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Alteration in Protein Metabolic Profiles in Liver Tissue of Rats during Dimethoate Toxicosis

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Abstract: *Dimethoate is the widely used organophosphorous insecticides in agriculture. The irrational use of Dimethoate in Yemen play a crucial role in the occurrence of many diseases affecting plants, animals and man. Dimethoate (DM) is used to kill mites and aphids among other insects and is applied on citrus, cotton, fruit, olives, potatoes, tea, tobacco and vegetables. The aim of the present work was to study biochemical changes that might occur in the liver of albino rats as a result of DM intoxication. In the present investigation the animals were treated with 1/10th of LD_{50} of DM via oral gavage (34.5mg/kg body weight. The first group animals were considered as control animals. Second group of animals were treated with Dimethoate via oral gavage (34.5mg/kg body weight which is 1/10th of LD_{50}) for 10 days, third and fourth groups of animals were administered for 20 and 30 days with an interval of 48h respectively. The DM treated groups are AST and ALT was selected in the present investigation showed an increment. The present findings indicate that chronic exposure to DM has clear toxic effect on the liver of albino rats.*

Key Words: *Dimethoate, Albino rat, liver, protein metabolic profile.*

I. Introduction

The control of insect pests relies heavily on the use of synthetic insecticides. But, their widespread use has led to some serious problems including toxic residues on grass and toxicity to non-target organisms such as mammals, birds and fishes **(**Zetter and Cuperus 1990: White 1995: and Riebeiro et al., 2003). OP compounds are currently among the most frequently used pesticides worldwide (Heudorf et al. 2006). The pollution of the environment plays a crucial role in the occurrence of many diseases affecting plants, animals and man. One of the main factors causing pollution of the environment is the irrational use of organophosphorus insecticides (Al-Haj et al., 2005). Toxicity of these OP compounds results in negative effects of many organs like liver, heart, kidney, nervous system and reproductive system (Ferah Sayim, 2007). Symptoms of acute poisoning of DM are common with all other OPs and revolve around cholinesterase inhibition. DM is highly mobile in the soil, labeled as a class II Moderately Toxic insecticide by (EPA) and is somewhat persistent, and is not often found in large quantities in water. It is however, highly toxic to honeybees, moderately to highly toxic to birds, and moderately toxic to aquatic organisms. DM is a widely used OP used to kill mites and aphids among other insects and is applied on citrus, cotton, fruit, olives, potatoes, tea, tobacco and vegetables. For humans, the main groups at risk of high rates of DM exposure are pesticide producers, pesticide workers and farm owners (Sharma et al. 2005). Dimethoate is an insecticide with anticholinesterase mode of action (De-Bleecker et al., 1993; and Dongren et al., 1999). Many alterations have been observed in organs of animals due to the organophosphorus insecticides (Betrosian et al., 1995; and Senanayke1998), specially CNS, (Desi et al., 1998; and Lengyl et al., 2005), liver (Gomes et al., 1999), and kidney (Kossmann et al., 1997).

The liver is the primary organ involved in xenobiotic metabolism and is a major target organ of OPs and drugs. Hence in the present study hepatotoxicity of DM was studied. Clinical biochemistry and hispathological evaluations are commonly used methods for detecting organ-specific effects related to OP exposure (Crissman et al. 2004). Begum and Vijavaraghaven (1995) observed that, the exposure of Dimethoate to the fresh water fish claries batrachus reduced the carbohydrate and proteins metabolism, and affect the aminotransferase activity in the liver. JYostana et al (2003), observed a significant biochemical and hematological alterations due to the exposure to the various pesticides. Significant damage in the hepatic cells glucose metabolism in liver was observed as the result of Diazionon administration (Fatima et al., 2006).

Despite DM's extensive use in crop protection and in the household, information on its health effects is still scarce. Sharma et al (2005) studied the effect of DM on the oxidative stress in albino rats. Sivapriya et al. (2006) studied the effect of DM in the liver and kidney of albino rats. Ferah Sayim (2007) studied the histopathological changes in the liver in DM exposed rats. Yahya et al. (2012) studied the effect of DM induced oxidative stress and morphological changes in the liver of guinea pig. Devi Srilakshmi Kala et al. (2013) studied the effect of DM on different regions of the brain in the albino rat.

II. Material and Methods

Test Chemical: Dimethoate Technical (94%) pure in crystalline form was obtained from Hyderabad chemical limited, Hyderabad A.P., India.

Animal model: Male adult Albino rat of 7 weeks old and aged 200 ± 20 g. were obtained from Indian Institute of Science (II.Sc.), Bangalore. They were housed at an ambient temperature 28 ± 2°C in a 12-h light/dark cycle and a minimum humidity of 40%. The animals had free access to commercial pellet diet supplied by Sai Durga Feeds and Foods, Bangalore, India and water ad libitium.

Experimental Design:

All the male healthy adult male albino rats were randomly divided into four groups having with six rats per group. The first group animals were considered as control animals. Second group of animals were treated with Dimethoate via oral gavage (34.5mg/kg body weight which is $1/10^{th}$ of LD_{50}) for 10 days, third and fourth groups of animals were administered for 20 and 30 days with an interval of 48h respectively.

Estimation of Aspartate aminotransferase (AST)

The activity of aspartate aminotransferase (AST) was assayed by the method described by Bergmeyer and Bernt (1965**).** 2 % w/v tissue homogenates of the selected tissues were prepared in 0.25 M ice cold sucrose solution. The homogenates were centrifuged at 1000xg for 15 minutes and supernatant was used for the enzyme assay. The incubation mixture of 2.0 ml contained 100 μ moles of phosphate buffer (Na_2HPO_4 + NaH_2PO_4) (pH 7.4), 100μmoles of L-aspartatic acid, 2 μ moles of α-keto glutarate and 0.5 ml of supernatant as enzyme source. After incubation for 30 minutes at 37°C, the reaction was stopped by the addition of 1 ml of ketone reagent (0.001 M, 2,4-dinitrophenyl hydrazine solution in 1 N HCl) and the contents were allowed to stay at laboratory temperature for 20 minutes. After 20 minutes of 10 ml of 0.4 N NaOH was added. The developed color was read at 545 nm in a spectrophotometer against a reagent blank.

Estimation of Alanine aminotransferase (ALT)

The activity of alanine aminotransferase (ALT) was assayed by the method of described by Bergmeyer and Bernt (1965**).** The incubation mixture of 2 ml contained 100 μ moles of DL-alanine, 100 μ moles of phosphate buffer (pH 7.4), 2 μ moles of α-ketoglutarate and 0.5 ml of the supernatant of the homogenate 2% w/v prepared in 0.25 M ice-cold sucrose solution, as enzyme source. The reaction mixture was incubated at 37°C for 30 minutes. The reaction was stopped by the addition of 1.0 ml of 2, 4-dinitrophenyl hydrazine solution prepared in 1 N HCl (ketone reagent). The color was developed by the addition of NaOH as described above for AST. The optical density was measured at 545 nm in a

Statistical treatment: The data was subjected to statistical treatment. One way analysis of variance (ANOVA) and S-N-K tests were performed using SPSS (ver. 12) in the personal computer and $p < 0.05$ was considered as statistically significant.

III. Results:

The results of protein metabolic profile of the control and experimental rats under Dimethoate are mentioned in Table (1 and 2.) the activities of ALT and AST the experimental rats exposed to Dimethoate showed statistically significant ($P < 0.01$) increased. Alteration in protein metabolic profiles was in the form of a dose – and time- dependent manner in treated rat liver tissues. Since proteins are involved in the architecture and physiology of the cell, they appear to occupy a key role in cell metabolism (Murray et al., 2007). Catabolism of proteins and amino acids make a major contribution to the total energy production in rats. Can be correlated with this fact. These results are in agreement with the earlier report of David et al. (2004), who demonstrated a similar situation in Cyprinus carpio exposed to Dimethoate.

ALT and AST enzymes are called the transferase enzymes, which are synthesis of amino acids and lysis of the amino acids. The elevation of AST and ALT activities observed in this study (Table1and 2). Offers an excellent corroboration of the above trend. This is a clear indication of shunting of amino acids into TCA cycle through oxidative deamination and active transamination. The status of protein metabolic profiles changes in liver tissues in the present study corroborates the findings of Begum et al. (2007**)** and Nagarjuna et al. (2008). At repeated dose levels of Dimethoate administered orally, a damaging effect on the cell metabolism occurs, thereby leading to impaired protein synthetic machinery. In conclusion, it can be stated that long term exposure to sub lethal doses of pyrethroid pesticides can result in cell metabolism toxicosis.

Table. 1 Changes in the Aspartate Aminotransferase in different tissues of Albino rats exposed to sub-lethal dose of Dimethoate

Tissues	Control	10 days	20 days	30 days	F ratio
Liver	1.235	1.545	1.602	1.855	8.074*
± SD	0.115	0.151	0.144	0.175	
(% Change)		(25.10)	(29.71)	(50.20)	
Heart	0.535	0.582	0.712	0.726	9.339*
± SD	0.043	0.048	0.075	0.063	
(% Change)		(8.78)	(33.08)	(35.70)	
Kidney	0.412	0.511	0.575	0.623	12.458*
± SD	0.033	0.052	0.055	0.059	
(% Change)		(24.03)	(39.56)	(51.21)	
Pancreas	1.015	1.125	1.411	1.623	50.533*
± SD	0.115	0.125	0.155	0.158	
(% Change)		(10.84)	(39.01)	(59.90)	

Values expressed in mg protein/g. wet weight of the tissue are Mean ± SD of six individual observations. Values in the parenthesis indicate % change over control. Mean values with the same superscript do not differ among themselves through S-N-K test.
*P < 0.01, **P<0.001

Table. 2 Changes in the Alanine Amino transferase in different tissues of Albino rats exposed to sub-lethal dose of Dimethoate

Tissues	Control	10 days	20 days	30 days	F ratio
Liver	7.128	8.677	8.988	11.500	10.161*
± SD	0.688	0.812	0.755	1.105	
(% Change)		(21.73)	(26.09)	(61.33)	
Heart	4.463	5.169	5.488	7.125	11.852*
± SD	0.325	0.488	0.512	0.699	
(% Change)		(15.82)	(22.97)	(59.65)	
Kidney	5.046	5.688	6.284	7.126	12.271*
± SD	0.423	0.512	0.564	0.703	
(% Change)		(12.72)	(24.53)	(41.22)	
Pancreas	6.885	7.850	8.650	9.330	11.114*
± SD	0.612	0.655	0.788	0.869	
(% Change)		(14.02)	(25.63)	(35.51)	

Values expressed in mg protein/g. wet weight of the tissue are Mean ± SD of six individual observations. Values in the parenthesis indicate % change over control. Mean values with the same superscript do not differ among themselves through S-N-K test.
*P < 0.01, **P<0.001

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