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Dimethoate-induced oxidative damage and biochemical changes in male rabbits

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ABSTRACT: Dimethoate is a commonly used in secticide for organophosphate and acaricide, used worldwide in agriculture, control of home pests, food safety and control of disease vectors. Manag ement of home rodents, food safety, and manage ment of disease vectors.The purpose of this study was to investigate dimethoate 's propensity to ind uce oxidative stress and changes in biochemical p arameters in male rabbits following oral exposure (3 months). Ten male New Zealand white rabbit randomly into two groups: (1): control group and (2): dimethoate treatment of rabbits. Exposure to dimethoate caused oxidative stress in plasma evidenced by an increase in the activities of blood plasma AST and ALT, (ɣ-GT) , TBARS and bilirubin while ALP were significantly ($P<0.05$) decreased compared with control group. The levels of, TC, TG, and LDL-c were significantly ($P<0.05$) increased, while HDL-c, were significantly ($P<0.05$) decreased in plasma.
Keywords: Dimethoate, thiobarbituric acid-reactive substances, enzyme activities, and New-Zealand white rabbits

I. INTRODUCTION

Wide spread use and disposal of organophosphorus compounds for pest control have resulted in the release of their residue into natural water, thus inducing an environmental problem and have been widely recognized as a health hazard[1]**.** Besides fatalities, caused by high dose, exposure of animals to low dose organophosphorus insecticides has been found to cause widespread effect on body including organ specific lesions in central nervous system[2]**,** liver[3]**,** kidneys and generalized effects like immunosuppression, teratogenesis, carcinogenesis and metabolic disorders[4]**.** Organophosphorus insecticide, dimethoate, is a systemic insecticide widely used in agriculture and domestic pest control[5]**.** It acts by interfering with the activities of cholinesterase activities and is toxic to insects, rodents, fish and humans[6]**.** Its chronic exposure has been associated with the critical increase in hepatopathy, nephropathy as well as diabetic mellitus in humans[7] and has been recognized as a possible human carcinogen[8]**.**

Several studies addressed the toxic effect of dimethoate on the functions of several mammalian organs including liver and kidney. Dimethoate was reported to alter the level of the marker parameters related to the liver and kidneys in rats and mice[3]**.** Significant increase in the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (ɣ-GT) as well as the decrease in the levels of cholinesterase, bilirubin, total protein and albumin in the serum were the major diagnostic symptoms of liver diseases in animals and human[9]**.** The increase in the uric acid and creatinine in the serum are the major symptoms of glomerular filtration damage[10]**.**

[11]found that daily oral administration of 20 mg/kg body weight dimethoate to males, adult Wistar albino rats caused hepatotoxicity as monitored by the increase in the levels of hepatic markers enzymes (ALT, AST, ALP and (ɣ-GT), as well as in bilirubin. Similarly,[12]**.** demonstrated significant increase in the levels of various serum marker enzymes of liver, including AST, ALT and ALP in response to oral administration of 1/50 LD_{50} dimethoate to guinea pigs. In addition,[13] showed that feeding of Wistar rats with dimethoate for two months induced a marked renal failure characterized by a significant increase in serum creatinine and urea levels.

II. MATERIALS AND METHODS

Materials

In this study dimethoate (purity 400g/L) was purchased from B &W agrochemichals

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(China). All other chemicals used in the experiment were of analytical grade. Mature male New Zealand White rabbits (age of 6 months and initial weight of (1.641 ± 27.2 Kg) were used. Ten mature male rabbits were randomly divided into couple equal groups (each five rabbits): Group I: Rabbits were used as control and received an equivalent volume of the vehicle (corn oil) alone by oral gavage daily for 12 successive weeks. Group II: Rabbits were treated with dimethoate. Dimethoate was given dimethoate daily by gavage at a dose of 43.2 mg/kg B.W/day (1/50 of DM) lethal dose[14], which dissolved in corn oil for 12 successive weeks

Blood and plasma sampling

At the conclusion of the test period, all rabbits were weighed at that point yielded beneath ether anesthesia.

Blood tests were collected in clean dry centrifuge tubes.. Plasma was separated by centrifugation at 3000 rpm for 10 minutes and then quickly frozen at -20°c for biochemical analysis.

Biochemical analysis

The other part of heparted blood samples were placed immediately on ice. Plasma was obtained by centrifugation of samples at 860 xg for 20 min, and was stored at -20°C until used for analyses. Stored plasma samples were analyzed for plasma total bilirubin was measured using the method of[15]. Gamma glutamyl transferase (**ɣGT)** using the method of Szasz/Persijn[16]. Plasma concentrations of cholesterol and triglycerides (TG) were determined according to the methods of[17] **and** [18]respectively. High-density lipoprotein (HDL) was determined according to the methods of[19]. Low-density lipoprotein (LDL) was determined by the calculation (cholesterol-(TG/5+HDL). Very low-density lipoprotein (VLDL) was calculated by dividing the values of TG by factor of 5.

The exercises of plasma aspartate transaminase (AST; EC 2.6.1.1) and alanine transaminase (ALT; EC 2.6.1.2) were tested by the strategy of Reitman and Frankel (1975).. Alkaline phosphatase (AlP; EC 3.1.3.1) activity was determined in plasma according to the method of [20]. Plasma thiobarbituric acid-reactive substances (TBARS) were measured by the method of [21].

Statistical analysis

Where applicable, statistical analysis was carried out in Minitab software; statistical significance was assessed using one way ANOVAanalysis.
After discovery ordinary dissemination to the information and suitable P<0.05consider note worthy.

III. RESULTS

Table 1 showed the overall means of the activities of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (AlP), gamma glutamyl transferase activity (ɣ-GT), Plasma thiobarbituric acid-reactive substances (TBARS) and bilirubin in blood plasma as affected by treatment with dimethoate throughout the 12-week experimental period. Treatment with DM resulted in significant (P<0.05) increase in the activities of blood plasma AST and ALT, (ɣ-GT) , TBARS and bilirubin while ALP were significantly (P<0.05) decreased compared with control group. Tables 2 illustrated the effect of dimethoate (DM) on the levels of total cholesterol (TC), triglyceride (TG), very low-density lipoprotein, high and low-density lipoprotein-cholesterol (HDL-c and LDL-c) in blood plasma of male rabbits. The levels of, TC, TG,and LDL-c were significantly (P<0.05) increased, while HDL-c, were significantly (P<0.05) decreased in plasma of rabbits treated with DM as compared with control group.

Table 1: Changes in the activities of plasma enzyme and the level of thiobarbituric acid-reactive substances (TBARS) of male rabbits treated with dimethoate

Parameters	**Animal Groups**	
	Control	**DM**
AST (U/L)	43.083 ± 0.460^{b}	46.890 ± 0.700^{a}
ALT (U/L)	46.191 ± 0.67^{a}	48.62 ± 1.14^{a}
ALP (U/L)	142.55 ± 0.79^{b}	135.81 ± 1.05^{b}
ɣ-GT (U/L)	7.1680 ± 0.066^{b}	7.5453 ± 0.114^{a}

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Bilirubin (mg/dl)	1.569 ± 0.009^{b}	1.650 ± 0.010^{a}
TBARS (nmol/ml)	1.684 ± 0.027^{a}	1.6637 ± 0.073^{a}

Values are means ± SEM of 5 rabbits in each group. Mean with different letters **(a- d)** are significantly difference ($p \leq 0.05$) at same raw. Mean with the same letters (a-d) are non-significantly difference ($p \geq 0.05$).

AST, aspartate amino transferas; ALT, alanin amino transferas; AlP, alkline phosphatase; **ɣ-GT,** gamma glutamyl transe activity; **T**BARS, thiobarbituric acid-reactive substances.

Table 2: Plasma lipid profiles of male rabbits treated with dimethoate

Parameters	**Animal Groups**	
	Control	**DM**
Cho	120.10 ± 1.925^{bc}	121.76 ± 1.812^{a}
TG	56.11 ± 1.007^{a}	59.12 ± 0.590^{a}
HDL	57.11 ± 1.007^{a}	54.01 ± 0.466^{b}
LDL	64.27 ± 1.22^{a}	65.89 ± 2.66^{a}
VLDL	11.42 ± 1.22^{a}	11.82 ± 2.66^{a}

Values are means ± SEM of 5 rabbits in each group. Mean with different letters **(a- d)** are significantly difference ($p \leq 0.05$) at same raw. Mean with the same letters (a-d) are non-significantly difference ($p \geq 0.05$).

Cho., cholosterol; TG, triglycerides; HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very low density lipoprotein.

IV. DISCUSSION

Data presented in this study showed that the mean levels of serum ALT, AST and ALP in the dimethoate-treated rabbits were significantly higher than those in the controls. Such elevation of liver enzymes as a result of dimethoate administration was documented by other authors[12,22-24]

Liver is the center of biotransformation and detoxification of foreign compounds and is the most vulnerable to the chemical assaults such as dimethoate poisoning[12,25,26]. Serum ALT, AST and, ɣ-GT are considered to be among the most sensitive markers employed in the diagnosis of hepatotoxicity[11,27]. Pesticide presentation causes liver harm and spillage of cytosolic proteins from hepatocytes and other body organs into blood[28,29]. Elevation of liver enzymes may also be due to increased gene expression due to long term requirement of detoxification of pesticides[30].

In contrast to elevation of transaminases, ɣ-GT and ALP was markedly decreased in dimethoate-treated rabbits compared to controls. Such inhibition in ChE in response to organophosphorus dimethoate administrated was obtained by[26,31].

Elevation in aminotransferases and phosphatases were observed in liver of female albino rats treated with organophosphates methyl parathion, monocrotophos and dimethoate[32]. The liver useful transaminases (AST and ALT) and antacid phosphatase(Highmountain) proteins action in serum are most habitually measured for determination ofliver maladies especially infe ctivehepatitis,alcoholiccitrrhosis,biliary obstacle, harmful hepatitis and liver cancer[33].

The previous liver utilitarian proteins are not discharged into the blood, any rise of their exercises inbloodis broughtabout from spilla ge of liver harm cells and from the disturbance and dysfunctions in lever functional enzymes[23]. Similarly, Triazophos and quinlophos also caused increasein liver enzymes[5.34]. In the present study oral administration of dimethoate caused gradual increase in bilirubin level throughout the experiment. Such increase was reported previously by[11,23,35] in dimethoate-intoxicated rats. The change in serum bilirubin which is accepted as indicator of liver function may provide further evidence on hepatotoxicity induced by the organophosphorus insecticide dimethoate[9,11].

Pesticides generally cause an increase in total cholesterol level[36]. In this think about, dimethoate caused an increment within the serum add up to cholesterol level.. Increased serum cholesterol can be attributed to the effects of the pesticide on the permeability of liver cell membranes[37]. Moreover, the increment within the level of serum add up to cholesterol may be ascribed to the blockage of the liver bile channels, causing a lessening or cessation of cholesterol discharge into the duodenum[33]. An increment within the serum cholesterol level may be a sign of liver harm[38]. In the present study, dimethoate caused decreases in the triglyceride and VLDL-cholesterol levels. Clinically, in parenchymal liver diseases, levels of these parameters decrease. Some different pesticides cause a decrease in the VLDL-cholesterol and triglyceride levels[36].

In conclusion,

The findings of this study indicate that it can be concluded that exposure of animals to di methoate is capable of inducing major hazardous lipid peroxidation alterations and certain biochem ical parameters.

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