SUBACUTE EFFECT OF TECHNICAL ALPHACYPERMETHRIN INSECTICID AND 10% EC. OF IT ON SOME LIVER, KIDNEY AND THYROID FUNCTIONS IN MALE ALBINO RATS

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Abstract

In the present study four equal groups of male experimental rats were orally treated with two doses of technical alphacypermethrin 96 %(10.5and5.25 ppm) and two other doses of its 10% EC. formulations (1.2and0.6 ppm) for 28 consecutive days, then blood samples were taken after two weeks from treatment and at the end of experiment. The plasma was separated and assayed for some parameters induct liver, kidney and thyroid functions. The results showed that in case of technical grade, a significant decrease in ALT enzyme activity caused by the high dose ,while significant increases in ALP, AChE enzyme activities occurred by the high and low doses after two weeks from treatment. The two used doses produced significant increase in plasma urea and uric acid concs. by the high dose after two weeks. Triiodothyronin hormone conc. was increased significantly in plasma with the two doses after two weeks then, decreased significantly with the low dose at the end of treatment, while thyroxin hormone conc. was decreased significantly by the low dose after 2 weeks, increased significantly by the two doses at the end of treatment. In case of 10%EC. formulation, significant decrease and increase were occurred in AST enzyme activity with the high dose after 2 weeks and at 28 days, respectively. Significant increase in ALP enzyme activity was recorded by the two doses after 2 weeks and with the high dose at the end of experiment. AChE enzyme activity was decreased significantly by the low dose at the end of treatment period. Significant increase in plasma urea conc. was occurred by the two doses at the two experimental periods. Plasma creatinine and thyroxin hormone concs. were decreased significantly by the low dose at the end of treatment period.

INTRODUCTION

Pyrethroids are highly active insecticides at considerable lower quantities (up to 100 kg/ha), compared to other insecticides. Therefore, their contribution to the contamination of the natural environment is smaller than that caused by other groups of pesticides (Lukowicz-Ratajczak and Krechniak 1991). Alphacpermethrin is a synthetic pyrethroid insecticide with a range of agricultural uses. It is also used to form a barrier to repel or kill termites. Like other pyrethroids, alphacypermethrin kills insects by affecting the salt balance (sodium channels) in nerve cells. It has a broad spectrum of activity against insects with the main toxic effect on the nervous system. The present study aimed to throw light on the toxicological effects of technical grade and

10%EC. of alphacypermethrin which were orally administered in two different doses each for 4 consecutive weeks on liver, kidney and thyroid functions in adult male albino rats.

MATERIALS AND METHODS

Chemicals:- Alphacypermethrin ((R)- cyano(3-phenoxyphenyl)methyl (1s,3s)-rel-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxlate)technical grade 96%and its E.C. formulation 10%(super alpha) were obtained from El-Help Co. (Egypt)and used in this study.

Experimental animals: - Adult male albino rats (Wister strain) weighting 120-150g were used in this study. Animals were acclimatized for 2 weeks prior to study under normal health conditions in the animal house of the Mammalian Toxicology Department, Central Agriculture Pesticides Laboratory, were fed on a normal commercial diet and were allowed free excess of water.

Experimental design: - 25 animals were randomly divided to five groups of equal fiv**e** rats each. The groups were treated as follows:

Group 1:- The animals were administrated the dose level10.5mg/kg b.w. (1/10determined LD50) of the technical alphacypermethrin as a high dose.

Group 2:-The animals were administrated the dose level 5.25mg/kg b.w. (1/20determined LD50) of the technical alphacypermethrin as a low dose.

Group 3:- The animals were administrated the dose level 1.2mg/kg b.w. (1/10determined LD50) of the formulation as a high dose.

Group 4:- The animals were administrated the dose level 0.6mg/kg b.w. (1/20determined LD50) of the formulation as a low dose.

Group 5:- The animals were received distilled water to be used as control. All groups were treated orally by metallic stomach tube for 28 consecutive days.

Blood sampling: - From each group of animals blood samples were obtained at two periods (14and 28 days) from the retro-orbital plexus of veins according to the method of Schermer (1967). The samples were collected in clean dry tubes, some containing heparin as anticoagulant and centrifuged at 600 g. for 15 min. then, serum and plasma were separated and kept in a deep freezer at - 20◦C until different parameters were carried out.

Biochemical analysis:- Diagnostic specified kits were used in this study to assay the different parameters where AST, ALT enzyme activities were determined as the method of Reitman and Frankel (1957) , ALP enzyme activity as the method of Hausamen et al., (1967), AChE enzyme activity as the method of Ellman et al., (1961), plasma urea conc. as the method of Caulombes and Farreau(1963), plasma

creatinine conc. as the method of Husdan and Rapaport(1968) and plasma uric acid conc. b the method of Fossati et al., (1980). Radioimmunoassay kits were used for determination serum thyroxin (T4) and triiodothyronin (T3) concs. as mentioned by Britton et al., (1975).

Statistical analysis: - Data were expressed as mean± SE and significant differences of values were calculated according to the student t-test (Snedecor and Cochran, 1970).

RESULTS AND DISCUSSION

Alphacypermethrin has been available commercially since the mid 1980s. It contains more than 90% of the insecticidally most active enantiomer pair of the four cis isomers of cypermethrin as a racemic mixture. Alphacypermethrin induced clinical signs, like those of cyano-containing pyrethroid. The observed signs included ataxia, abasia, gait abnormalities, choreoathetosis, tip-toe walking, and increased salivation, lacrimation, piloerection, tremor and clonic convulsions (Rose1982).

Tables1and 2 contain the effect of the two used forms of alphacypermethrin on some plasma enzymes where significant decrease and significant increase in ALT and ALP enzyme activities were produced by the high dose of technical grade respectively, also a significant increase in AChE enzyme activity by the low dose after two weeks from treatment. The formulation caused a significant decrease in AST enzyme activity by the high dose and a significant increase in ALP enzyme activity by the two used doses after two weeks of treatment, while at the end of treatment period significant increases in AST and ALP enzyme activities were noticed with the high dose and a significant decrease in AChE enzyme activity by the low dose. Changes in plasma enzyme activities by alphacypermethrin were reported by Manna et al., (2004) (increased AST, ALT and ALP) after single oral dose of 145mg/kg b.w. exposure and by Manna et al., (2004 and 2006) (increased AST, ALT and ALP) after treatment by the dose level 14.5mg/kg b.w. for 30, 60 days respectively. The four determined enzyme activities represent the functional status of the liver and the increase value of their activities is related to the intensity of liver cellular damage and the decrease is related to damage in protein metabolism process.

Tables 3and 4 showed the effect of alphacypermethrin technical or formulation on some kidney function parameters where, the technical affected after two weeks of treatment only by the two doses on plasma urea conc. (significant increase) and by the high dose on uric acid conc. (significant increase). The formulation increased significantly the urea conc. by the two used doses at the two experimental periods and decreased significantly the creatinine conc. by the low dose at the end of treatment

period. These data suggest relatively more kidney damage by the formulation than the technical grade. Pickering (1982) showed increases in urea conc. in male rats fed 400mg/kg diet also Green(1993) noticed increased urea levels in males and females mice treated with 200,400,600,800,1200 and 1600 mg alphacypermethrin /kg diet without clear dose relation.

Tables 5and 6 represent the effect of alphacypermethrin technical and formulation on T3, T4 hormones. Data indicated significant increase in T3 conc. by the two doses of the technical after 2 weeks and a significant decrease with the low dose at 28 days, while T4 conc. was decreased significantly by the low dose after 2 weeks and increased significantly with the two doses at the end of treatment period. In case of formulation, only significant decrease in T4 conc. was noticed with the low dose at the end of experiment. These results reflected more thyroid hormones disruption by the technical than the formulation. Some endocrine effects of pyrethroid in animal studies were proved by Akhtar et al., (1996) and Kaul et al., (1996). As WHO had classified these substances as moderate hazardous (WHO 1996) other studies are required to cover all its hazardous effect and suggest the ideal application which minimizes its danger.

Table (1) Effect of orally administrated Alphacypermethrin 96% on some plasma enzymes in male rats.

Periods / Parameter	14days			28 days		
	Control	Low	High	Control	Low	High
ALT U / L	65.33 ± 5.66	63.92 ± 5.95	44.74 ± 3.24**	43.19 ± 3.25	38.67 ± 0.88	37.24 ± 5.49
AST U / L	99.30 ± 10.69	109.487 ± 11.58	120.58 ± 9.66	111.92 ± 6.67	105.80 ± 6.24	123.55 ± 10.51
ALP U / L	189.19 ± 26.86	210.55 ± 27.69	245.35 ± 14.11*	174.478 ± 4.65	174.47 ± 29.731	219.738 ± 22.476
AChE U / L	483.00 ± 55.52	981.51 ± 85.90**	584.41 ± 43.28	503.75 ± 30.81	536.97 ± 77.19	543.62 ± 47.29

Table (2) Effect of orally administrated Alphacypermethrin 10% on some plasma enzymes in male rats.

Periods / Parameter	14 days			28 days		
	Control	Low	High	Control	Low	High
ALT U / L	63.79 ± 2.91	64.26 ± 8.62	51.69 ± 6.81	65.69 ± 4.27	87.48 ± 4.19	87.6 ± 12.06
AST U / L	145.192 ± 10.57	139.69 ± 9.65	117.92 ± 8.58*	87.54 ± 6.91	96.85 ± 6.81	152.92 ± 8.27**
ALP U / L	63.20 ± 2.30	85.70 ± 3.35**	155.47 ± 16.64**	127.21 ± 3.55	135.436 ± 16.98	187.952 ± 16.93**
AChE U / L	389.13 ± 14.90	386.85 ± 7.92	422.48 ± 35.17	433.34 ± 48.51	331.67 ± 20.87*	406.49 ± 22.49

Data expressed as mean ± SE . ** Significante difference at P<0.01. * Significante difference at P<0.05 .

U = unit of enzyme activity = the amount of the enzyme that catalyzes the conversion of 1 micro mole substance per minute.

Table (3) Effect of orally administrated Alphacypermethrin 96% on kidney function parameters in male rats.

Parameter \ Periods	14 days			28 days		
	Control	Low	High	Control	Low	High
Urea mg/dl	20.507 ± 1.10	29.970 ± 2.49**	30.856 ± 1.19**	27.967 ± 1.82	25.712 ± 2.64	26.125 ± 2.05
Creatinine mg/dl	0.59 ± 0.08	0.58 ± 0.042	0.59 ± 0.04	0.61 ± 0.11	0.42 ± 0.024	0.57 ± 0.04
Uric acid mg/dl	2.569 ± 0.17	2.602 ± 0.33	4.001 ± 0.31**	2.491 ± 0.21	2.504 ± 0.26	2.51 ± 0.50

Table (4) Effect of orally administrated Alphacypermethrin 10% on kidney function parameters in male rats.

Parameter \ Periods	14 days			28 days		
	Control	Low	High	Control	Low	High
Urea mg/dl	21.428 ± 0.87	27.259 ± 1.99*	29.972 ± 2.25**	19.807 ± 1.95	25.097 ± 1.19*	29.419 ± 0.49**
Creatinine mg/dl	0.491 ± 0.039	0.444 ± 0.075	0.468 ± 0.008	0.421 ± 0.019	0.304 ± 0.023**	0.444 ± 0.007
Uric acid mg/dl	2.197 ± 0.11	2.039 ± 0.18	2.123 ± 0.23	3.058 ± 0.26	3.611 ± 0.20	3.144 ± 0.24

Data expressed as mean ± SE . ** Significante difference at P<0.01. * Significante difference at P<0.05 .

Table (5) Effect of orally administrated Alphacypermethrin 96% on plasma T3, T4 hormones in male rats.

Periods / Parameter	14 days			28 days		
	Control	Low	High	Control	Low	High
Triiodothyronin (T3) ng/dl	64.41 ± 2.86	95.3 ± 9.75**	86.56 ± 11.02*	83.92 ± 4.61	67.54 ± 7.37*	83.58 ± 5.73
Thyroxine (T4) ug/dl	4.94 ± 0.36	1.39 ± 0.09**	5.2 ± 0.82	3.80 ± 0.65	5.55 ± 0.53*	7.08 ± 0.63**

Table (6) Effect of orally administrated Alphacypermethrin 10% on plasma T3, T4 hormones in male rats.

Periods / Parameter	14 days			28 days		
	Control	Low	High	Control	Low	High
Total Triiodothyronin (T3) ng/dl	68.71 ± 8.07	70.42 ± 9.54	71.83 ± 10.28	66.99 ± 11.12	72.79 ± 11.71	57.88 ± 10.02
Total Thyroxine (T4) ug/dl	2.71 ± 0.50	3.65 ± 0.45	2.93 ± 0.57	4.19 ± 0.49	2.59 ± 0.28**	3.75 ± 0.70

Data expressed as mean ± SE . ** Significante difference at P<0.01. * Significante difference at P<0.05 .

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التأثيرتحت الحاد لخام مبيد الالفاسيبرمثرين ومستحضر ١٠% منه مركز قابل للاستحلاب على بعض وظائف الكبد والكلى والغدة الدرقية فى ذكور لفئران التجارب

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عوملت فى هذة الدراسة ٤ مجموعات متساوية العدد من ذكور فئران التجارب البالغة بتركيزين من الفاسيبرمثرين الخام ٩٦% (١٠,٥و ٥,٢٥ جزء فى المليون) وتركيزين أخرين من المستحضر ١٠%مركز قابل للاستحلاب(١,٢و٠,٦ جزء فى المليون) كلا على حده لمدة ٢٨ يوم متواصلة وأخذت منها عينات الدم بعد أسبوعين من المعاملة وفى نهايتها وفصلت البلازما وقدرت بها بعض الانزيمات والمكونات والهرمونات لدراسة التأثير على وظائف كل من الكبد والكلى والغدة الدرقية. أظهرت النتائج أنه فى حالة المعاملة بالخام حدث نقص معنوى فى نشاط أنزيم الانين ترانسفيريز بواسطة التركيز العالى بعد أسبوعين من المعاملة وزيادةمعنوية فى نشاط أنزيم الكالين فوسفاتيز وأنزيم أسيتيل كولين أستيريز بواسطة التركيز العالى والمنخفض على التوالى أيضا بعد أسبوعين من المعاملة. أحدث ايضا كلا التركيزين ارتفاع معنوى فى تركيز اليوريا فى البلازما وفى تركيز حمض اليوريك بواسطة التركيز العالى فقط بعد اسبوعين من المعاملة. أما تركيز هرمون ترای ايودوثيرونين فقد زاد معنويا فى البلازما بواسطة كلا التركيزين بعد أسبوعين من المعاملة وأنخفض معنويا بواسطة التركيز المنخفض فى نهايتها فى حين أنخفض معنويا تركيز هرمون الثيروكسين بواسطة التركيز المنخفض بعد اسبوعين من المعاملة ثم أظهر أرتفاعا معنويا بواسطة كلا التركيزين فى نهايتها. وفى حالة المستحضر وجد أنخفاض معنوى ثم ارتفاع معنوى فى نشاط انزيم اسبارتات ترانسفيريز بواسطة التركيز العالى بعد أسبوعين من المعاملة وفى نهايتها على التوالى وأيضا وجد أرتفاع معنوى فى نشاط أنزيم الكالين فوسفاتيز بواسطة كلا التركيزين بعد اسبوعين من المعاملة وبواسطة التركيز العالى فقط فى نهايتها وانخفض كذلك معنويا نشاط أنزيم أسيتيل كولين أستيريز بواسطة التركيز المنخفض فى نهاية المعاملة . كذلك ظهر ارتفاع معنوى فى تركيز اليوريا فى البلازما بواسطة كلا التركيزين فى كلا فترتى الاختبار وأنخفض معنويا تركيز الكرياتينين وهرمون الثيروكسبن فى البلازما بواسطة التركيز المنخفض فى نهاية المعاملة.