Advance Research in Agriculture and Veterinary Science
Adv. Res. Agri. Vet. Sci. Vol. 1, No. 1, 2014: 44-46
Academy for Environment and Life Sciences, India
Available at www.aravs.org

ORIGINAL ARTICLE

TOXICITY AND BIOCHEMICAL EFFECT OF ZIRAM IN WISTAR RAT

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KEYWORDS
Ziram,
Biochemical,
Acute,
Subchronic,
LD50,
Wistar Rat.

Article History:
Received on
20 Jan 2014

Accepted on
27 Jan 2014

Published on
10 Feb 2014

ABSTRACT: Ziram, a dithiocarbamate fungicide was used for estimation of acute toxicity (LD50) and effect of ziram on biochemical parameters protein and lipids in serum of Wistar rats. LD50 was estimated by log-dose/ probit regression method. Rats were administered dose orally equivalent to LD25 for acute (1 and 2 day) and LD5 for subchronic (15, 30 and 60 day) treatment, through gabage tube. Control was also run for each treatment simultaneously. Biochemical analysis show the increase in total protein and albumin while decrease in case of globulin. Alteration in biochemical parameter resulted imbalance between protein synthesis and utilization.

INTRODUCTION

India's economy is based on agriculture. In agricultural developmental process the use of pesticide work as an agent to kill or control undesired pests, such as insects, weeds, rodents, fungi and other organism, which increases the food production reported by Abhilash and Singh, (2009). Wide spread use of pesticides in agriculture has increases the intoxication to mammals.

Dithiocarbamate fungicides are used in agriculture for protection of crop and seeds from fungi as Franekic *et al.*, (1994). Ziram, a dithiocarbamate is also used to treat a variety of fungal disease of potatos, nuts, some fruits and grains. Human exposure of ziram may occur orally by ingesting treated crop or by inhalation proposed by Caldas *et al.*, (2001). Very few studies are published on the effect of ziram exposure and its effect on mammals.

The present study is aimed to the lethal toxicity and biochemical effect of ziram after short and long duration exposure on protein and lipid contents of serum in mammals (Wistar rats).

MATERIAL AND METHODS

Wistar albino rats [*Rattus norvegicus* (Berkenhout)] have been selected from inbred colony. Healthy adult rats of almost equal size and weight (120±5) irrespective of sexes were selected randomly. The rats were maintained in polypropylene cages and acclimatized at temperature 25±5^{0}c, relative humidity 60±5% and a photoperiod of 12 hr/day. The rats were provided food and water *ad libitum*.

Ziram [zinc bis (dimethyldithiocarbamate)] was purchased from FIL Industries Ltd. Jammu in powder form and a solution was made in warm ground nut oil.

LD_{50} of ziram has been estimated by log-dose/probit regression line method given by Finney, (1971). Biochemical assessment has been done after acute (1 and 2 days) and sub-chronic (15, 30 and 60 days) treatments. LD_{25} dose(694.77mg/kg b.wt.) was introduced orally through gavage tube for acute treatment, once and effect was observed after 24 hr and 48hr. LD_5 dose (284.31mg/kg b.wt.) was introduce for sub-chronic 60 days treatment and effect was observed after 15th, 30th and 60th days exposure. Ground nut oil was used as vehicle. Controls run for each treatment with same amount of vehicle *i.e.* ground nut oil. Recovery assessment for acute and sub-chronic treatment was carried out for 7 and 45 days simultaneously. Rats were sacrificed by chloroform anesthesia. The

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serum total protein was estimated by Biuret method described by Henry *et al.*, (1974), total lipid was estimated by method described by Zollner and Kirsch, (1962), serum cholesterol was estimated by the method of Wybenga and Pileggi, (1970), serum Triglyceride was estimated by GPO-PAP method described by Schettler and Nussel, (1975) and HDL was estimated by the Wybenga and Pileggi, (1970). The experimental data were analyzed for mean value and standard error (Mean ± SE) for all groups, and comparison made by one way parametric ANOVA and followed by HSD Tukey test.

RESULT AND DISCUSSION

The estimated LD_{50} of ziram after experiment was found to be 1305 mg/kg body weight, which was dose dependent. LD_{50} of ziram (fungicides) was reported 1400 mg/kg body weight as describe by Gupta and Agrawal, (2007), which is nearly same and support the present finding.

The result of effect of ziram exposure on protein and lipid contents was observed (table 1). Total protein and albumin level in serum decrease significantly after acute and sub-acute treatment with compare to control value, whereas increase in serum globulin is observed at highly significant level with compare to control.

Mohsen, (2000) reported that mancozeb fungicides at different doses induced a significant decrease in the level of serum protein content. The decrease in total protein might be due to decreased rate of protein synthesis by inactivating several different transcription factor reported by Haddad, (2002). Lambda-cyhalothrin-intoxicated rabbits showed increase in their total protein and albumin in serum described by Basir *et al.*, (2011). Al-Amaudi, (2012) observation also supports the present findings who observed the decreased level of total protein and albumin after exposure of metalaxyl fungicides on albino rat.

Findings show significant increase in total lipid and total cholesterol after acute and subacute ziram treatment on rat. Hyperlipidemia and hypercholestremia may be due to acceleration of acetyl-CoA, which is known to be the precursor of cholesterol biosynthesis proposed by Al-Amaudi, (2012). An elevated amount of cholesterol was observed in rats after treated with carbamate fungicides by Veerappan *et al.*, (2011). Result of present study also reveals a significant increase in triglyceride, VLDL and non-significant increase in LDL. A significant decrease was found in HDL after ziram fungicides treatment in both acute and subacute exposure. The observed alterations in serum biochemical parameters after ziram intoxication are suggestive of liver dysfunction in rats.

Table 1: Serum biochemical changes after Ziram treatment on rats

parameter	treatment	1 day	2 day	7 day (R)	15 day	30 day	60 day	45 day (R)
Total protein (g/dl)	Control	6.32 ± 0.74	6.37 ± 0.45	6.87 ± 0.38	6.46 ± 0.38	6.56 ± 1.32	6.63 ± 0.43	6.28 ± 0.40
	Treatment	6.13 ± 0.46^{c}	5.54 ± 0.75^{a}	6.89 ± 0.69^{c}	6.23 ± 0.62^{b}	5.87 ± 0.75^{a}	6.18 ± 0.78^{b}	6.09 ± 1.10^{c}
Albumin (g/dl)	Control	3.65 ± 0.72	3.93 ± 0.30	3.84 ± 0.64	4.13 ± 0.45	4.06 ± 0.34	4.25 ± 0.75	3.46 ± 0.12
	treatment	3.00 ± 0.37^{b}	3.08 ± 0.60^{b}	3.80 ± 0.34^{c}	4.20 ± 0.62^{c}	4.24 ± 0.42^{c}	3.42 ± 0.46^{b}	3.41 ± 0.26^{c}
Globulin (g/dl)	Control	2.67 ± 0.28	2.44 ± 0.75	3.04 ± 0.82	2.33 ± 0.96	2.50 ± 0.61	2.38 ± 1.03	2.82 ± 0.64
	Treatment	3.10 ± 0.37^{b}	2.46 ± 0.57^{c}	3.09 ± 0.46^{c}	2.03 ± 0.60^{b}	1.63 ± 0.53^{a}	2.76 ± 0.88^{b}	2.68 ± 1.02^{b}
Total lipid (mg/dl)	Control	303.08 ± 7.73	312.60 ± 4.71	297.36 ± 2.45	325.07 ± 2.92	320.97 ± 1.16	342.08 ± 3.88	335.65 ± 1.54
	Treatment	426.37 ± 3.5^{b}	486.42± 4.11^{b}	318.47 ±3.55^{c}	439.24 ± 4.02^{b}	498.52 ±3.08^{b}	594.18 ±2.58^{a}	368.72 ± 2.85^{c}
Total cholesterol (mg/dl)	Control	117.11 ± 0.99	118.25 ± 0.97	119.81 ± 0.95	120.12 ± 0.46	119.07 ± 0.96	118.59 ± 1.32	121.67 ± 1.62
	Treatment	146.25 ± 1.34^{b}	126.78 ±1.25^{c}	114.10 ± 1.10^{c}	177.39 ± 2.08^{b}	156.45 ±1.65^{b}	226.38 ±1.36^{a}	128.62 ± 1.78^{c}
Triglyceride (mg/dl)	Control	97.60 ± 1.03	101.58 ± 0.91	97.28 ± 1.06	103.50 ± 0.99	96.42 ± 0.85	90.47 ± 0.83	95.37 ± 0.93
	Treatment	146.52 ± 1.46^{b}	164.11 ±1.65^{b}	95.62 ± 1.86^{c}	107.28 ± 2.06^{c}	156.62 ±1.78^{b}	171.68 ±2.08^{b}	99.47 ± 2.16^{c}
VLDL (mg/dl)	Control	19.52 ± 0.73	20.28 ± 0.51	19.46 ± 0.86	20.70 ± 1.09	19.22 ± 0.65	17.87 ± 1.03	19.07 ± 0.43
	Treatment	28.67 ± 0.67^{b}	32.49 ± 1.06^{b}	19.34 ± 0.93^{c}	20.78 ± 0.76^{c}	31.53 ± 0.47^{b}	35.05 ± 0.38^{a}	20.38 ± 1.04^{c}
HDL (mg/dl)	Control	44.75 ± 0.87	44.84 ± 0.90	45.62 ± 1.21	48.46 ± 0.84	47.87 ± 0.48	43.53 ± 0.74	50.08 ± 0.74
	Treatment	42.62 ± 0.75^{b}	44.31 ± 0.86^{c}	44.42 ± 1.02^{c}	42.32 ± 1.40^{b}	44.42 ± 0.88^{b}	40.49 ± 0.89^{b}	49.98 ± 0.89^{c}
LDL (mg/dl)	Control	52.84 ± 0.34	53.13 ± 1.45	54.73 ± 2.05	50.96 ± 1.62	51.98 ± 0.82	57.19 ± 1.48	52.52 ± 0.86
	Treatment	73.96 ± 2.17^{c}	49.98 ± 2.20^{c}	50.34 ± 1.40^{c}	114.29 ± 0.96^{a}	80.50 ± 1.33^{b}	150.84 ±2.55^{a}	58.26 ± 2.60^{c}

Each value is a mean ± SE, n = 5, Statistical difference from control: a= highly significant at P<0.01, b= significant at P<0.05, c= non-significant at P>0.05, general mean= average mean of each treatment days.

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