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POOR ANTEDOTAL EFFECTS OF COPPER AND MANGANESE ON RATS EXPOSSED TO ACUTE DOSE OF DICHLORVOS

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ABSTRACT

Aim: This study examined the antidotal effect of copper and manganese as an alternative to atropine sulphate in dichlorvos toxicity.

Background: Acute pesticide poisoning is a major public health concern today in developing countries. Studies have shown the importance of antioxidants in health and disease that they could help prevent a host of chronic and degenerative disorders that might occur due to adverse effects of chemicals and other toxic agents in the system. Hence the need to assess the antidotal effects of some metals. **Methods**: Lethal and sublethal doses of dichlorvos was determined in a pilot study to be 18.5mg/kg and 14.5mg/kg respectively. Twenty rats divided into five groups of four albino rats per group were used for the study. Group 1 was given 14.8mg/kg of dichlorvos alone. Group 2 was given 1 ml of atropine sulphate (1.5mg/kg) after injection of dichlorvos (14.8mg/kg). Group 3 was given 1 ml of copper (0.025mg/kg) after the injection of dichlorvos (14.8mg/kg). Group 4 was given 1ml of manganese (0.01mg/kg) after the injection of dichlorvos (14.8mg/kg). Group 5 was given 1ml of manganese (0.025mg/kg) and 1 ml of copper (0.01mg/kg) after the injection of dichlorvos (14.8mg/kg). The symptoms of acute dichlorvos poisoning observed in the rats were straub tail, muscle fasciculation, piloerection, lacrimation, defecation, excessive salivation, whole body tremor, micturition, restlessness, pupil constriction, respiratory distress, gasping, convulsion and death. **Results**: The haematological result in acute toxicity

study showed a statistically significant decrease ($p<0.05$) in the mean values of the circulating red blood cells (RBC), white blood cells (WBC), haemoglobin (HB), packed cell volume (PCV), and platelet that was dose dependent. Also obtained was a significant dose dependent increase ($p<0.05$) in the biochemical parameters; aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), urea and creatinine in the copper, manganese and copper and manganese combined treated rats when compared with the atropine treated and control rats ($p<0.05$). There was however a significant decrease ($p<0.05$) in the mean value of serum cholinesterase in all treated groups. These effects were observed to gradually and significantly increase ($P<0.05$) in the copper, manganese, copper and manganese treated groups and least in atropine treated and control groups. **Conclusion**: The use of trace elements copper, manganese, and copper and manganese when compared with atropine were not able to reduce the impact of dichlorvos-induced toxicity in the rats.

KEYWORDS: Dichlorvos toxicity, respiratory distress, gasping, convulsion and death.

INTRODUCTION

Pesticides are chemicals developed to help provide man a clean and healthy environment by getting rid of insects and pest that could cause harm to farm products, man and other animals in the ecosystem (Prakasam, *et al.*, 2001. Exposure to pesticides had been found to produce adverse effects in exposed populations including humans such exposures can result in ill health and even death (John *et al*., 2001).

The benefits derived from pesticides can be cancelled out by the harm done to our health and those of other animals in the ecosystem if not properly handled. The potential adverse impact of pesticides on human health is likely to be higher in developing countries like Nigeria, due to easy availability of these highly hazardous chemical products and its low risk awareness among the populace especially local farmers.

Pesticide poisoning is a worldwide problem and an important cause of premature mortality accounting for estimated 200,000 deaths every year in developing countries (Michael *et al*., 2008).

Acute pesticide poisoning is a major public health concern today in developing countries, accounting for a proportion of recorded death cases. In this regard, their widespread use in

industrialized and developing counties have led to the concern over their effects on human and other animals exposed to them (Kumar *et al.*, 2010).

Poisoning due to organophosphate pesticides is treatable with atropine sulphate; pralidoxime chloride (2-PAM chloride) may also be used as an effective antidote in addition while maintaining full atropinisation (Debra, 2003; Kumar *et al.*, 2010).

Studies have shown the importance of antioxidants in health and disease that they could help prevent a host of chronic and degenerative disorders that might occur due to adverse effects of chemicals and other toxic agents in the system (Wintergerst *et al.*, 2007). A wide range of vitamins, enzymatic, and non enzymatic antioxidants have been reported to prevent the destructive effect of free radicals generated by toxic chemicals in the body (Colbert, 2000).

The human body has a large array of endogenous antioxidant defenses against oxidative stress, including antioxidant enzymes such as superoxide dismutase, catalase, and various peroxidases, as well as small molecule with antioxidant activity such as glutathione (Jason and Masson, 2004; DasGupta *et al*., 2006; Korotkova *et al*., 2008).

There have been reports on the toxicological effects of dichlorvos in animal studies and the use of atropine sulphate in the treatment of both acute and chronic toxic effects of dichlorvos (Raina *et al.*, 2008,Walker, 2001).

The present study looked at the possible use of antioxidant properties of copper and manganese singularly and in combination as an alternative remedy to atropine in the management of rats exposed to acute dichlorvos poisoning.

MATERIALS AND METHODS

3.1 Test Animals

A total of fifty-four (54) albino rats (*ratus ratus*) of 0.2kg average weight were obtained from University of Port Harcourt animal house were used for this study. The animals were housed in polypropylene cages under hygienic conditions and were acclimatized for 2 weeks prior to commencement of the study. The rats were maintained on standard laboratory feed and water *ad libitum* throughout the experimental period.

3.2 Pilot Study

A pilot study was carried out to establish the dose of dichlorvos that would cause 100% death. Twenty four rats made up of four rats per group were used for the study, the albino rats of average weight 0.2kg were injected intraperitoneally with 1ml of 11.10, 14.80 18.5, 22.2 and 25.6mg/kg dichlorvos respectively. 100% death occurred in rats that received 18.5mg/kg and above of dichlorvos. The LD_{100} was therefore obtained for dichlorvos as 18.5mg/kg and sublethal dose as 14.5mg/kg. 1ml of 0.9% saline was injected intraperitoneally into the control rats.

3.3.1 Determination of LD_{50} of dichlorvos (Acute Toxicity Test)

Six groups of male albino rats made up of five rats per group were weighed. Rats of similar average weight were placed into one group. Six cages were arranged and grouped as A, B, C, D, E and F. Dose levels of 3.7, 7.4, 11.1, 14.8 and 18.5mg/kg doses of dichlorvos were administered respectively using the intraperitoneal route.

The sixth group (control rats) was given sterile saline water using the same route. The rats were closely observed over 24 hours for sign and symptoms of dichlorvos toxicity. All the symptoms of toxicity, time of onset and duration were observed and recorded. The number of rats that died within 24 hours was recorded; acute toxic symptoms were scored according to order of severity. LD_{50} of dichlorvos was calculated using Arithmetic method of Karber and finally rated using Matsumara (1975) toxicity rating method.

3.3.2 Determination of effect of Antidotal Therapy on Acute dichlorvos Toxicity

This experiment was carried out to determine the effectiveness of the antidotal therapy atropine sulphate compared with those of trace elements; copper and manganese singularly and in combination after administration of sub-lethal dose of dichlorvos (dose that caused 80% death). Five groups made up of four albino rats per group were used for the study. Group 1 was given 14.8mg/kg of dichlorvos alone. Group 2 was given 1 ml of atropine sulphate (1.5mg/kg) after injection of dichlorvos (14.8mg/kg). Group 3 was given 1 ml of copper (0.025mg/kg) after the injection of dichlorvos (14.8mg/kg). Group 4 was given 1ml of manganese (0.01mg/kg) after the injection of dichlorvos (14.8mg/kg). Group 5 was given 1ml of manganese (0.025mg/kg) and 1 ml of copper (0.01mg/kg) after the injection of dichlorvos (14.8mg/kg). Signs and symptoms of toxicity observed and noted for all the groups.

The effect of antidotes on dichlorvos poisoning were observed and recorded.

Blood samples were collected from the respective rat groups into plain containers for haematological biochemical analysis.

3.4 Statistical analysis

Statistical analyses were carried out on the biochemical and haematological data obtained using Microsoft Excel statistical tools (2003 version). The mean, standard deviation, standard error of mean were calculated: correlations between the biochemical and haematological parameters were determined. The values were presented as means ± standard error of mean (SEM) and compared by student's statistical test. $P<0.05$ was accepted as statistically significant level.

RESULTS

4.1 Acute toxicity study: The result of the acute toxicity study carried out on albino rats using Arithmetic method of karber indicated LD_{50} value of dichlorvos to be 11.47mg/kg (Table 4.1). Dichlorvos injected intraperitoneally at dose levels 0, 3.7, 7.4, 11.1, 14.8 and 18.5 mg/kg respectively into the albino rats caused a dose dependent effect on the rats. The sign and symptoms of toxicity and the time of onset of toxicity in the rats increased with increased dose level of dichlorvos as well as the number of dead rats. The clinical signs and symptoms of toxicity included straub tail, muscle fasciculation, piloerection, lacrimation, defecation, excessive salivation, whole body tremor, micturition, restlessness, pupil constriction, respiratory distress, gasping and convulsion and death; the rats were considered dead when they failed to respond to agitation. The above signs and symptoms were observed to be rapid at dose levels 14.8 and 18.5mg/kg of dichlorvos. Dichlorvos induced death in acute poisoning was observed between 5 minutes and 60 minutes after single exposure and it was dose dependent. Group 1 and 2 albino rats injected with 3.7 and 7.4 mg/kg dichlorvos intraperitoneally, both caused 0% death, group 3 and 4 albino rats injected with 11.1 and 14.8mg/kg dichlorvos respectively caused 60% death with survival time 6-8 minutes and 80% death with survival times of 2-4 minutes respectively. Group 5 albino rats injected with 18.5mg/kg dichlorvos caused 100% death with survival time less than 1 minute (Table 4.2).

Table 4 .1 Determination of Median Lethal Dose (LD_{50}) of Dichlorvos

Cages	Dose level mgkg-1	Dose Diff mgkg-1	No. Dead	Mean Dead	Dose Diff x mean dead
1	0	0	0	-	0
2	3.7	3.7	0	0	0
3	7.4	3.7	0	0	0
4	11.1	3.7	3	1.5	5.55
5	14.8	3.7	4	3.5	12.95
6	18.5	3.7	5	4.5	16.65

LD_{50} Determination

$$LD_{50} = LD_{100} - \frac{\text{sum of dose difference x mean dead}}{\text{No of rat}}$$

$LD_{100} = 18.5$

No of rat = 5

(Dose difference x mean dead) = 35.15

$$LD_{50} = \frac{(35.15)}{5} = 7.03$$

$LD_{50} = 18.5\text{-}7.03$

= 11.47mg/kg

18.5mg/kg dichlorvos was obtained as the dose of dichlorvos that caused 100% death (LD_{100}) Furthermore; LD_{50} study gave 11.47mg/kg as the dose of dichlorvos that caused 50% death in the albino rats (the median lethal dose).

Table 4.2: Percentage Survival in Acute Dichlorvos Poisoning

Group	Number of Death	Percentage survival (%)
Control	0	100
Dichlorvos dose		
3.7 mg/kg	0	100
7.4 mg/kg	0	100
11.1 mg/kg	3	40
14.8 mg/kg	4	20
18.5mg/kg	5	0
n = 5 Where n are no of rats.		

Table 4.3: Symptoms of Acute Dichlorvos Poisoning

Group	Micturition	Restlessness	Respiratory Distress	Pupil Constriction	Convulsion
Control	0.50 ± 0.22	1.0 ± 0.32	0. 8 ± 0.41	0.40 ± 0.22	0.00± 0.00
Atropine	0.40 ± 0.22^{ns}	0.80 ± 0.32^{ns}	0. 60 ± 0.41^{ns}	0.40 ± 0.20^{ns}	0.00 ± 0.00^{ns}
Copper	2.00 ± 0.25^{a}	3.00 ± 0.22^{a}	2.60 ± 0.00^{a}	3.00 ± 0.00^{a}	2.50 ± 0.25^{a}
Manganese	1.80 ± 0.20^{a}	2.40 ± 0.20^{a}	2.60 ± 0.00 ^{a}	2.80 ± 0.00^{a}	2.60 ± 0.25^{a}
Copper + Manganese	2.10 ± 0.20^{a}	2.80 ± 0.20^{a}	2.80 ± 0.00^{a}	2.60 ± 0.00^{a}	2.40 ± 0.25^{a}

n=5 a - P<0.05 = significant ns – not significant

4.2 Antidotal Effects

Antidote effect of copper and manganese singularly and in combination against acute toxicosis induced by dichlorvos in male albino rats was evaluated and compared with that of the standard antidote atropine. The effectiveness of the antidotal therapy was based on the mean number of symptoms alleviated and percentage survival produced (Table 4.3). Atropine administered intraperitoneal at 1.5mg/kg compared with copper and manganese singularly and in combination administered at 0.025mg/ml and 0.01mg/ml respectively given 5minutes after a single acute dosing of 14.8mg/kg dichlorvos showed that atropine gradually and significantly decreases (P<0.05) all symptoms of poisoning and the occurrence of toxic manifestation in the rats over a period of 60 minutes. The symptoms of acute dichlorvos poisoning observed in the rats included; straub tail, muscle fasciculation, piloerection, lacrimation, defecation, excessive salivation, whole body tremor, micturition, restlessness, pupil constriction, respiratory distress, gasping and convulsion and death. These effects were observed to gradually and significantly increase (P<0.05) in the copper, manganese, copper and manganese treated groups and least in atropine treated and control groups. Treatment with atropine gradually reduced the severity of dichlorvos - induced toxicosis. The use of trace elements copper, manganese, and copper and manganese when compared with atropine were not able to reduce the impact of dichlorvos-induced toxicity in the rats.

The reduction in cholinesterase (ChE) activity occurred in all rats dosed with dichlorvos regardless of the antidotal therapy as compared to the control group. The antidote did not protect the rats against ChE inhibition caused by the dichlorvos dosing. Rats dosed with dichlorvos and then treated with copper and manganese, singularly and in combination had significantly lower ChE activity in the plasma when compared with the atropine group.

4.3 Biochemical Parameter Values in Acute Dichlorvos Poisoning

Table 4.4 showed biochemical indices ALT, AST, GGT, ALP, cholinesterase, creatinine and urea values obtained in albino rats exposed to acute toxic effect of dichlorvos at doses of 3.7, 7.4, 11.1, 14.8 and 18.5mg/kg respectively on blood samples. Statistically significant dose dependent increases in ALT, AST, GGT, ALP urea and creatinine, were observed ($P< 0.05$) when compared with control value. There was a significant decrease in cholinesterase levels ($P< 0.05$) that was dose dependent when compared with the control value.

Table 4.4: Acute Toxic Effect of Dichlorvos on Liver Enzymes (mean±SEM)

Group	1	2	3	4	5	6
Doses Mg/kg	0 (Control)	3.7	7.4	11.1	14.8	18.5
ALT (U/L)	24±0.6	39±1.5 ^{ns}	45±0.5 ^{a}	52±2.5 ^{a}	70± 1.2 ^{a}	81±1.5 ^{a}
AST (U/L)	27.5±1.2	40± 0.9 ^{ns}	55±1.0 ^{a}	65±0.8 ^{a}	80±0.5 ^{a}	95±1.0 ^{a}
GGT (U/L)	5±0.33	6±0.58 ^{ns}	6.5±0.8	15±0.5 ^{a}	20±0.9 ^{a}	27±0.9
ALP (U/L)	40±1.0	55±0.60^{ns}	69±1.0 ^{ns}	75±1.6 ^{a}	80±1.2 ^{a}	95±1.5
CHE X 10^3	2.9±0.5	2.00±0.3 ^{ns}	1.93±0.3 ^{ns}	1.8±0.6 ^{a}	1.6± 0.5 ^{a}	1.4±0.6 ^{a}

n=5 a - $p<0.05$ = significant ns – not significant SEM = standard error of mean
Where n are no of rats.

4.4 Haematological Parameter Values in Acute Dichlorvos Poisoning

Table 4.5 showed haematological indices RBC, HB, PCV, Total WBC and Platelet levels obtained in albino rats exposed to acute dichlorvos poisoning. Statistically dose dependent decreases were observed in the RBC, HB and PCV values obtained ($P< 0.05$) for the exposed albino rats when compared to the control rats. While statistically dose dependent increases were observed in the WBC and platelets values ($P < 0.05$) when compared with the control value

Table 4.5 Toxic Acute Effect of Dichlorvos on Hematological Parameters (mean±SEM)

Groups	1	2	3	4	5	6
Doses mg/kg	0 (control)	3.7	7.4	11.1	14.8	18.5
RBC $X10^{12}$/I	7.8 ±1.0	7.2±1.2 ^{ns}	6.9±0.5 ^{ns}	5.0±0.8^{a}	4.32± 1.2^{a}	3.78 ±1.0^{a}
HB g/dl	17.5±0.5	15.7±0.9 ^{ns}	14.7±1.0^{ns}	12.8±0.6^{a}	12.0±0.8^{a}	11.5±1.0^{a}

PCV %	52±0.6	47±0.5^{ns}	45±0.8^{ns}	38 ±0.5^{a}	36±0.9^{a}	33±0.9^{a}
WBC X10^{9}/I	9.0±1.0	9.7±0.6 ^{ns}	10.5 ±1.0^{ns}	13.2 ±1.5^{a}	15.5±1.2^{a}	17.0 ±1.5^{a}
PLT X10^{9}/I	40±1.0	42±0.6^{ns}	48±1.0^{ns}	53±1.6^{a}	59±1.2^{a}	65±1.5^{a}

n=5 a - P<0.05 = significant ns – not significant SEM = standard error of mean
Where n are no of rats.

DISCUSSION

The median lethal dose (LD_{50}) of dichlorvos from the acute toxicity study in the albino rats using intraperitoneal route was calculated to be 11.47mg/kg. This suggests that dichlorvos is highly toxic when ranked against the international classification of chemical toxicity by Matsumura (1975). The symptoms of toxicity observed in the experimental rats following acute dichlorvos poisoning included restlessness, micturition, defecation, pupil constriction, muscle weakness, respiratory distress, gasping, convulsion and death. These were scored and found to be dose dependent. Convulsion appeared to be very prominent at higher doses. These symptoms of toxicosis could be attributed to the inhibitory action of dichlorvos on the enzyme cholinesterase thereby leading to accumulation of acetylcholine at nerve endings. These symptoms largely agreed with those reported by Mohammed *et al.,* (2008), Kaur *et al.*, (2007) and in the literature by USEPA, (2006). The manifestations of the toxic symptoms were observed to be dose-related, at high doses all the rats that convulsed died. This apparently was due to excessive stimulation of the central nervous system. At lower doses mild poisoning occurred with symptoms characteristic of muscaranic and less of nicotinic effect. However, at high doses convulsion seemed to predominate which was largely due to considerable central nervous system stimulation. In the animals that died, the common cause of death was asphyxia, due to respiratory failure or cardiac arrest and this was produced within minutes after administration of dichlorvos. This finding is in agreement with the report in the literature by USEPA (2006) and also agrees with the finding by Iyaniwura et al., (1991). Dichlorvos inhibits the enzymes acetyl cholinesterase and cholinesterase activities in brain, plasma and red blood cells resulting in accumulation of acetylcholine at cholinergic synapses which in turn over-stimulates and then paralyzes cholinergic transmission. Dichlorvos poisoning manifest predominantly muscaranic effect and to a lesser effect nicotinic symptoms. These effects may be attributed to the fact that dichlorvos is poorly lipid soluble and penetrate the blood-brain barrier poorly (Taylor, 1985).

The result obtained from the administration of the antidotes; atropine, copper and manganese singularly and in combination after a single acute dose of 14.8mg/kg dichlorvos showed that symptoms of poisoning developed few minutes after dosing and death occurred within a short time, but when the rats survived prognosis improved and recovery appeared complete.

Dichlorvos poisoning results in the inhibition of the enzyme acethylcholinesterase (AChE) thereby leading to the accumulation of acetylcholine at nerve endings (synapses), causing overstimulation and subsequent disruption of transmission in both the central and peripheral nervous systems (Erdman, 2004). Treatment with the antidote atropine was able to alleviate the toxic effects of dichlorvos on the experimental rats. Atropine a muscarinic antagonist blocks the action of acetylcholine thereby preventing lethality that could result from dichlorvos poisoning. This finding is consistent with those reported by Yurumez *et al*., (2007) and that of Chedi and Aliyu, (2010). The symptoms of dichlorvos toxicity observed were predominantly muscarinic with little nicotinic effects; atropine therefore blocked the muscarinic receptors, thus eliminating the agonistic effect of acetylcholine on these receptors. This would explain the high percentage of survival observed in the atropine treated rats compared to the trace element treated rats. The trace elements copper and manganese singularly and in combination could not reverse the cholinergic and muscarinic effects of dichlorvos in the poisoned rats nor confer protection on the rats' organ, hence all the rats that convulsed in these groups died. Treatment with atropine however reversed the toxic effects of dichlorvos on the poisoned rats and also confer some degree of protection on the rats organ.

The biochemical parameters monitored in the study were aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), urea, creatinine and cholinesterase. The serum levels of these enzymes; ALT, AST, GGT, ALP and cholinesterase are often measured clinically as part of diagnostic liver function tests. In assessing the extent of liver involvement in acute dichlorvos poisoning in the course of this work, the serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyltransferase (GGT) and cholinesterase were measured. There was statistically significant increase ($p<0.05$) in the mean concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma glutamyltransferase (GGT) in the male albino rats exposed to dichlorvos poisoning that was dose dependent in the acute toxicity test when compared with their corresponding control rat group as shown in table 4.4. Serum ALT and

AST activities frequently serve as an index of liver injury (De Boer *et al.*, 2000); they are usually released in the liver when parenchyma cells of the liver become necrotic due to toxic cell destruction. The activity of either enzymes especially AST could be raised in extra-hepatic condition; AST is present in red blood cells and since dichlorvos induced haemolysis in the experimental rats which led to an increased rate of red blood cell destruction; this could explain the higher level of AST obtained in comparison with ALT. The increase in the levels of ALT and AST alongside ALP and GGT could reflect inflammatory disease or cholestatic liver disease. The result of the current study coincide with previous studies (Manal et al., 2008; Hernadez *et al*., 2006; Campbell and Ofurum, 1986) that showed significant increase in liver enzymes in rats and humans exposed to pesticides. Studies by Dede and Chike, (2000) and Sharpe et al., (1996) also indicated increased activity of these enzymes; ALT, AST alongside ALP following hepatocellur damage in fish and albino rats exposed to toxic substances.

Measurements of serum cholinesterase activity in this study serve as a sensitive measure of the synthetic capacity of the liver, the statistically significant decrease ($p<0.05$) in the mean serum concentration of the enzyme compared to the control as presented in table 4.4 may reflect impaired synthesis of the enzyme by liver. Cholinesterase level in serum is useful as a test of liver function, as an indicator of possible insecticide poisoning, or for the detection of patients with atypical forms of the enzyme. The spread of values encountered in apparently healthy people is wide, ranging between 2000 and 12000 U/L. A fall in the enzyme level below 670 U/l is significant at 95% confidence level according to Beckett *et al.*, (2005). 30 to 50% decrease in serum cholinesterase level is observed in acute hepatitis and in chronic hepatitis of long duration. 50 to 70% decrease may occur in advanced cirrhosis and carcinoma with metastases to the liver. In the present study the mean concentration of cholinesterase was significantly decreased in all the rat groups (treated and untreated) compared to the control. This is attributed to the inhibitory effect of dichlorvos on acetyl-cholinesterase that can be reversed by all treatment leading to accumulation of acetylcholine at nerve synapses.

The renal function test, serum urea and creatinine levels in the acute toxicity study as presented in table 4.4, increased with increase dose of dichlorvos, the levels were significantly elevated ($p<0.05$) in the dichlorvos poisoned rats and those treated with copper and manganese singularly and in combination compared with the values obtained in the

control group. The kidney besides performing physiological functions, eliminate foreign compounds and their metabolites from the body. The assay of urea and creatinine is often used as a test of renal function to access the functioning ability of the kidneys. Increase in their activity in the serum may indicate renal dysfunction.

Haematological parameters serve as important indices in the monitoring and management of health status. The haematological parameters monitored in this study includes; red blood cells (RBC), haemoglobin (Hb), packed cell volume (PCV), total white blood cell count (WBC) and platelet count. The results obtained in table 4.5 showed significant increase in the mean values obtained for total WBC and platelet count ($p<0.05$) which was found to be dose dependent in the acute toxicity study; with high levels observed in rats exposed to high doses of dichlorvos. The increase in the total white blood cell count (WBC) could be attributed to the rats' defense mechanism in response to the invading xenobiotic (dichlorvos).

Furthermore there was statistically significant decrease ($p<0.05$) in the mean values of the circulating red blood cells, haemoglobin and packed cell volume that was also dose dependent. This finding indicates a state of anaemia which could arise as a result of excessive destruction of erythrocytes by dichlorvos at a rate that exceeds the bone marrows capability to compensate or offset for the blood loss. These findings corroborated with those reported by Mohssen, (1997) and Dede and Kagbo, (2001). Erythrocytopenia observed in this study could be attributed to the suppressing effect of dichlorvos on erythropoiesis. The toxicity of dichlorvos on haemopoietic cells in the bone marrow could be due to metabolites of dichlorvos that are produced in relatively high concentration and act in synergistic manner to disrupt the mechanism that regulate blood cell formation.

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