

CARTAP AND CARBOFURAN INDUCED ALTERATIONS IN SERUM LIPID PROFILE OF WISTAR RATS

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ABSTRACT

Wistar rats of 6-8 weeks in age weighing between 120-150 g were exposed to the fixed doses of each of the carbamate pesticides such as cartap (50% LD₅₀) and carbofuran (50% LD₅₀) as well as a combination of these two with 25% LD₅₀ of each for one week. The effect of treatments was studied in terms of serum lipid parameters such as high-density lipoprotein, total cholesterol, triglyceride, low-density lipoprotein and very low-density lipoprotein. Treatment with individual doses of carbofuran (50% LD₅₀) and cartap (50% LD₅₀) caused significant alterations in the levels of serum lipid parameters. The pesticides treatment resulted in marked decrease in the level of serum high-density lipoprotein where as that of other lipids got significantly elevated. Further, the rats exhibited relatively higher impact of pesticides when treated with the compounds in combination (25% LD₅₀ of each). The results indicated that these compounds when used together may exert enhanced effect on the levels of serum lipids in rat.

KEY WORDS

Cartap, Carbofuran, Lipid, Triglyceride, Wistar rats.

INTRODUCTION

Carbamate pesticides are extensively used in agriculture due to their rapid degradability and low toxicity to non-target species. Their widespread and indiscriminate application poses serious health hazard to humans and animals (1). Carbamates have been reported to have high mammalian toxicity, and the main target organs are brain, liver, skeletal muscles, and heart (2, 3). Their primary mechanism of toxicity is the reversible inhibition of serine group of acetylcholinesterase via carbamoylation at the nerve terminals (4).

In addition to inhibition of acetylcholinesterase activity, carbamates affect many nonspecific sites. Liver is the primary site involved in the metabolism of various drugs and chemicals

including carbamates (5). In addition, kidney and reproductive functions have been reported to be adversely affected with carbamate exposure to rats (6, 7). Cholesterol and triglyceride levels have been reported to be elevated in liver after carbofuran exposure (8). Another anticholinesterase compound, chloropyrephos has been reported to cause hyperlipidemia in rats (9).

Lipophilic nature of carbamates may render them with the ability to interact with the serum and tissue lipids. Carbamates have been reported to cause alterations in the levels of total serum lipids, glucose and protein levels in rats (10). Moreover, in India and many other developing / developed countries the application of pesticide cocktails takes place. Keeping aforementioned facts the current study was aimed to determine effect of two carbamate pesticides on serum lipid parameters by exposing the rat with these compounds individually and also in combination to assess if there are any individual as well as additive or synergistic effects in this experimental animal.

MATERIALS AND METHODS

Animals: Male albino rats (Wistar strain) weighing between

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120 and 150 g inbred in the Central Animal House of the University were used. Animals were housed in polypropylene cages, fed with standard pellet diet (Ashirwad Industries, Kharar, India), and had free access to drinking water. Carbofuran (technical grade, purity 99.8%) was a kind gift from Rallis India Limited (Bangalore, India). The protocols used in the study were according to the guidelines for use and care of laboratory animals and were approved by the institutional ethics committee. Animals were divided into four groups as following:

Group 1: Animals in this group received 0.5 ml of groundnut oil orally for 1 week; Group 2: Animals in this group-received cartap (CT) 195 mgkg⁻¹ equivalent to 50% of its LD₅₀ dissolved in 0.5 ml of groundnut oil orally for 1 week; Group 3: Animals in this group-received carbofuran (CF) 4 mgkg⁻¹ equivalent to its 50% LD₅₀ dissolved in 0.5 ml of groundnut oil orally for 1 week; Group 4: Animals in this group received a combination of cartap (CT) 97.5 mgkg⁻¹ and carbofuran (CF) 2 mgkg⁻¹ each equivalent to its 25% LD₅₀ dissolved in 0.5 ml of groundnut oil orally for 1 week.

Biochemical Assays: Blood samples were collected in sterile eppendorf tubes from the tail vein of the rat. Serum was separated after coagulation of blood. Serum lipids, total cholesterol (TC), high density lipoprotein (HDL) cholesterol and triglyceride (TG) levels in serum were measured spectrophotometrically by the method described elsewhere (14-15) using standard kits of Bayer Diagnostics India Limited. However, very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) cholesterol were calculated by Friedwald's formula: (VLDL = TG/5 and LDL = TC - VLDL + HDL) (16).

Statistical Analysis: The values were expressed as mean ±

SD. The data were subjected to one way ANOVA followed by a post hoc Newman-Keuls Multiple Comparison Test for comparison between groups and values having p < 0.05 were considered significant.

RESULTS AND DISCUSSION

Cartap and carbofuran pesticides when administered individually as well as in combination caused significant alterations in the serum lipid profile. The data from Tables 1 and 2 reflected marked alterations in the levels of different serum lipids. The serum HDL was found to be decreased by 24, 20 and 36% due to CT, CF and CT+CF treatment in group 2, 3 and 4, respectively. However, serum triglyceride (TG) level got elevated by about 16 % in CT and CF treated groups. The CT+CF treated group exhibited a drastic increase (87%) in the level of serum TG. The total cholesterol (TC) concentration in the rat serum was found to be enhanced by 25 and 16% in the CT and CF treated groups, respectively. The CT+CF group on the other hand reflected an increase of 31% in TC level. A very sharp increase of 84% was observed in the level of serum low density lipoprotein (LDL) due to CT treatment. The treatment with CF could cause relatively small increase (21%) in the level of serum LDL. The treatment of rat with a combination of CF and CT (CF+CT) exhibited significant increase (46%) in the serum LDL content. The VLDL concentration got elevated by 17, 16 and 25% CT, CF and CT+CF treated groups, respectively. The changes observed in present investigation indicated an elevation of lipid profile in rats exposed to different sub lethal doses of the pesticides. The effect of these compounds was more marked when the pesticides were used in combination than their individual treatments. Hyperlipidemic effect has also been reported in

Table 1: Effect of carbamate pesticides levels in Wistar rats treated for seven days (carbofuran and cartap) on the serum lipid profile

| Pesticide Treatment (mg kg ⁻¹ body wt.) | HDL (mg/dl) | | Triglycerides (mg/dl) | | Total Cholesterol (mg/dl) | |
|---|--------------|----------------------------|-----------------------|-----------------------------|---------------------------|------------------------------|
| | Day 1 | 1 Week | Day 1 | 1 Week | Day 1 | 1 Week |
| Group 1 | 24.95 ± 3.82 | 25.32 ± 5.23 ^{ns} | 136.65±9.39 | 137.89 ± 8.58 ^{ns} | 174.88 ± 8.92 | 170.16 ± 10.31 ^{ns} |
| Group 2 Cartap (195) | 23.58 ± 4.17 | 17.89 ± 5.1 ^a | 136.69±10.02 | 158.67 ± 8.32 ^a | 158.78 ± 8.31 | 198.68 ± 10.39 ^a |
| Group 3 Carbofuran (4) | 22.98 ± 3.42 | 18.49 ± 2.64 ^a | 138.72 ± 8.39 | 160.31 ± 7.56 ^a | 166.77 ± 9.8 | 193.54 ± 12.4 ^a |
| Group 4 Cartap (97.5) + Carbofuran(2) | 22.08 ± 4.0 | 14.11 ± 3.7 ^b | 137.16 ± 10.7 | 170.58 ± 7.9 ^c | 159.17 ± 6.42 | 209.03 ± 10.7 ^b |

Serum lipid concentrations have been monitored spectrophotometrically as described in Materials and Methods section. The values represent the average of three independent experiments. The pesticides doses when used independently represent 50% of their respective LD₅₀ values, whereas in combination 25% of their LD₅₀ value has been used. ^{ns} Represents day 7 values, not significant from the corresponding values at day 1. ^a Corresponds to the day 7 value significantly different from its corresponding value on day 1 @ p<0.001. ^b Represents the day 7 value significantly different from its corresponding value on day 1 @ p<0.01 and ^c denotes day 7 value significantly different from its corresponding value on day 1 @ p<0.05.

Table 2: Effect of carbamate pesticides levels in Wistar rats treated for seven days (carbofuran and cartap) on the serum lipid profile

| Pesticide Treatment (mg kg ⁻¹ body wt.) | LDL (mg/dl) | | VLDL (mg/dl) | |
|---|----------------|----------------------------|--------------|---------------------------|
| | Day 1 | 1 Week | Day 1 | 1 Week |
| Group 1 | 122.86 ± 7.53 | 114.27 ± 5.7 ^{ns} | 27.07 ± 5.32 | 27.57 ± 3.4 ^{ns} |
| Group 2 Cartap (195) | 108.07 ± 7.53 | 199.10 ± 9.32 ^a | 27.13 ± 4.53 | 31.73 ± 5.1 ^a |
| Group 3 Carbofuran (4) | 116.05 ± 5.32 | 140.99 ± 8.43 ^a | 27.74 ± 2.62 | 32.06 ± 5.4 ^a |
| Group 4 Cartap (97.5) + Carbofuran(2) | 110.26 ± 10.31 | 160.26 ± 4.9 ^b | 27.43 ± 2.48 | 34.11 ± 2.12 ^c |

Serum lipid concentrations have been calculated as described in Materials and Methods section. The values represent the average of three independent experiments. The pesticides doses when used independently represent 50% of their respective LD₅₀ values, whereas in combination 25% of their LD₅₀ value has been used. ^{ns} Represents day 7 values, not significant from the corresponding values at day 1. ^a Corresponds to the day 7 value significantly different from its corresponding value on day 1 @ p<0.001. ^b Represents the day 7 value significantly different from its corresponding value on day 1 @ p<0.01 and ^c denotes day 7 value significantly different from its corresponding value on day 1 @ p<0.05.

rats due to treatment with an organophosphate pesticide, mirex (17). The elevation in serum total lipids and total cholesterol may be attributed to the stimulation of catecholamines, which stimulate lipolysis and increase fatty acid production. The elevation in total serum cholesterol level that observed in present investigation could be due to blockage of liver bile ducts causing reduction or cessation of its secretion to the duodenum subsequently causing cholestasis. The results from the present investigation were also in the conformity with that reported by Gupta et al (11) in the serum of carbofuran treated mice. The disruption of formation of lipoprotein has been reported by Hassan et al, (18) as one of the factors leading to accumulation of cholesterol in carbofuran treated mice. The aforesaid changes could be due to increased tissue lipogenesis via acceleration of acetyl CoA (19). Since the treatment of the rats with a combination of CT and CF registered marked hyperlipidemic effect, it could be possible that the exposure to both of these compounds may play significant role in aggravating certain diseases such as atherosclerosis, chronic renal failure and diabetes associated to increased level of serum lipids in the body. The results from the present study showing alterations in the level of lipoproteins due to the treatment of the experimental animal with twin carbamate compounds could be exploited as a potential biomarker of pesticide toxicity in human beings.

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