Afr. J. Med. Med. Sci. (2018) 47, 185-194

Hepatotoxicity and clastogenicity of dichlorvos at high doses in male Wistar rats

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Abstract

Introduction: Dichlorvos (2, 2-dichlorovinyl dimethyl phosphate (DDVP) is widely used in Nigeria for the preservation of stored grains, especially dry beans. Residues of this organophosphate pesticide may therefore inadvertently be present in such products. The present study investigates the hepatotoxic and clastogenic effects of high doses of DDVP in rats as a mimic to its indiscriminate use on store products.

Methods: Male rats (100-150 g) were randomly divided into six groups of five each. Treatments (p.o) were as follows: Group 1-distilled water; Group 2 (control)-corn oil; Groups (3-5)-varying doses of DDVP (5-20 mg/kg b.w) and Group 6-(2.5 mg/kg) sodium arsenite. After 28 days, indices of hepatotoxicity [serum activities of gamma-glutamyl transferase (γGT), alkaline phosphatase (ALP), alanine and aspartate aminotransferases (ALT and AST)] and clastogenicity [relative number of micronucleated polychromatic erythrocytes (mPCEs)] were determined.

Results: DDVP at all the tested doses induced significant ($p < 0.05$) increase in activities of γGT, ALP, ALT and AST. It also significantly ($p < 0.05$) induced mPCEs formed in the bone marrow as compared with the control. The level of induction was dose dependent in both cases. In addition, there was significantly ($p < 0.05$) higher number of hepatic cells in the cell/mm^2 assay for the group treated with DDVP. Histopathological analysis of liver samples from the treated groups revealed lesions corroborating the biochemical indices above.

Conclusion: Findings from this study suggest that DDVP has clastogenic and hepatotoxic effects in rats. There is therefore a need for strict regulatory control and monitoring of the use and residues of DDVP in stored products.

Keywords: *Aminotransferases, Micronucleated polychromatic erythrocytes (mPCEs), DDVP.*

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Résumé

Introduction : Le dichlorvos (2, 2-dichlorovinyl diméthyle phosphate) (DDVP) est largement utilisé au Nigéria pour la conservation des grains entreposés, en particulier des haricots secs, et des résidus de ce pesticide organophosphoré peuvent donc être présents par inadvertance dans ces produits. Cette étude présente enquête sur les effets hépatotoxiques et de clastogènes à fortes doses de DDVP chez les rats, comme une imitation de son utilisation sans discernement sur les produits en réserve.

Méthodes : Des rats mâles (100-150 g) ont été divisés au hasard en six groupes de cinq chacun. Les traitements (p.o) étaient les suivants: Groupe 1 - eau distillée; Groupe 2 (témoin) - huile de céréale; Groupes (3-5) - doses variables de DDVP (5-20 mg / kg de poids corporel) et du groupe 6- arsénite de sodium (2,5 mg / kg). Après 28 jours, indices d'hépato-toxicité [activités sériques du gamma-glutamyl transférase (γGT), la phosphatase alcaline (ALP), l'alanine et l'aspartame aminotransférase (ALT et AST)] et la clastogénicité [nombre relatif d'érythrocytes polychromatiques micro-nucléés (mPCEs)] ont été déterminées.

Résultats : Le DDVP à toutes les doses testées a induit une augmentation significative ($p < 0,05$) des activités de γGT, ALP, ALT et AST. Il a également induit significativement ($p < 0,05$) des mPCEs formés dans la moelle osseuse par rapport au témoin. Le niveau d'induction dépend de la dose dans les deux cas. En outre, il y avait un nombre significatif ($p < 0,05$) plus élevé de cellules hépatiques dans le test cellule/mm^2 pour le groupe traité avec DDVP. L'analyse de l'histopathologie des échantillons hépatiques des groupes traités a révélé des lésions corroborant aux indices biochimiques ci-dessus.

Conclusion : Les résultats de cette étude suggèrent que le DDVP a des effets clastogènes et hépatotoxiques chez les rats. Il existe donc un besoin de contrôle réglementaire strict et de surveillance de l'utilisation et des résidus de DDVP dans les produits stockés.

Mots - clés: *taminotransférase, micro-nucléés érythrocytes polychromes (mPCEs), DDVP*

Introduction

Significant progress has been made in understanding the molecular basis of cancer and other diseases. This often involves defects in diverse number of genes [1]. Such defects can be initiated by environmental, biological, physical and chemical agents. Some of the agents are deliberately taken as with excessive ethanol in drinks while others, are inadvertently introduced into the biological system. Pesticides that are used in crop processing and production belong to the latter category. Increasing use of pesticides in agriculture has been attributed as a factor behind recent all year food availability and increase in agricultural productivity [2].

One such pesticide is dichlorvos (2, 2-dichlorovinyl dimethyl phosphate, DDVP), an organophosphate pesticide that is effective against aphids, spider, mites, caterpillars, thrips, and white flies [3, 4]. It is used for space treatment during food processing, handling, and in storage plants, feedlots, stockyards, corrals, holding pens, animal buildings, poultry houses, as well as commercial and institutional buildings. In Nigeria, it is widely used in the preservation of stored grains especially dry beans. European Union recently placed a ban on importation of Nigerian dry beans due to presence of high concentration of DDVP beyond permissible limit of 0.01 mg/g [5, 6].

Although there are concerns regarding the environmental and ecological impact of DDVP, only little is known about its toxicity in the mammalian system [7, 8]. There is a need for increased understanding of the toxic effects of this class of chemicals used indiscriminately in food preservation in order to define the health risk associated with exposure to them. This study was designed to assess the hepatotoxic and clastogenic effects of DDVP when administered at high doses in experimental male Wistar rats.

Materials and methods

Test substances

Dichlorvos (2, 2-dichlorovinyl dimethyl phosphate) was purchased from Amenss Agrochemicals, Mokola Ibadan. The stock solution was prepared by making up 0.5 ml of dichlorvos (1 g/ml) to 50 ml using corn oil to give a concentration of 10 mg/ml.

Kits and Chemicals

Aspartate aminotransferase (AST), alanine aminotransferase and γ-glutamyl transferase kits were purchased from Randox Laboratories, United Kingdom. May Grünwald stain, DPX mountant, Giemsa stain, and colchicine were from Sigma Chemical Co. USA.

Experimental animals and treatments

Thirty male albino rats weighing between 100-150 g were obtained from Olufarms, Ibadan; and housed in the experimental animal facility of our department. The animals were kept under the condition of 12 hours light/ dark cycle and temperature of 28 ± 2 °C with free access to feed pellets (Vita Feeds, Mokola, Ibadan) and water *ad libitum* throughout the duration of the experiments.

The rats were divided into six groups of five rats each and treated as follows:

Group 1: Given distilled water

Group 2: Given corn oil only.

Group 3: Administered DDVP at 5 mg/kg body weight

Group 4: Administered DDVP at 10 mg/kg body weight

Group 5: Administered DDVP at 20 mg/kg body weight

Group 6: Given sodium arsenite at 2.5 mg/kg body weight (this is 1/10th LD_{50} in rats [9].

Sodium arsenite was used as a standard genotoxin and hepatotoxin [10, 11]. The test substances were administered every other day for a period of four weeks by oral gavage. Experimental animals were treated and sacrificed following standard rules laid down by the University Ethics Committee on the treatment of experimental animals.

Serum samples preparation

The rats were sacrificed by cervical dislocation. Through cardiac puncture, blood was collected from each of the sacrificed animals into plain tubes and allowed to clot at room temperature for about 2 hours. The clotted blood samples were centrifuged at 3000 g for 10 minutes at 4 °C using Beckman L5-50B ultracentrifuge (Ramsey, MN, USA). The supernatant (the serum) was separated and used immediately or stored at -20 °C until required.

Biochemical assays

Micronuclei assay

The method of Schmid [12] was adopted in the preparation of bone marrow smears. The femurs were removed from the sacrificed rat and stripped clean of muscle. A pair of scissors was used to make an opening in the iliac region of the femur. A small pin was then introduced into the marrow canal at the epiphyseal end. As the pin was pushed inside the canal, the marrow exuded through the hole at the iliac end. The marrow was placed into a slide and a drop of fetal calf serum was added to the smear using a Pasteur pipette. The marrow and fetal calf were mixed to homogeneity using a clean edge of another

slide. The homogeneous mixture was then spread on the slide as a smear and allowed to dry. The cells on the slides were viewed under light microscope to detect the presence of micronucleated polychromatic erythrocytes (mPCEs). Micronuclei and mPCEs stain blue while mature erythrocytes stain red. Tally counter was used to aid the scoring of mPCEs.

Protein determination

The protein concentrations of the various samples were determined by Biuret method as described by Gornal and his research group [13]. Potassium iodide was added to the reagent to prevent precipitation of Cu^{2+} ions as cuprous oxide. In some cases the serum or supernatants from liver homogenate were diluted 100 times with distilled water. Then, 1 ml of the original or diluted sample was taken and added to 3 ml of Biuret reagent. The determination was done in triplicates. The mixtures were incubated at room temperature for 30 minutes after which the absorbance was read at 540 nm using distilled water as blank. The protein concentration for each of the samples was obtained by extrapolated from the standard curve.

Enzyme assay

Gamma glutamyl transferase activity (ãGT)

Serum ãGT was assayed using the reconstituted ãGT diagnostic reagent following the method of Szasz [14].

Alanine amino transferase (ALT) and aspartate amino transferase (AST) activities

Serum ALT and AST activities were assayed according to Reitman and Frankel [15] by monitoring an intensely coloured hydrazone read at 546 nm using a Spectronic-20 spectrophotometer (Thermo Scientific, Surrey, UK).

Determination of lipid peroxidation

Lipid peroxidation level was determined by measuring the thiobarbituric acid reactive substances (TBARS) produced during lipid peroxidation. An aliquot of 0.4 ml of the sample was mixed with 1.6 ml of Tris-KCl buffer to which 0.5 ml of 30 % TCA was added. 0.5 ml of 0.75 % TBA was added and placed in a water bath for 45 minutes at 80 °C. This was then cooled on ice and centrifuged at 3000 g for 10 minutes. Clear supernatant was collected and absorbance measured against reference blank of distilled water at 532 nm. The MDA (malondialdehyde) level was calculated according to an established method [16].

Histopathological analysis

Liver tissues from the animals were immersed in 10 % buffered formal-saline. These were left for 24 hours for fixation of the organs after which cross-sections of the organs were cut at 3 mm thickness and placed in a processor overnight. In the processor, the tissues were placed first in 70 % alcohol for 2 hours, followed by 90 % alcohol for another 2 hours, xylol for 4 hours, and finally, in wax for 5 hours. The tissues were removed, embedded in molten fibro wax and allowed to solidify under a running tap. The tissues, mounted on wooden blocks, were then chilled on ice. Sections of the tissue were cut at a thickness between 3 and 5 mm using the rotary microtome and then allowed to float in 20 % alcohol, followed by water at 58°c (in an incubator). It was then placed on albumized glass slides and dried on a hot plate at 60 °C. The slides so prepared were initially placed in xylol and washed with decreasing concentration of absolute alcohol, 90 % alcohol, 80 % alcohol and finally, 70 % alcohol. They were washed in water stained with Cole's haematoxylin, washed again with water, followed by 1 % hydrochloric acid, running tap water and rinsed in saturated lithium carbonate. These glass slides were transferred to 1 % aqueous solution of eosin for 2 minutes, and washed in a running tap. They were cleaned, mounted on Depex after treatment in absolute alcohol. The slides were finally allowed to dry on the bench at room temperature and then viewed under the microscope.

Cells per mm² analysis

The numbers of hepatocytes per mm² on stained slices, prepared from the liver were counted under a Nikon light microscope at x400 with the aid of a grid and tally counter.

Haematological analysis

White blood cell (WBC) (total and differential), total red blood cell (RBC), haemoglobin (Hb), packed cell volume (PCV), and platelets were determined from blood samples collected in EDTA bottles using standard techniques.

Statistical analysis

Data were expressed as mean ± standard deviation and analysed by one-way analysis of variance (ANOVA) followed by least significant difference (LSD) to test for significant differences among the groups of rats using Statistical Package for Social Sciences (SPSS) program. P values less than 0.05 were considered statistically significant.

Results

Administration of sodium arsenite (2.5 mg/kg body weight), used as standard toxicant in this study, resulted in significant ($p<0.05$) reduction in percentage change in body weight compared with the group given distilled water only (Group 1). Also, administration of DDVP in corn oil, at all doses, caused significant ($p < 0.05$) reduction in the percentage change in body weight when compared to the control Group 2 treated with corn oil (Fig. 1).

In addition, findings from the micronucleus assay showed that DDVP at all doses tested, induced formation of micronuclei at levels similar to sodium arsenite. The number of mPCEs scored per 1000 PCEs in the bone marrow cells of rats in each of the treated groups (Groups 3 -6) were significantly higher than observations made in the respective control (Groups 1 and 2) (Fig. 2). Furthermore, administration of sodium arsenite at 2.5 mg/kg body weight or DDVP (at 10 mg and 20 mg/kg body weight)

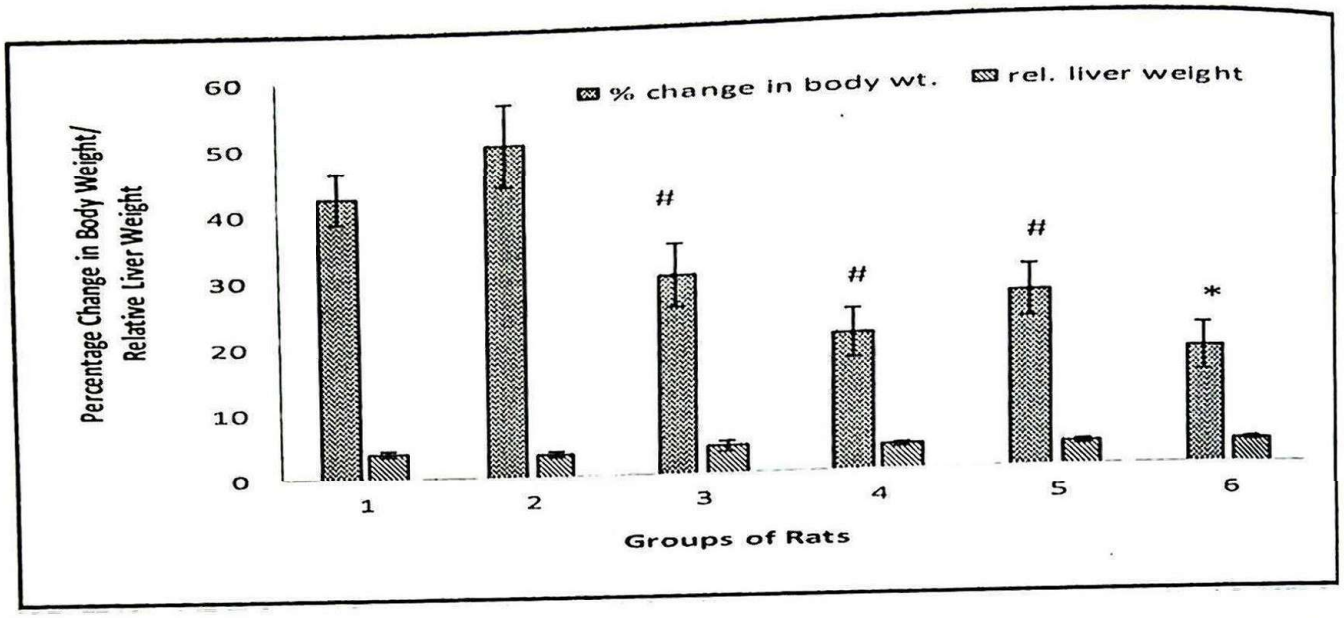

Fig. 1: Effects of DDVP on percentage change in body weight and relative liver weights of rats. Values are mean + SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only (corn oil was used as vehicle for DDVP); group 3 rats were treated with DDVP at 5 mg/kg; group 4 rats were treated with DDVP at 10 mg/kg; group 5 rats were given DDVP at 20 mg/kg; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite dissolved in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

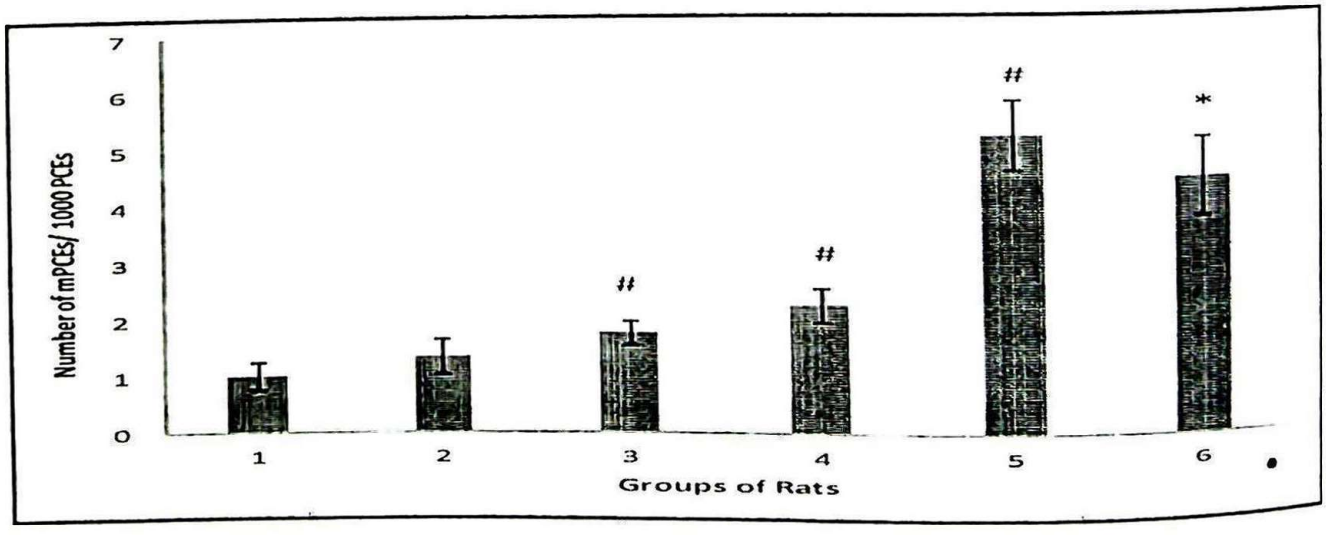

Fig.2: Induction of micronuclei formation in the bone marrow cells by DDVP. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with DDVP at 5 mg/kg; group 4 rats were treated with DDVP at 10 mg/kg; group 5 rats were given DDVP at 20 mg/kg; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite dissolved in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

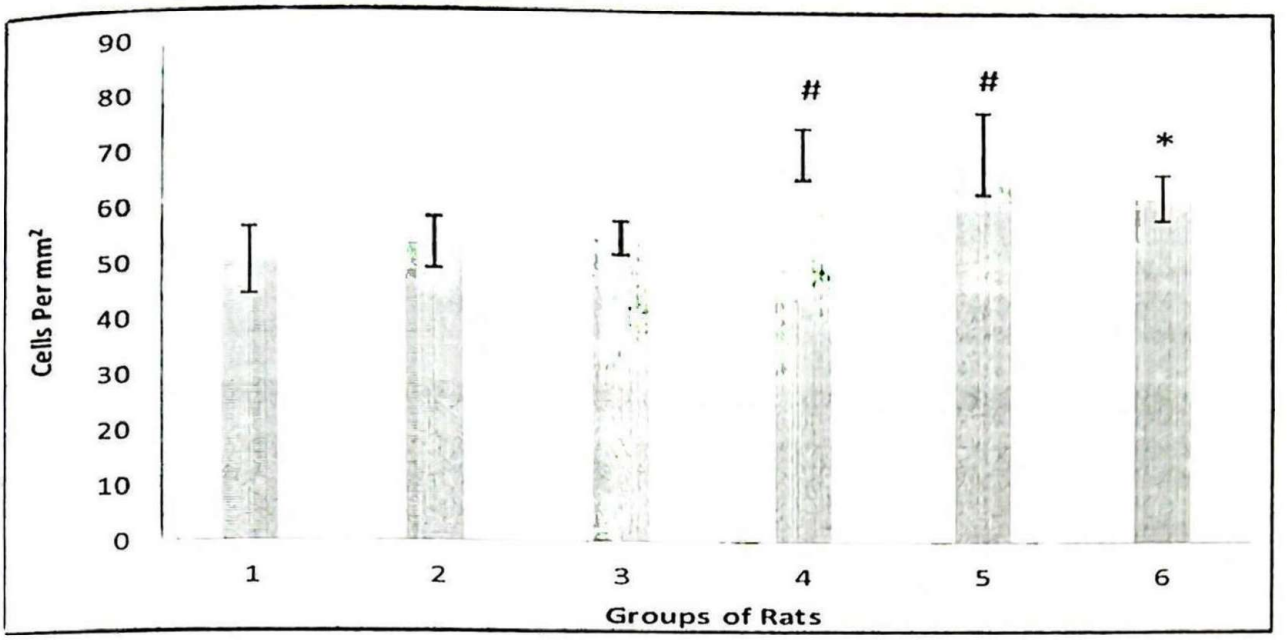

Fig. 3: High doses of DDVP induced hepatic cells proliferation in rats. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

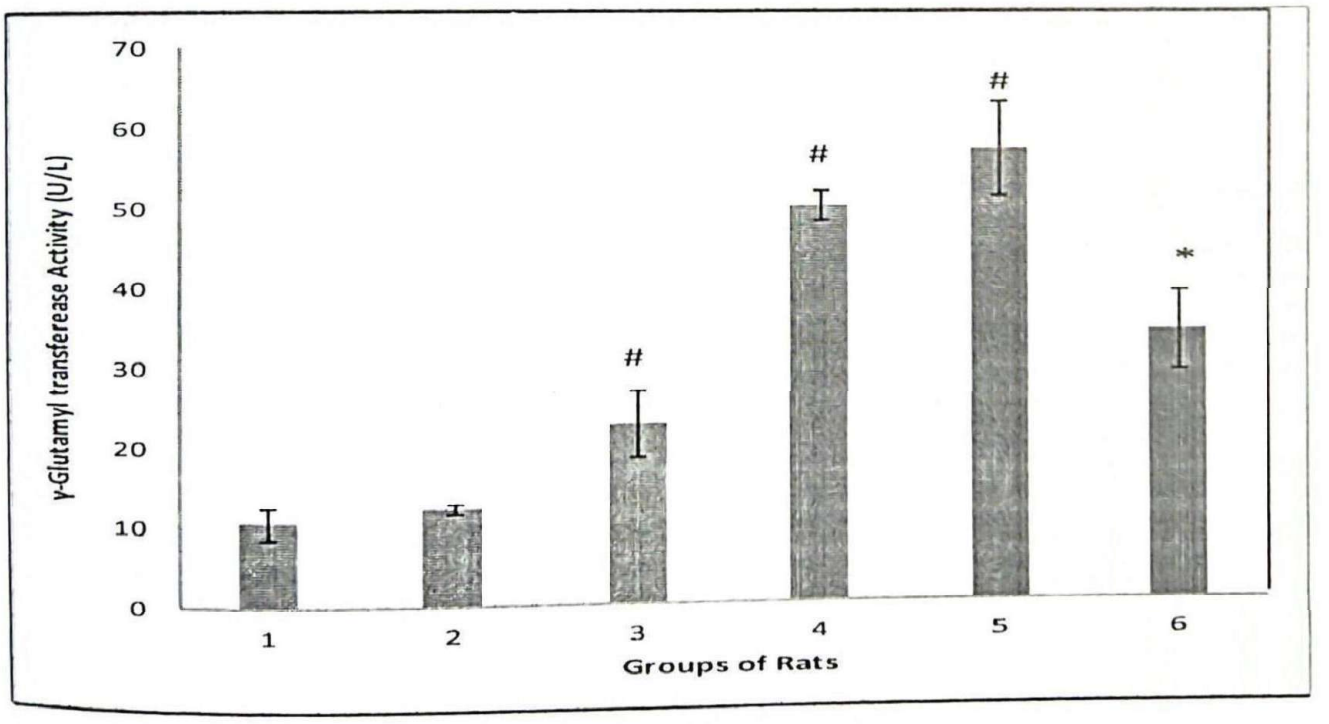

Fig. 4: Effects of DDVP on serum ã-glutamyl transferase activity in rats. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

triggered significant increase in the liver cell per mm² compared with the control group (Fig. 3).

Treatment of rats with sodium arsenite or DDVP (at all doses) produced significant increase in mean serum ãGT activities compared with the control groups treated with distilled water or corn oil alone. The increase in the enzyme activity in groups treated with DDVP is dose dependent (Fig. 4). Observation made with AST and ALT activities (Fig.5). and ALP activity (Figure 6) in the treated

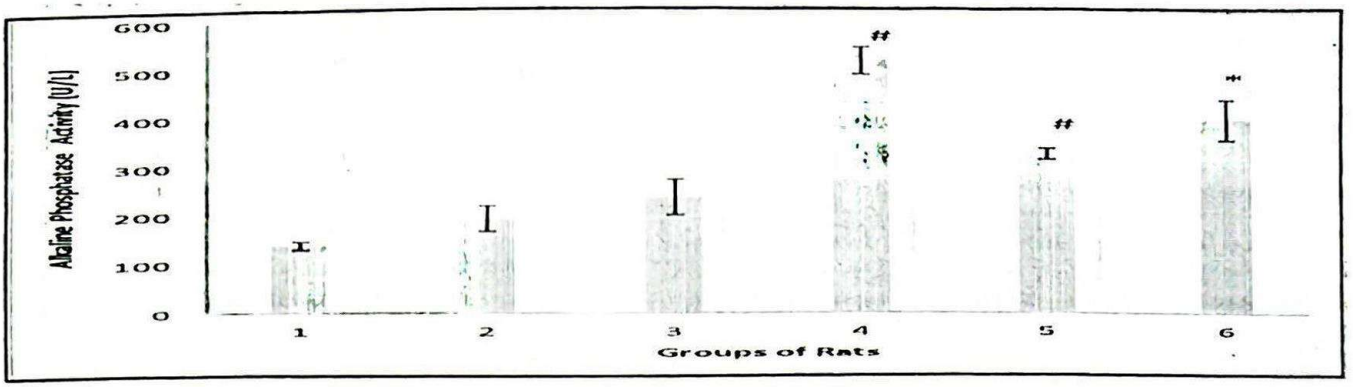

Fig. 5: Effects of DDVP on serum alkaline phosphatase activity in rats. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

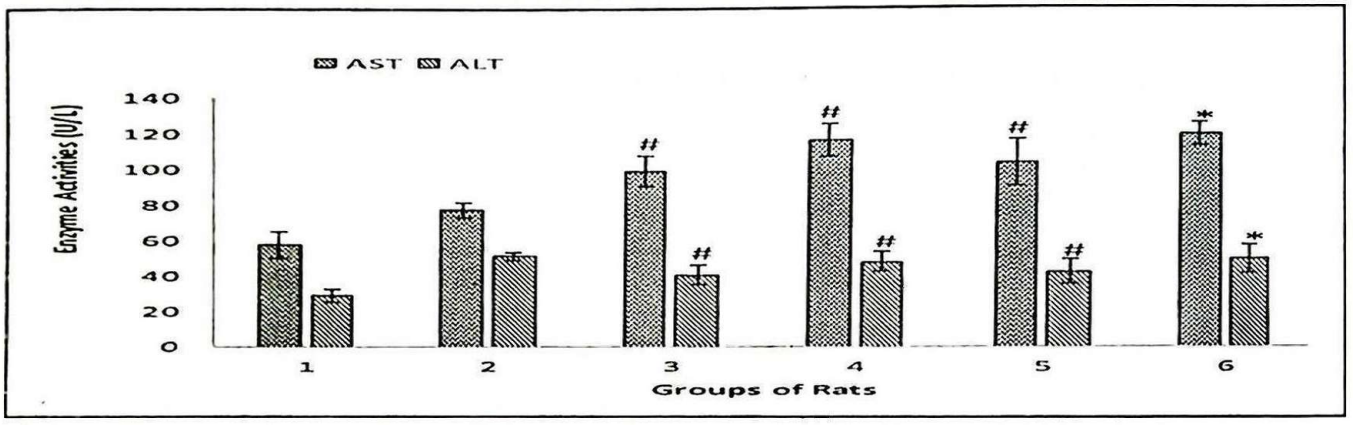

Fig.6: Administration of DDVP produced raised serum alanine and aspartate aminotransferases (ALT and AST) activities in rats. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

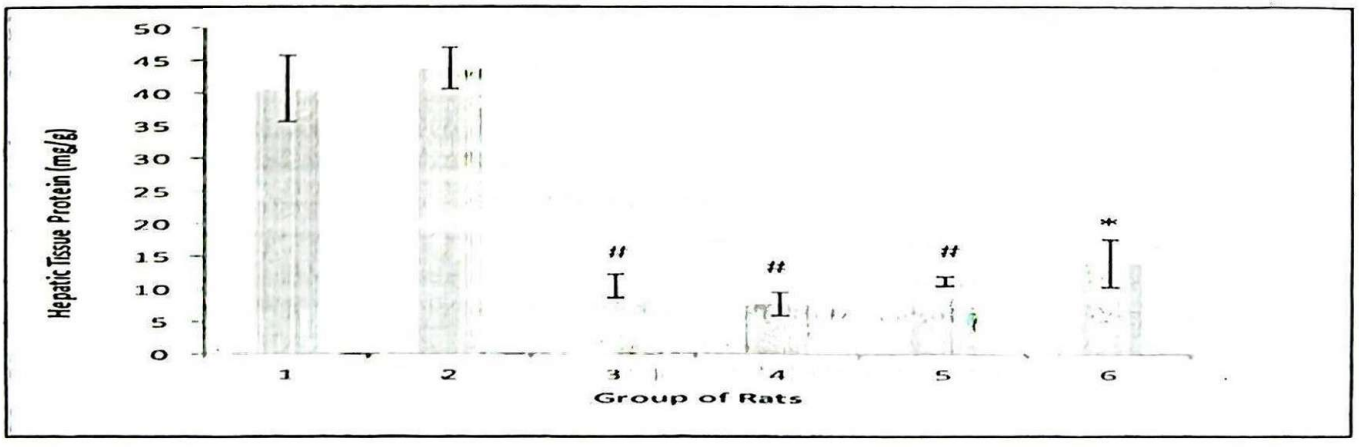

Figure 7: Effect of DDVP on tissue hepatic protein in rats. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water # = significantly different ($p < 0.05$) from control group 2 * = significantly different ($p < 0.05$) from control group 1.

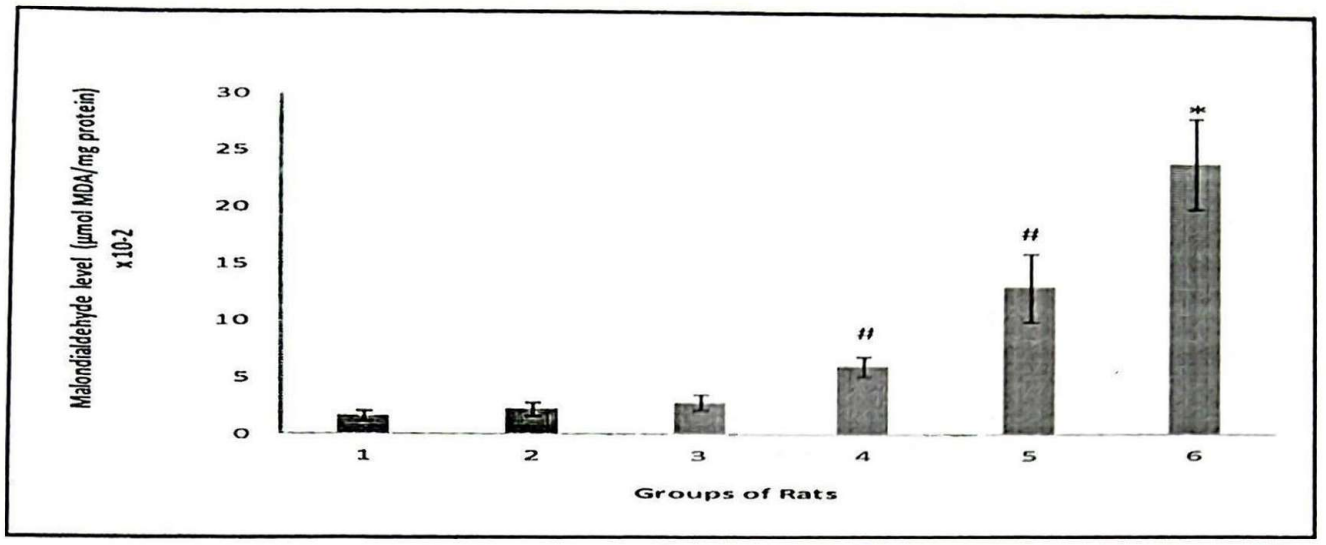

Fig. 8: Lipid peroxidation index (MDA) in rats treated with DDVP. Values are means ± SD (n =5); group 1 represents negative control given distilled water; group 2 rats were given corn oil only; group 3 rats were treated with 5 mg/kg DDVP; group 4 rats were treated with 10 mg/kg DDVP; group 5 rats were given 20 mg/kg DDVP; group 6 served as positive control group treated with 2.5 mg/kg sodium arsenite in distilled water. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1.

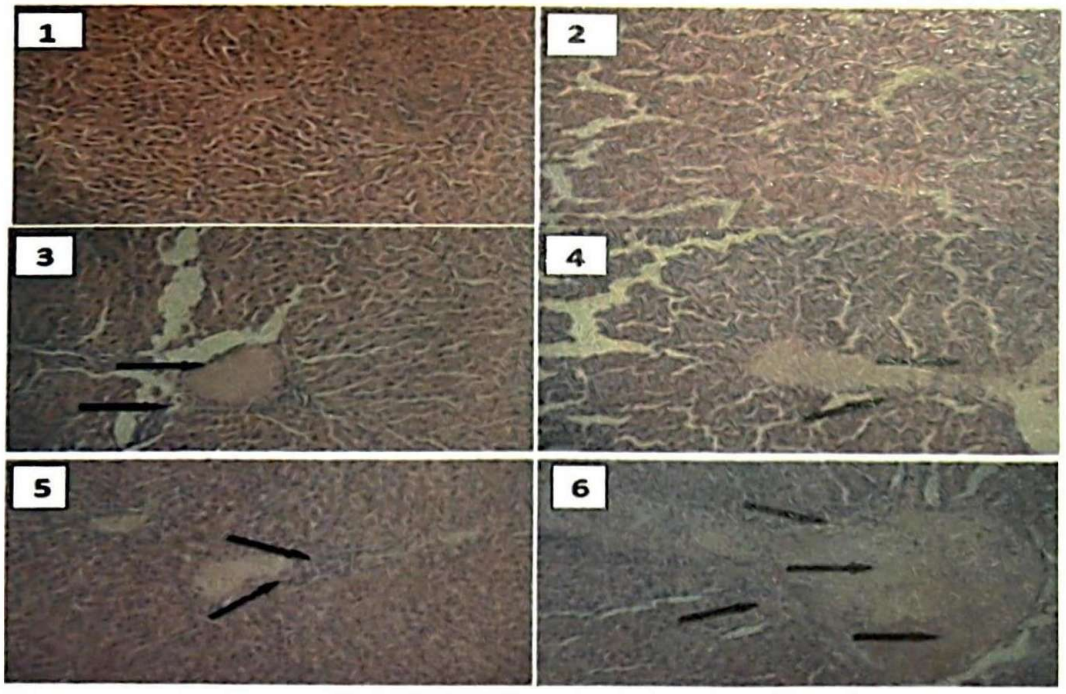

Fig. 9: Selected photomicrograph of the liver sections (x40) rats treated and untreated with DDVP. Negative control group (1) distilled water: no visible lesions seen. Negative control group (2) rats given corn oil only: no visible lesions seen. Rats treated 5 mg/kg DDVP (3): There is moderate portal fibroplasia and cellular infiltration by mononuclear cells. Rats treated with 10 mg/kg DDVP (4): There is mild to moderate periportal infiltration by mononuclear cells. Rats given 20 mg/kg DDVP (5): There is extensive and sinusoidal congestion with periportal and some extent of diffuse cellular infiltration. Positive control group (6) (Rats treated with 2.5 mg/kg sodium arsenite): There is very severe portal congestion, cellular infiltration and fibroplasia.

and control groups followed pattern similar to the findings for ãGT activity. Moreover, significant reduction ($p<0.05$) in total hepatic protein was observed in all the groups treated with sodium arsenite or DDVP compared with the negative control (Fig.7). On the other hand, lipid peroxidation, measured as µmol MDA/mg protein, increased significantly ($p<0.05$) in groups treated with sodium arsenite (group 6) and DDVP (at 10 mg or 20 mg/kg body weight) (groups 4 and 5) compared with the control. There was no significant difference ($p>0.05$) between groups treated with DDVP at 5 mg/kg and control (Fig.8).

The histological assessment for liver integrity showed that while groups 1 and 2 given distilled water and corn oil alone respectively had no visible lesion, rats treated with 5 mg/kg DDVP (group 3) showed a moderate portal fibroplasia and cellular infiltration by mononuclear cells. Rats treated with 10 mg/kg DDVP (group 4) showed a mild to moderate periportal infiltration by mononuclear cells. In rats given 20 mg/kg DDVP (group 5), there is an extensive and sinusoidal congestion with periportal and some diffuse cellular infiltration. In the positive control (group 6), treated with 2.5 mg/kg sodium arsenite, there is very severe portal congestion, cellular infiltration and fibroplasias (Figure 9).

The effect of DDVP treatment on rats' haematological parameters is shown on Table 1. Overall, administration of DDVP did not produce significant effects ($p>0.05$) on RBC counts, PCV and Hb values compare with the control given corn oil only. However, at all doses of DDVP, WBC increased significantly ($p<0.05$) compared with control (Table 1).

pesticide for the duration of exposure has no effect on the overall liver mass turnover.

It was observed that treatment with DDVP (at 10 and 20 mg/kg body weight) produced increased liver cell counts compared with the control, suggesting that the insecticide is able to promote hepatocytes proliferation. The induction of increased liver cell populations in the exposed animals may be an adaptation by the rats to get rid of the potentially toxic insecticides. Benford and others [17] have also demonstrated an enforced cell proliferative property of dichlorvos in B6C3F1 strain of mice. However, another research group [18] has reported DDVP induction of cell death *in vitro*. In addition, we observed that the administration of (DDVP) or sodium arsenite promotes significant ($p<0.05$) formation of micronuclei in the polychromatic erythrocytes (PCEs) of the rats bone marrow cells suggesting that DDVP caused chromosome aberrations and nuclear anomalies during mitosis. This is consistent with earlier observations made with sodium arsenite [11,19] and carbofuran [20]. Similar findings were also reported

Table 1: Effects of Dichlorvos on Haematological parameters of Wistar male rats

Groups	Treatment	RBC	WBC	PCV	Hb
1	Distilled water	7.30±0.14	7383.3±275.4	44.3±1.20	59.63±4.52
2	Corn oil	7.51±0.05	5533.33±464.6	45.33±1.15	15.6±0.1
3	5 mg/kg DDVP	7.75±0.13	10466.67±202.1#	44±1.73	13.93±0.95#
4	10 mg/kg DDVP	7.76±0.30	8566.67±208.2#	47±1.00#	15.43±0.15
5	20 mg/kg DDVP	8.41±0.27	7150±132.3#	49.67±2.89	17.1±1.15
6	2.5 mg/kg S.A.	8.11±0.31*	5850±475.2*	48.67±1.53	16.23±0.25*

*DDVP= 2, 2-dichlorovinyl dimethyl phosphate; S.A. = sodium arsenite. # = significantly different ($p < 0.05$) from control group 2. * = significantly different ($p < 0.05$) from control group 1. Values are means ± SD (n =5).*

Discussion

This study was designed to investigate hepatotoxicity and clastogenicity of high doses of DDVP in Wistar rats using sodium arsenite as standard toxicant [10,11]. Our findings showed a significant decrease in percentage body weight change in the groups treated with sodium arsenite and DDVP compared with the control groups. This suggests that DDVP or sodium arsenite, within the duration of the study, exert detrimental effects on the systemic activities in the body of experimental rats. Moreover, a loss of appetite was observed in the rats administered the chemicals. However, there was no significant difference in the relative liver weights between the groups of rats treated with sodium arsenite or DDVP compared with the control groups indicating that the in the culture of human peripheral blood lymphocytes with DDVP [21].

Serum enzymes, ãGT, ALP, AST and ALT, activities are used in the diagnosis of hepatic injuries and diseases, and elevation in the levels of these enzymes is an indication of a liver lesion [22-24]. The finding in the present study, showing that DDVP induces activities of the transaminases in treated groups of rats compared with the observation made with the control group, suggests that orally administered DDVP is hepatotoxic in the animals and causing damage to the liver cells resulting in the release of these enzymes into the blood. Moreover, histopathological analyses of the liver sections indicated that DDVP (and sodium arsenite) induced degeneration in the liver cells. Observations

range from a mild to severe periportal infiltration of mononuclear cells, an extensive and severe sinusoidal congestion, diffuse cellular infiltration, severe central venous and portal congestion and cellular infiltration and fibroplasia. Hepatotoxicity of DDVP in the aquatic organism, *Misgurnus anguillicaudatus*, has also been reported recently [25].

The observed total hepatic protein in the treated groups was found to be much lower than the control group. This finding is similar to earlier observation [26] which was reported as a significant decrease in protein level in *Channa gachua* exposed to DDVP. In addition, DDVP along with other insecticides have been reported to alter metabolism of proteins, glucose and fats [27]. Moreover, treatment with DDVP or sodium arsenite resulted in a significant increase in the level of lipid peroxidation products (TBARS) compared to the control groups. Several studies have also associated the toxicity of DDVP to its induction of oxidative stress [28-31].

Administration of DDVP did not produce significant effect on RBC count, PCV and Hb in the experimental rats ($p > 0.05$) compare with control. Significant decrease in mean corpuscular volume after five weeks of exposure to DDVP has been reported [32]. The disparities between the findings in this report and that of Edem and co-workers [32] may be due to differences in route of exposure and duration of exposure to DDVP. On the other hand, we recorded that DDVP at all doses enhanced the WBC counts ($p < 0.05$) compared with control group treated with corn oil only. This suggests that DDVP is recognised by the body defense as foreign or pathogenic leading to proliferation of WBC. This finding supports the carcinogenic potential of long term intoxication of DDVP [33].

In conclusion, the findings from this study suggest that DDVP has clastogenic and hepatotoxic effects in rats and may be carcinogenic long term. Considering the profile of toxicities of DDVP in experimental rats, it could constitute a big risk to human health. There is therefore an urgent need for strict regulatory control for the use of DDVP for food preservation, and effective monitoring system of its residues in stored products before they gain access to the consumers. This regulation will not only provide health safety measures but will enhance the international consumer confidence and provide a much needed thriving source of foreign exchange for developing countries.

Acknowledgments

We would like to thank Messrs E. Sabo, I. Adebiyi and O. Ajiboye for their technical assistant in the course of the research that generated the data in this article.

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