out that the production of active oxon from pesticide within the brain and the sensitivity of brain acetylcholine to inhibition are the most important factors determining the avian toxicity. Durham and Ecobichon, (1986)[4] showed that toxic effect of fenitrothion elicit delayed neurotoxicity in chicks., where it interact with a specific enzyme (Ca ++ / calmodulin kinase 2) responsible for phosphorylation of cytoskeleton proteins which result in disassembly of those proteins that accumulate in the distal portion of the axons accompanied by swelling and degenerative changes which extended from the periphery towered the cell body. (Carlton & McGavin, 1995)[3].

Carbofuran is an anticholine esterase carbamate, which is enormously used in agriculture. Therefore, it may result in accidental poisoning due contamination of feed with carbofuran or its metabolites. The changes detected in the liver, kidney, heart and brain were accounted by Gupta, (1994)[21] to the fact that these organs underwent characteristic changes in LDH (Lactate dehydrogenase) isoenzymes patterns indicating tissue specific damage. Also, he pointed out that the leakage of creatine phosphokinase and lactic dehydrogenase enzymes and their isoenzymes from tissue into serum is due to depletion of adenosine triphosphate (ATP) and phosphocreatine enzymes (PCr) which are required to retain intracellular constituents by maintaining cell membrane permeability and integrity.

The severe pericellular and perivascular oedema encountered in the brain of hens treated with fenitrothion and those treated with carbofuran pesticide was considered by Jones et al., (1997)[23] as a sign of intoxication condition. On the other hand, Gupta et al, (1991)[16] speculated that the disorders of lipid levels in carbofuran treated chicks particularly in brain may be associated with central nervous system depressant action and structural and functional toxicity of other tissues.

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