



Hormones and Signaling

Elixir Hormo. & Signal. 84 (2015) 33801-33804

Elixir
ISSN: 2229-712X

Effect of Vitamin E on Hepatic Enzymes of Albino Rats Treated With Alpha Cypermethrin

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ARTICLE INFO

Article history:

Received: 7 February 2015;

Received in revised form:

8 July 2015;

Accepted: 18 July 2015;

Keywords

Alpha cypermethrin,
Hepatic,
Vitamin E.

ABSTRACT

The study was carried out to ascertain the antioxidant effect of vitamin E on sub-acute toxicological effects of alpha cypermethrin in male albino rats using hepatic enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (Alkphos) as indicators. Nine albino rats divided into 3 groups were fed diets mixed with vitamin E for 2 weeks to saturation prior experiment were administered with alpha cypermethrin intraperitoneally at concentrations of 50, 100 and 500mg /kg concentrations while the 4th group of 3 albino rats were fed normal rat diet with distilled water and injected with physiological saline and compared with albino rats fed normal rat diets administered with alpha cypermethrin intraperitoneally at similar concentrations. The result showed dose dependent significant increases in mean \pm SEM Aspartate transaminase, Alanine transaminase and Alkaline phosphatase in the cypermethrin treated when compared with the vitamin E treated male albino rats ($P < 0.05$). Alpha cypermethrin elicited severe dose dependent changes in the hepatic enzymes, while treatment with vitamin E reduced enzyme activities in male albino rats with milder alterations. The results of this study have shown that vitamin E conferred some level of protection on Alpha cypermethrin treated male albino rats.

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Introduction

The first pyrethroid was developed in 1973 and commercialized as fenvalerate in 1978. At the moment, the class of pyrethroids includes 42 active ingredients (NPTN, 1998). The pyrethroids are neurotoxins, and based on their structure and on toxic signs in the rat are classified into two groups namely type I and type II compounds. Type I pyrethroids, which do not contain an alpha-cyano group in their molecule are allethrin, resmethrin, D-phenothrin, permethrin and mainly cause tremors (T-syndrome). Type II pyrethroids, which contain an alpha-cyano group are deltamethrin, cypermethrin, cyfluthrin and fenvalerate and cause choreoathetosis and salivation. Pyrethroids have emerged as a new class of agricultural pesticides and have found wide use over organochlorine and organophosphate pesticides. Pyrethroid pesticides show high toxicity to a wide range of insects, including resistant strains, low toxicity to mammals and birds and rapid biodegradability (Parker et al., 1984 Kale et al., 1999; el-Tawil et al., 2001). Apart from their use in agriculture, pyrethroids are essential in public health programmes e.g. vector control programmes (Zaim and Jambuligam, 2004).

However, Alpha-cypermethrin (α -CP) is the most potent cypermethrin and has broad-spectrum use in agriculture, domestic and veterinary applications due to its high bioefficacy, enhanced stability and considerably low mammalian toxicity. The serum lactate dehydrogenase (LDH), isocitrate dehydrogenase (ICH) and amylase activities were significantly elevated, suggestive of liver and possible pancreatic malfunction. The glutamate oxaloacetate transaminase (GOT) and creatine phosphokinase (CPK) activities decreased. Histological changes were marked by hypertrophied hepatic cells and nuclei (Shakoori et al., 1988). Alphamethrin is metabolized in mammals and readily excreted through the

gastrointestinal tract and kidney (Ivie et al., 1980; Saka and Popoova, 1996).

Vitamin E is one of four fat-soluble vitamins. The vitamin has eight different isoforms (vitamers) grouped into alpha, beta, gamma or delta. A large body of research currently focuses on the alpha tocopherol form of vitamin E, which is the most biologically active (Traber, 1999). Vitamin E is a very powerful antioxidant. Other well-known antioxidants are Vitamin C, beta carotene and others. Antioxidants are nutrients that inhibit some of the damage caused by toxic by-products released when food is metabolised to energy or the body fights off infection (Rimm et al., 1993).

The aim of this study is to investigate the effects of alpha tocopherol on Renal and liver function of male Albino rats treated with cypermethrin using Alkaline phosphatase (Alk Phos), Alanine amino transferase (ALT), Aspartate aminotransferase (AST), Creatinine (Cr) and Urea (Ur) as indicators.

Materials and Methods

Alpha cypermethrin was bought from a pest control company along Trans-Amadi, Port Harcourt. It was stored in a 1 litre industrial bottle and was well stoppered.

Test animals

Eighty (80) male albino rats of average weight 200g were obtained from the animal house of the department of Pharmacology and Toxicology, University of Port Harcourt. These rats were acclimatized to laboratory conditions for a period of 14 days before the study.

Animal studies Seventy two (72) male wistar rats divided into 2 treatments of 4 groups of 9 rats each for cypermethrin and vitamin E treated were fed with normal rat diet and diet mixed with vitamin E for cypermethrin and vitamin E treated respectively for two weeks.

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Table 1. Effect of vitamin E on AST activities in cypermethrin treated rats

Concentration (g/Kg)	First week			Second Week			Forth week		
	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value
0	10.± 5.0	9 ± 0.58	P>0.05	8.00± 1.16	12.00±1.16	P>0.05	12± 1.16	7.± 0.58	P<0.05
50	74 ± 3.46	67± 4.04	P>0.05	52 ± 4.62	72 ± 6.93	P>0.05	76 ± 2.31	54±3.46	P<0.05
100	143 ± 13.28	135±8.66	P>0.05	137 ± 9.82	143± 13.28	P>0.05	131 ± 0.58	138±5.77	P>0.05
500	154 ± 26.56	149±10.97	P>0.05	172 ± 6.93	151± 5.20	P>0.05	183 ± 9.82	144±13.85	P<0.05

Table 2. Effect of vitamin E on ALT activities in cypermethrin treated rats

Concentration (g/Kg)	First week			Second Week			Forth week		
	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value
0	9± 0.58	12± 1.15	P<0.05	11± 0.58	10± 2.89	P>0.05	10± 2.89	12± 1.16	P>0.05
50	133 ± 19.05	65 ± 8.66	P<0.05	128 ± 1.16	58± 10.39	P<0.05	117 ± 7.51	43 ± 4.04	P<0.05
100	146 ± 3.46	123± 3.27	P>0.05	149 ± 121.12	121± 8.66	P>0.05	138 ± 5.77	120±11.54	P<0.05
500	137 ± 9.80	135± 8.66	P>0.05	156 ± 13.86	128± 1.15	P>0.05	160 ± 11.54	116 ± 2.30	P<0.05

Table 3. Effect of vitamin E on Alkaline Phosphatase activities in cypermethrin treated rats

Concentration (g/Kg)	First week			Second Week			Forth week		
	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value	Cypermethrin treated	Vitamin E treated	P value
0	18± 1.15	15± 2.89	P>0.05	21± 0.58	20± 5.78	P>0.05	15± 2.89	13± 1.73	P>0.05
50	52 ± 4.62	48 ± 4.62	P>0.05	55 ± 2.89	51 ± 5.19	P>0.05	57 ± 4.04	46 ± 3.46	P<0.05
100	49 ± 0.58	52 ± 6.92	P>0.05	60 ± 5.77	57.33±5.46	P>0.05	53 ± 1.73	44 ± 8.08	P>0.05
500	325 ± 14.43	286±8.08	P>0.05	406 ± 3.46	293 ± 53.69	P>0.05	384 ± 48.50	248±20.78	P>0.05

Alpha cypermethrin were administered intraperitoneally at concentrations of into 3 rats each to 3 groups per treatment at 1, 2 and 4 week periods while the rats in the last groups per treatment were administered with 0.9% normal saline at 1, 2 and 4 week periods. The animals were sacrificed and blood specimens for biochemical analysis collected.

Biochemical Studies

Determination of ALT and AST was done by monitoring the concentrations of pyruvate hydrazone formed with 2, 4 dinitrophenylhydrazine. 0.5ml of buffer solution was dispensed into test tubes labeled blank, sample, control blank and control respectively for AST and ALT respectively. 0.1ml of sample and control was dispensed into their respective test tubes. All the tubes were incubated at 37°C for 30minutes. 0.5ml of 2, 4 dinitrophenylhydrazine was dispensed into all test tubes. 0.1ml of sample and control was dispensed into their respective blank test tube. The contents of each test tube was mixed and allowed to stand for 20minutes at 25°C. 5ml of 0.4N sodium hydroxide was added to each tube, mixed and read at 550nm against the respective blank prepared. The activity of the unknown was extrapolated from the calibration curve already prepared (Reitman, and Frankel, 1957).

Alkaline Phosphatase activity was done by Phenolphthalein Monophosphate method. The test tubes were respectively labeled sample, standard and control. 1.0ml of distilled water was pipetted into each tube followed by a drop of the substrate into each test tube. All the test tubes were incubated at 37°C for 5minutes. 0.1ml of sample, standard and control were dispensed into their respective test tubes. The test tubes were incubated at 37°C for 20minutes. 5ml of colour developer was added to each test tube, mixed, and read at 550nm using water as blank. The activity of sample was calculated using the absorbance of sample against absorbance of standard multiplied by concentration of standard (Babson et al 1966).

Statistical analysis

The biochemical data were subjected to some statistical analysis. Values were reported as Mean ± SEM while student's t-test was used to test for differences between treatment groups using Statistical Package for Social Sciences (SPSS) version 16. A value of P<0.05 was accepted as significant.

Results

There was dose dependent increase in AST activities (u/l) at first week in cypermethrin treated albino rats with concentrations of 74 ± 3.46, 143 ± 13.28 and 154 ± 26.56 at cypermethrin concentrations of 50, 100, 500mg/kg respectively while the vitamin E treated rats had 67 ± 4.04, 135 ± 8.66 and 149 ± 10.97 respectively. The controls (0g/kg) for cypermethrin and Vitamin E treated were 10.± 5.0 and 9 ± 0.58 respectively. At week 2, the AST activities (u/l) were 52 ± 4.62, 137 ± 9.82 and 172 ± 6.93 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 72 ± 6.93, 143 ± 13.28 and 151 ± 5.20. The controls (0g/kg) were 8.00 ± 1.16 and 12.00 ± 1.16 for cypermethrin and Vitamin E treated respectively.

At week 4, the AST activities (u/l) were 76 ± 2.31, 131 ± 0.58 and 183 ± 9.82 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 54 ± 3.46, 138 ± 5.77 and 144 ± 13.85. The controls (0g/kg) were 12 ± 1.16 and 7.± 0.58 for cypermethrin and Vitamin E treated respectively as shown in table 1 below.

There was dose dependent increase in ALT activities (u/l) at first week in cypermethrin treated albino rats with concentrations of 133 ± 19.05, 146 ± 3.46 and 137 ± 9.80 at cypermethrin concentrations of 50, 100, 500mg/kg respectively while the vitamin E treated rats had 65 ± 8.66, 123 ± 13.27 and 135 ± .66 respectively. The controls (0g/kg) for cypermethrin and Vitamin E treated were 9 ± 0.58 and 12 ± 1.15 respectively.

At week 2, the ALT activities (u/l) were 128 ± 1.16, 149 ± 121.12 and 156 ± 13.86 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 58 ±

10.39, 121 ± 8.66 and 128 ± 1.15 . The controls (0g/kg) were 11 ± 0.58 and 10 ± 2.89 for cypermethrin and Vitamin E treated respectively.

At week 4, the ALT activities (u/l) were 117 ± 7.51 , 138 ± 5.77 and 160 ± 11.54 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 43 ± 4.04 , 120 ± 11.54 and 116 ± 2.30 . The controls (0g/kg) were 10 ± 2.89 and 12 ± 1.16 for cypermethrin and Vitamin E treated respectively as shown in table 2.

There was dose dependent increase in Alkaline phosphatase activities (u/l) at first week in cypermethrin treated albino rats with concentrations of 52 ± 4.62 , 49 ± 0.58 and 325 ± 14.43 at cypermethrin concentrations of 50, 100, 500mg/kg respectively while the vitamin E treated rats had 48 ± 4.62 , 52 ± 6.92 and 286 ± 8.08 respectively. The controls (0g/kg) for cypermethrin and Vitamin E treated were 18 ± 1.15 and 15 ± 2.89 respectively.

At week 2, the Alkaline phosphatase activities (u/l) were 55 ± 2.89 , 60 ± 5.77 and 406 ± 3.46 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 51 ± 5.19 , 57.33 ± 5.46 and 293 ± 53.69 . The controls (0g/kg) were 21 ± 0.58 and 20 ± 5.78 for cypermethrin and Vitamin E treated respectively.

At week 4, the Alkaline phosphatase activities (u/l) were 57 ± 4.04 , 53 ± 1.73 and 384 ± 48.50 at 50, 100, 500mg/kg cypermethrin respectively while the respective vitamin E values were 46 ± 3.46 , 44 ± 8.08 and 248 ± 20.78 . The controls (0g/kg) were 15 ± 2.89 and 13 ± 1.73 for cypermethrin and Vitamin E treated respectively as shown in table 3 below.

Discussion

Alpha cypermethrin is the most potent of all the pyrethroids. This is because of its ability to cause a longer protraction of sodium permeability of the nerve membrane during excitation (Exttoxnet, 1994, EPA, 2000).

Alpha cypermethrin caused induction of enzymes such as AST, ALT and ALK Phos in this study while supplementation of diets with vitamin E reduced the induction of the enzymes such as AST, ALT and ALK Phos in this study. This is suggestive of protection against alpha cypermethrin toxicity. Liver is the central organ of metabolism and act as an organ of storage. Many potentially toxic substances are metabolized by cells especially by the hepatic parenchyma cells. Metabolic action by the hepatic parenchyma cells has been regarded as an important defense system against toxicants and the transformations involved have been referred to as detoxification (Zimmerman, 1974). Elevated serum activity of the two aminotransferases (AST and ALT) is the most frequently measured indicator of liver disease (Reichling and Kaplan, 1988). The treatment with alpha cypermethrin increased the liver AST which treatment while Vitamin E reduced the enzyme. This may be as result of antioxidant nature of the vitamin E. AST is also diffusely represented in the heart, skeletal muscle, kidneys, brain and red blood cells while ALT has low concentrations in skeletal muscle and kidney (Wroblewski 1958); an increase in ALT serum levels is therefore more specific for liver damage. The level of serum ALT activity has been reported to be increased as a result of liver injury in patients developing severe hepatotoxicity (Beckett et al., 1989). ALT might have leaked from damaged cells, due to increased permeability of the hepatocellular membrane, or due to necrosis, indicating organ dysfunction (McIntyre and Rosalki 1992). Elevation of alanine amino transferase (ALT) activity appears to reflect hepatic disease and it is more specific for hepatic disease than aspartate amino transferase (AST) because of the biological location of the enzymes (Dede et al., 2001). These results also showed that the mean activities of the

enzymes of the vitamin -E treated were lower in comparison with those of the Alpha cypermethrin male albino rats.

Conclusion

The results of this study have shown that alpha cypermethrin caused induction of hepatic enzymes (AST, ALT and Alkaline Phosphatase), suggestive of liver dysfunction while the antioxidant vitamin E reduced the induced enzymes.

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