World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Ameliorative effects of selenium against cypermethrin induced toxicity of tissue minerals in vital organs of Sprague Dawley rats

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World Journal of Advanced Research and Reviews, 2022, 16(03), 505–517

Publication history: Received on 26 October 2022; revised on 13 December 2022; accepted on 15 December 2022

Article DOI: https://doi.org/10.30574/wjarr.2022.16.3.1310

Abstract

Introduction: Alpha-cypermethrin (Pyrethroid insecticide) is widely used in disease vector control, agriculture, home pest control and protection of foodstuff across the world. Due to its unchecked and widespread use, non-target organisms are also getting affected by its toxic effects.

Objectives: This investigation was aimed to determine the preventive potential of selenium on changes in tissue minerals induced by a short-term (21 days) oral treatment of cypermethrin in Sprague-Dawley rats.

Methodology: Female rats (n=20) were equally divided into four groups. Group 1 received corn oil (1 ml), Group 2 was administered 55 mg/kg/bw of cypermethrin, 1 ppm of sodium selenite was administered to Group 3 and Group 4 was given both cypermethrin and sodium selenite. Concentration of tissue minerals (Se, Na, K, Mg, Cu and Zn) were determined in the brain, heart, liver, kidney, spleen and blood through atomic absorption spectrophotometry.

Results: Results showed that cypermethrin administration caused significant changes in trace metals and electrolytes in some of the tissues while most tissues' concentrations remained unaffected.

Conclusion: The present study showed that selenium can be effective in the protection of cypermethrin induced toxicity. However further studies can be conducted to analyze the effects of different doses of selenium on cypermethrin induced toxicity in tissue minerals.

Keywords: Cypermethrin; Selenium; Pyrethroid; Atomic absorption spectrophotometry

1. Introduction

To protect their crops, humans are utilizing pesticides as early as 2500 BC. Elemental sulfur dusting was the first known pesticide used in Sumeria about 4,500 years ago. Toxic chemicals including lead, mercury and arsenic were being applied on crops to kill pests by the 15th century. Nicotine sulfate extracted from tobacco leaves was used as an insecticide in the 17th century. Two more natural pesticides were introduced in the 19th century including rotenone which is derived from the roots of tropical vegetables and pyrethrum which is obtained from chrysanthemums [1]. Pesticides contributes valuably to human health by reducing the incidence of vector-borne diseases and increasing food and fiber production [2]. However, several environmental concerns are raised due to the use of pesticides. More than 98% of sprayed insecticides and 95% of herbicides reach a destination other than their target species, including non-

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target species, water, air, bottom sediments and food [3]. When other areas are contaminated by pesticides carried as particles in wind, "pesticide drift" occurs. Some pesticides cause soil contamination by acting as organic pollutants and also one of the reasons of water pollution. Pesticides exposure during manufacturing, transport or during and after use is dangerous for workers, consumers and bystanders [4]. Unfortunately, there is not much information available on chronic human diseases caused by pesticide exposure [5], however the acute toxicity of most pesticides is well documented [6]. According to an estimate, ~4% of all human cancers is caused by occupational exposure to different types of pesticides [7].

1.1. Trace Minerals

Many key functions in the body relating to production of energy, connective tissue strengthening and brain neurotransmitters etc. are performed by copper. It is also part of some enzymes which are responsible for biochemical reactions in the body. A shortage of red blood cells and an inability to produce superoxide dismutase (SOD), an important antioxidant enzyme, has been linked to a deficiency of copper [8,9].

Among its many roles, magnesium acts as an important mineral for nerves and muscles. Magnesium is present primarily in bone and also in the cells of all soft tissues. It facilitates about 300 basic enzymatic reactions particularly those related to metabolism and acts as a co-factor for various ATP-dependent reactions [10]. Increased extracellular fluid (ECF) concentration of magnesium depresses activity of the nervous system and its deficiency leads to muscle weakness, tetany, tachycardia and ventricular fibrillation [11].

Potassium performs numerous important functions in the body including helping in digestion, providing electrolytic charge (ions) to the cells, storing and processing carbohydrates, and supporting the nervous system. Muscle tissue contains most of the total body potassium which is a great attractant of oxygen. Potassium works with sodium to maintain blood pressure and proper body fluids distribution in the body. Excessive perspiration, uncontrolled diabetes, intestinal tract diseases and problems, can result in potassium depletion which may cause muscle cramping and fatigue among other symptoms [10].

Selenium plays an important role in reducing free radicals induced tissue damage by acting as an enzyme co-factor. Athletes are particularly interested in antioxidant qualities of selenium along with vitamins such as C and E. It has been shown by preliminary studies that selenium may help the immune system and aid in the prevention of cancer and other degenerative disorders. It also helps to protect cells from environmental damage [12].

Sodium is important in facilitating the transmission of nerve impulses, and in maintenance of a proper pH balance in the body. People experiencing electrolyte loss and dehydration due to diarrhea, use of diuretics, heavy perspiration and other conditions may feel muscle weakness and cramping, fatigue and convulsions in severe cases [10].

Zinc is important for the proper function of several enzymes including those involved in tissue and bone growth and repair, wound healing, cell respiration, regulation of blood pressure and heart rate. Zinc along with copper is important in the formation of connective tissues and the protein fibers present in bone, ligaments, cartilage, skin and teeth [10].

2. Material and methods

2.1. Animals

Albino Sprague-Dawley rats (8-10 weeks old) used in the experiment were purchased from National Institute of Health, Islamabad having approximately 180 g average body weight. They were acclimatized for a week and maintained under standard laboratory conditions in the Animal House facility of Quaid-i-Azam University, Islamabad. They were fed standard rat chow and water *ad libitum*. Throughout the experiment, average temperature of 25°C was maintained with air condition system. The light-dark photoperiod was 12 hrs. All animal handling and subsequent killings were performed according to the guidelines provided by the ethics committee of the Department of Zoology, Quaid-i-Azam University, Islamabad.

2.2. Chemicals

In this experiment, alpha cypermethrin [(RS)-cyano-(3-phenoxyphenyl) methyl-(IRS)-cis-trans-3-(2,2 dichloroethenyl)-2,2-dimethyl-cyclopropane carboxylate] and sodium selenite Na_2SeO_3 (Surechem, England) were employed.

Ripcord (commercial pyrethroid product) was used as test compound which was acquired from the local market. A mixture of petrol and xylene 820 g/l and 10% cypermethrin 100 g/l was contained in Ripcord (Basf Aktiengesellschaft, Germany). All the other reagents used were obtained from Sigma and of analytical reagent grade (St. Louise, U.S.A).

2.3. Experimental design and treatment

20 mature female rats were taken to determine the effect of cypermethrin with or without selenium on the tissue minerals and randomly split into four equal groups having 5 rats each.

Group one served as control. However, groups two, three and four were given Cypermethrin (55 mg/kg body weight), sodium selenite (1 ppm) or their combination, respectively.

A low dose of 55 mg/kg body weight was used for this sub-chronic study (for 21 days) as the oral LD_{50} in female and male rats were found to be 150 to 500 and 187 to 326 mg/kg [13, 14] respectively.

Oral administration of cypermethrin in corn oil (1 ml) was done by gavage. Control animals received a subsequent amount of corn oil daily. Selenium was given as sodium selenite (Na_2SeO_3) in drinking water for 21 days.

Dose administration was done on the daily basis in the morning to non-fasted rats. The actual volume given was based on body weight which was taken daily during the dosing period.

2.4. Dissections

At the end of the experiment (i.e. 21 days), the animals were sacrificed according to the guidelines provided by National Institute of Health, Islamabad. Tissues including brain, heart, liver, kidney, ovary, spleen and blood were separated out to prepare digests for the detection of injected metal and to determine the concentration of essential elements.

2.5. Atomic Absorption Spectrophotometry

2.5.1. Sample Preparation and Metal Estimation

For brain, heart, liver, kidney, ovary, spleen and blood determination, wet tissue weight and volume of blood was recorded. 0.5 gm of tissue was digested with 10 ml of 69% concentrated HNO_3 (Merck, Germany) employing a Microwave Digestion System (MARS, CEM, USA). Temperature was set at 200 °C (maximum), and the power was 1200 watts. Samples were run for five minutes. Digested samples were filtered with Whattman filter papers (125 mm). Distilled water was added in each filtrate to make the final volume of 30 ml; samples were ready at this stage for atomic absorption spectrophotometry.

2.6. Methodology of the Technique

2.6.1. Preparation of Standard Solutions for Different Metals

Following formula was used to prepare the standard solutions of each metal salt (1000 ppm):

$$\frac{\text{Molecular weight of salt}}{\text{Molecular weight of sample}} = X$$

X grams of salt were dissolved in 1000 ml – dH_2O to make 1000 ppm solution.

In order to calibrate the instrument, diluted solutions having concentration from 1 ppm to 10 ppm were used. Following formula was employed to make different dilutions:

$$C_1V_1 = C_2V_2$$

Where concentration and volume of the stock solution of standard were represented by C_1 and V_1, whereas the required concentration and volume are represented by C_2 and V_2 respectively.

2.7. Determination of Metal Concentration

The standard solutions of varying concentrations were used to make calibration curves in order to determine metal concentration. All the tissues' digests were subjected to air/acetylene fast sequential flame atomic absorption spectrometer (Varian, AA240 FS, and USA).

Following metals were determined: Selenium (Se), Magnesium (Mg), Zinc (Zn), Sodium (Na), Potassium (K) and Copper (Cu).

Following formula was used to convert concentrations that were obtained in ppm (mg/L) into microgram/gram of tissue:

$$\text{Metal conc. (ppm)} \times \frac{\text{Final volume of solution}}{\text{Sample weight/volume}} = \text{Metal conc. } \mu g/g$$

2.7.1. Instrument Parameter for Element Analysis

Specific instrument parameters for each metal are summarized below (Table 1).

Table 1 Wavelength and detection limit of elements

Element	Wavelength [λ Max (nm)]	Detection Limit μg/L
Zinc (Zn)	213.9	1.0
Sodium (Na)	589	0.2
Potassium (K)	766.5	3.0
Copper (Cu)	324.7	3.0
Magnesium (Mg)	285.2	0.3
Selenium (Se)	422.7	1.0

2.8. Statistical analysis

Data are expressed as mean ± standard error of mean (SEM). GraphPad Prism 5 was used for the statistical analysis. Single factor analysis of variance (ANOVA) was used to assess the statistical significance of differences between the means.

The parameters of treatment groups were compared to those of control using Dunnett test. Comparison among different treatment groups was carried out by Tukey's test. A difference of $P < 0.05$ was considered significant.

3. Results

3.1. Copper (Cu) Concentration

3.1.1. Cypermethrin treatment group

In cypermethrin alone treated group, there was an increase in the concentrations of copper element in all the tissues studied including brain, heart, liver, kidney and blood of female rats except spleen which showed highly significant ($p = 0.001$) increase in comparison to control (Fig.1).

3.1.2. Sodium selenite treatment group

A non-significant decrease in copper concentration was shown by liver and brain. While the heart, spleen, blood and kidney tissues showed increase of copper concentration when compared to control (Table 2).

3.1.3. Cypermethrin + sodium selenite treatment group

An increase in copper concentration (non-significant) occurred in brain, blood, spleen and heart. While liver and kidney copper levels decreased non-significantly in comparison to the control group (Table 2).

3.2. Magnesium (Mg) concentration

3.2.1. Cypermethrin treatment group

The animals exposed to cypermethrin alone showed non-significant increase of Mg concentration when compared to the control group, in the brain, spleen and heart tissues. In contrast, liver, kidney and blood showed non-significant decrease in the Mg concentration than that of the control group (Table 3).

3.2.2. Sodium selenite treatment group

All the selected tissues i.e., brain, heart, liver, kidney and blood of the sodium selenite exposed group showed a non-significant decrease of Mg concentration as compared to the control group except spleen which showed highly significant decrease as compared to control and cypermethrin treated groups ($p = 0.01$ and $p = 0.001$ respectively) (Table 3).

3.2.3. Cypermethrin + sodium selenite treatment group

The magnesium concentration of the combined treatment group decreased significantly ($p < 0.05$) in liver, kidney, blood and non-significantly in brain and heart tissues when compared to the control group. In spleen it was highly significant ($p = 0.001$) when compared to control and cypermethrin treated rats (Fig.2).

3.3. Zinc (Zn) concentration

3.3.1. Cypermethrin treatment group

Zn concentration decreased non-significantly in the brain, heart and liver tissues of the animals exposed to cypermethrin alone as compared to the control group. Zn concentration of the blood, spleen and kidney increased non-significantly than that of the control group (Table 4).

3.3.2. Sodium selenite treatment group

In the sodium selenite alone treatment group, there occurred a non-significant ($p > 0.05$) decrease in the Zn concentration of the brain, liver, kidney, spleen and blood when compared to the control group. While a significant ($p < 0.01$) decline of Zn concentration in spleen observed when compared to cypermethrin treated group. Heart tissue remained indifferent in Zn concentration from the control group (Table 4).

3.3.3. Cypermethrin + sodium selenite treatment group

The animals exposed to a combination of cypermethrin + sodium selenite showed a non-significant increase of Zn concentration of brain when compared to the control while significant increase of Zn when compared to cypermethrin and sodium selenite alone groups ($p < 0.05$). Heart Zn concentration was increased significantly ($p < 0.05$) than that of the control, cypermethrin and sodium selenite alone groups. A significant ($p < 0.01$) decrease of Zn concentration in spleen observed when compared to cypermethrin treated group. Among other tissues, liver and kidney showed a decrease in the Zn concentration while blood showed an increase in Zinc level than the control group (non-significant) (Table 4).

3.4. Selenium (Se)

3.4.1. Cypermethrin treatment group

The animals exposed to cypermethrin alone showed a decrease in selenium concentration in all the tissues observed including liver, kidney, heart, spleen, brain and blood (Table 5).

3.4.2. Sodium selenite treatment group

All the tissues of animals exposed to sodium selenite alone showed an increase in selenium concentration as compared to control group (non-significantly). Spleen showed significant increase as compared to cypermethrin treated group ($p = 0.01$) (Fig 4).

3.4.3. Cypermethrin + sodium selenite treatment group

In experimental rats treated with a combination of cypermethrin and sodium selenite, selenium concentration decreases in brain and blood tissues. Heart, liver, kidney and spleen showed an increase in selenium level when

compared to control group. Spleen showed significant increase as compared to cypermethrin treated group ($p = 0.05$) (Fig. 4).

3.5. Sodium (Na) concentration

3.5.1. Cypermethrin treatment group

Sodium concentration decreases in heart and liver tissues of rats treated with cypermethrin (non-significantly) while significantly ($p < 0.01$) in brain tissue. In kidney, blood and spleen there was a non-significant ($p > 0.05$) increase in sodium concentration when compared to control (Fig. 5).

3.5.2. Sodium selenite treatment group

In the sodium selenite treatment group, Na concentration showed a non-significant decrease in the kidney, liver, spleen and heart while significant decrease in brain ($p < 0.01$). The concentrations of sodium rise in blood in comparison to the control group (non-significantly) (Table 6).

3.5.3. Cypermethrin + sodium selenite treatment group

There was a decrease of the Na concentration, when compared to the control rats, in the heart, liver and spleen tissues of the experimental group exposed to a combination of cypermethrin and sodium selenite. In contrast, an increase of Na concentration was observed in the kidney and blood of the combined treatment group. Brain showed significant ($p = 0.01$) decrease in this group as well (Table 6).

3.6. Potassium (K) concentration

3.6.1. Cypermethrin treatment group

A significant increase occurred in the K concentration of the liver tissues ($p < 0.05$) while a non-significant increase occurred in the brain and kidney tissues than that of the control group. In contrast a significant decrease of K concentration was noticed in the heart and blood ($p < 0.05$) and a non-significant decrease occurred in the spleen ($p > 0.05$) than the control tissues (Table 7).

3.6.2. Sodium selenite treatment group

In all the tissues observed, there was a decrease in K concentration except kidney where its concentration increases as compared to control group (Fig. 6).

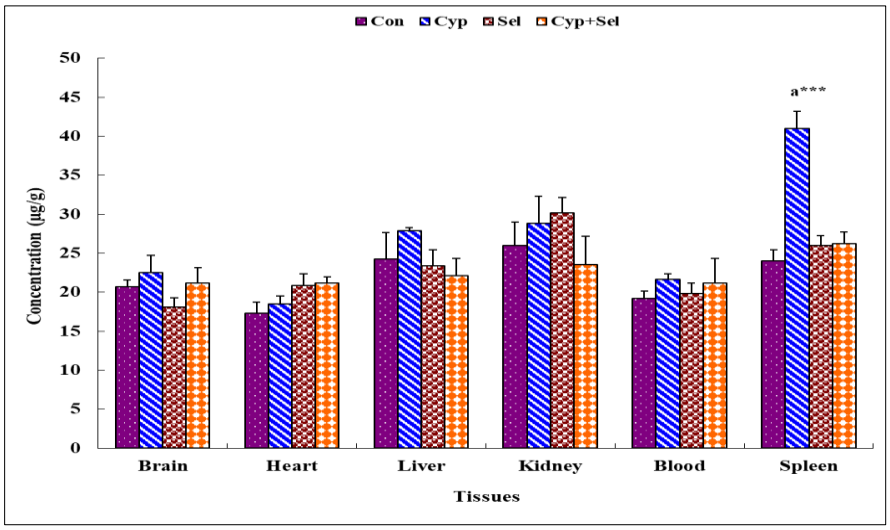
3.6.3. Cypermethrin + sodium selenite treatment group

Potassium concentration increased in the brain, liver, spleen and kidney while decreased in heart and blood from the control group (Fig. 6).

Table 2 Copper concentration (μg / g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	20.680 ± 0.897	22.491 ± 2.22	18.100 ± 1.154	21.136 ± 2.021
Heart	17.308 ± 1.434	18.456 ± 1.049	20.856 ± 1.523	21.142 ± 0.835
Liver	24.226 ± 3.435	27.878 ± 0.385	23.366 ± 2.051	22.150 ± 2.167
Kidney	26.007 ± 2.957	28.86 ± 3.439	30.187 ± 1.918	23.521 ± 3.664
Spleen	24 ± 1.435	41.03 ± 2.198[a***]	25.967 ± 1.318	26.210 ± 1.513
Blood	19.19 ± 0.917	21.631 ± 0.732	19.825 ± 1.363	21.170 ± 3.166

Values are given as SEM (n=5), $p < 0.05$; [a] significantly different from Control; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$



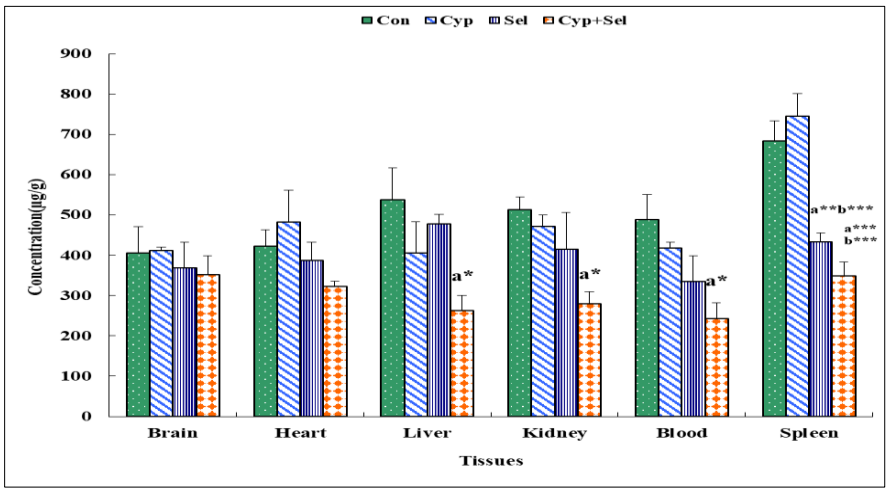
a Significantly different from Control; * p < 0.05; ** p < 0.01; *** p < 0.001

Figure 1 Concentration of Copper (Cu) (µg/g) in different tissues of female Sprague-Dawley rats from control and experimental groups

Table 3 Magnesium concentration (µg / g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	405.3 ± 65.74	411.528 ± 9.031	368.58 ± 63.68	352.176 ± 47.3
Heart	422.796 ± 40.97	483.012 ± 79.08	387.276 ± 45.86	323.004 ± 12.67
Liver	537.852 ± 78.64	406.068 ± 76.83	477.924 ± 24.34	262.92 ± 38.33^{a*}
Kidney	513.696 ± 31.41	472.548 ± 27.22	415.728 ± 90.13	280.188 ± 29.21^{a*}
Spleen	684 ± 49.96	746.1 ± 55.23	432.795 ± 22.28 ^{a**b***}	349.34 ± 34.30 ^{a***b***}
Blood	488.34 ± 62.39	418.632 ± 14.14	334.476 ± 64.49	243.048 ± 38.6^{a*}

Values are given as SEM (n=5), p < 0.05; [a] significantly different from Control; [b] significantly different from Cypermethrin; * p < 0.05; ** p < 0.01;*** p < 0.001



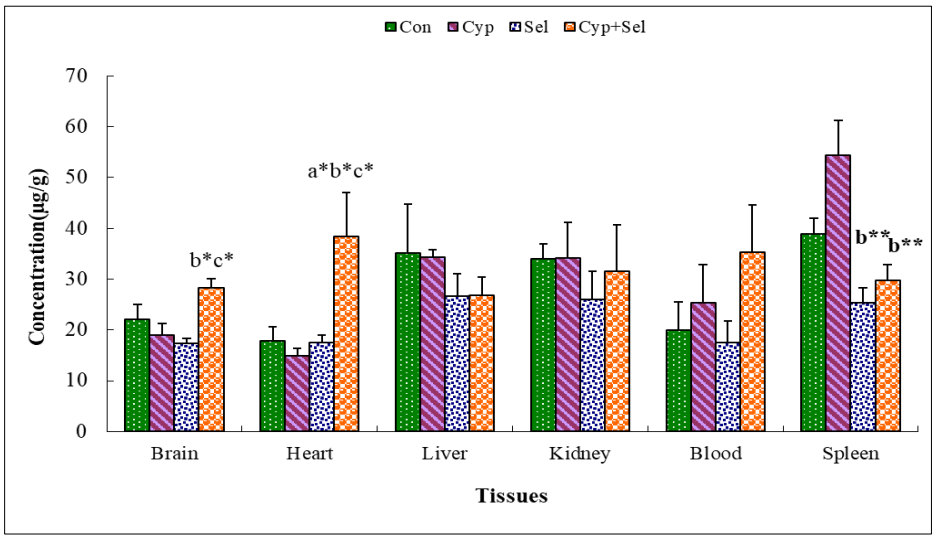
[a] Significantly different from Control; [b] Significantly different from Cypermethrin; * p < 0.05; ** p < 0.01;*** p < 0.001

Figure 2 Concentration of magnesium (Mg) (µg/g) in different tissues of female Sprague Dawley rats from control and experimental groups

Table 4 Zinc concentration (µg / g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	22.058 ± 2.889	18.944 ± 2.343	17.298 ± 0.9615	28.995 ± 1.763 $^{b*\,c*}$
Heart	17.832 ± 2.766	14.865 ± 1.431	17.454 ± 1.492	38.419 ± 8.607^{a*b*c*}
Liver	35.134 ± 9.636	34.382 ± 1.434	26.64 ± 4.419	26.846 ± 3.513
Kidney	33.955 ± 3.034	34.113 ± 7.107	26.052 ± 5.446	31.480 ± 9.227
Spleen	38.86 ± 3.040	54.35 ± 6.910	25.37 ± 2.918 ^{b**}	29.691 ± 3.203 ^{b**}
Blood	20.004 ± 5.466	25.279 ± 7.548	17.448 ± 4.337	35.337 ± 9.182

Values are given as SEM (n=5), $p < 0.05$; a significantly different from Control; b significantly different from Cypermethrin; c significantly different from Selenium; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$



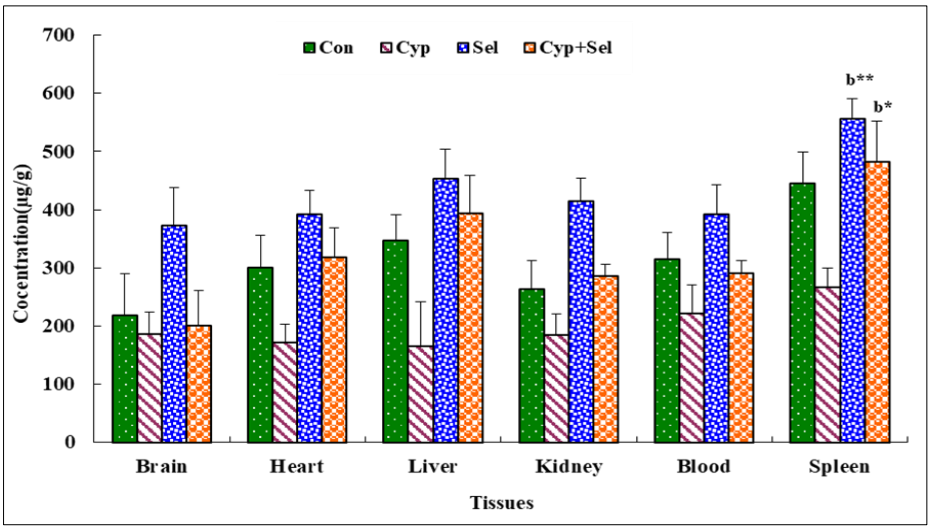
a Significantly different from Control; b Significantly different from Cypermethrin; c Significantly different from Selenium; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$

Figure 3 Concentration of Zinc (Zn) (µg/g) in different tissues of female Sprague Dawley rats from control and experimental groups

Table 5 Selenium concentration (µg / g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	219.1 ± 71.24	186.1 ± 38.63	372.1 ± 66.27	200.0864 ± 61.08
Heart	299.8 ± 56.58	171.1 ± 32.24	392.6 ± 41.03	318.865 ± 50.36
Liver	347.3 ± 44.57	165 ± 76.18	453.8 ± 49.45	394.2328 ± 64.46
Kidney	264.2 ± 48.67	185.3 ± 35.24	414.2 ± 39.62	285.9856 ± 20.35
Spleen	4445 ± 547.9	2671 ± 324.5	5567 ± 348.1 ^{b**}	4822.448 ± 708.5 ^{b*}
Blood	315.6 ± 45.61	221.6 ± 49.56	391.7 ± 51.28	290.872 ± 21.02

Values are given as SEM (n=5), $p < 0.05$; b Significantly different from Cypermethrin; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$



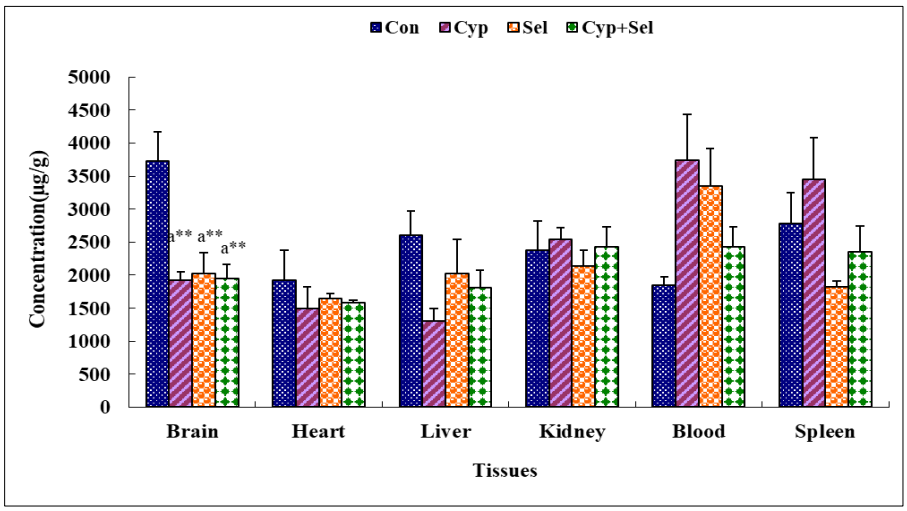
a Significantly different from Control; b Significantly different from Cypermethrin; * p < 0.05; ** p < 0.01;*** p < 0.001

Figure 4 Concentration of Selenium (Se) (µg/g) in different tissues of female Sprague- Dawley rats from control and experimental groups

Table 6 Sodium concentration (µg /g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	3731 ± 437.8	1925.402 ± 124.1^{a**}	2023.438 ± 312.4^{a**}	1947.3 ± 214.2^{a**}
Heart	1921.206 ± 461	1499.299 ± 323.2	1651.47 ± 68.62	1576.993 ± 37.75
Liver	2607.929 ± 368	1309.365 ± 178.8	2029.212 ± 507.7	1806.976 ± 270.5
Kidney	2376 ± 439.1	2537 ± 185	2144 ± 238.9	2432.314 ± 296.4
Spleen	2775 ± 472.7	3449 ± 630.8	1822.02 ± 88.61	2356.43 ± 385.8
Blood	1847.788 ± 120.5	3741.083 ± 698.2	3347.092 ± 574.8	2433.914 ± 300.6

Values are given as SEM (n=5), p < 0.05; a significantly different from Control; * p < 0.05; ** p < 0.01;*** p < 0.001



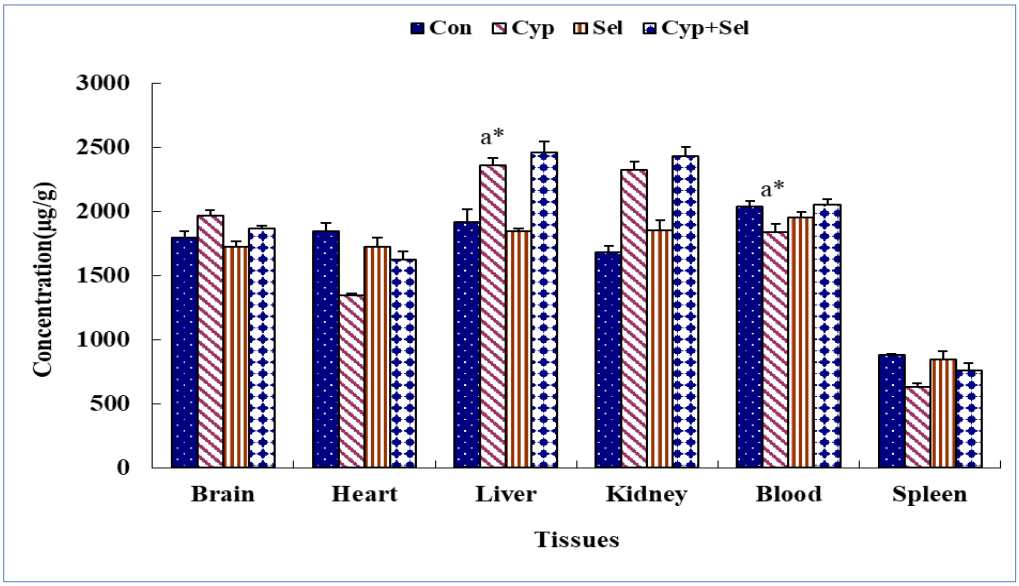
a Significantly different from Control; * p < 0.05; ** p < 0.01;*** p < 0.001

Figure 5 Concentration of Sodium (Na) (µg/g) in different tissues of female Sprague-Dawley rats from control and experimental groups

Table 7 Potassium concentration (µg / g wet weight) in vital tissues of control and experimental groups

Organs	Control	Cypermethrin	Selenium	Cypermethrin + Selenium
Brain	1791.40 ± 53.86	1967.65 ± 43.83	1723.75 ± 39.62	1867.65 ± 21.02
Heart	1847.10 ± 61.36	1341.60 ± 16.07[a*]	1724.7 ± 69.58	1623.2 ± 66.86
Liver	1917.6 ± 95.94	2359.87 ± 53.2 [a*]	1847.6 ± 21.81	2458.2 ± 89.29
Kidney	1677.79 ± 55.81	2327.2 ± 60.3	1850.05 ± 82.66	2433 ± 71.35
Spleen	2036 ± 43.34	1840.80 ± 64.43	1952 ± 43.85	2052 ± 41.81
Blood	876.96 ± 6.9	632.10 ± 29.35 [a*]	842.3 ± 66.30	759.96 ± 56.19

Values are given as SEM (n=5), $p < 0.05$; a Significantly different from Control; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$



a Significantly different from Control; * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$

Figure 6 Concentration of Potassium (K) (µg/g) in different tissues of female Sprague Dawley rats from control and experimental groups

4. Discussion

In several areas of Pakistan and other agricultural countries, the issue of protection against pesticides' exposure through drinking water, food and many other sources has assumed considerable importance in view of the widespread effects of pesticide poisoning of large number of human population. Prevention of pesticide toxicity through selenium as a nutritional supplement may be a possible option.

Selenium is an important dietary nutrient for all mammalian species [15]. Selenium compounds are also toxic for intact animals as well as in cultured cells [16]. It is well known that at supranutritional doses, selenium has a pronounced chemoprotective effect on carcinogen-induced cancers [17]. Selenium toxicity depends both on the chemical form and quantity of the element consumed [18-21].

The aim of this study was to evaluate the effect of selenium co-administration on the levels of essential mineral elements in the case of cypermethrin toxicity. Copper concentration increased in the brain and liver in cypermethrin treated group while decreases in selenium treated group. In combined group, the value remains close to normal. Copper is an important metal which participates in several enzymatic reactions. The role of the liver as a detoxifying and storage organ might be indicated by the high levels of copper in the liver, by virtue of metallothioneins or other metal-binding proteins [22].

In heart, copper concentration increases non-significantly in all treated groups. In kidney, its level increases both in cypermethrin and selenium alone treated groups while remains close to normal in combined treated group. In blood, copper concentration increases in cypermethrin and combined treated group while remains unaltered in selenium alone treated group.

Magnesium is present primarily in the bone and in the cells of all soft tissues and is vital for calcium metabolism. Magnesium concentration increased in cypermethrin alone treated group while decreased in selenium alone and in selenium + cypermethrin combined group in heart and brain tissues. In liver and kidney, its concentration decreases non-significantly in cypermethrin and selenium alone treated groups while significantly ($p < 0.05$) in combined group.

Increased ECF concentration of Mg, depresses activity of the nervous system and skeletal muscle contraction [23]. Magnesium is an enzymatic cofactor for enzymes involved in metabolism, DNA replication and RNA synthesis [10]; raised Mg concentration might have altered numerous cellular reactions which should be investigated further.

In brain, Zinc concentration decreases both in cypermethrin and selenium treated groups (non-significantly); but in combined group the values were raised significantly ($p < 0.05$) in comparison to other treated groups. In liver, all the treated groups showed decrease in the levels of zinc. Liver is mainly concerned with the filtration of blood and removal of debris.

Zinc decreases in heart in cypermethrin treated group, remained unaffected in selenium treated group while increases significantly in combined treated group when compared to all the other treated groups. Zinc is a cofactor of many enzymes (especially in carbonic anhydrase in RBCs) and acts as an electron acceptor [10]. Zinc concentration increases in selenium alone and combined treated groups when compared to control.

Spleen is the major tissue that degrades hemoglobin and filter blood. In spleen, the concentration of zinc increases in cypermethrin treated group while decreases non-significantly in other groups as compared to control and significantly ($p < 0.05$) when compared to cypermethrin treated group.

In blood, the concentration of zinc increases in cypermethrin and combined treated group while decreases in selenium alone treated group as compared to control values. Zinc induces metallothionein (MT) production. MT synthesis occurs primarily in the organs of absorption and excretion, but they also occur in the blood [24].

The concentration of selenium in cypermethrin treated group decreased as in the combined treatment group. In selenium alone treated group, there was an increase in selenium levels of blood. The same trend was present in selenium concentrations among different treatment groups in the rest of the body tissues observed. It clearly indicates that cypermethrin disrupts the normal metal concentration which was brought closer to control values by selenium co-administration.

Electrolytes are necessary for maintaining body homeostasis; of which sodium and potassium are the major electrolytes that regulate membrane potentials as well as cellular fluid volumes and are responsible for regulating the transmission of nerve impulses and muscular contraction; regulate blood pressure and hypertension [25]. Potassium is most abundantly found as intracellular cation, and only about 2% of total body potassium is extracellular. Cell membrane polarization is strongly influenced by the ratio between ICF and ECF potassium concentrations, which in turn affects essential cell processes, like the conduction of nerve impulses and contraction of muscle cell (including myocardial). Thus, relatively small changes in plasma potassium concentration can have important clinical manifestations.

Sodium is predominantly found in the extracellular fluid (ECF). The volume of extracellular fluid is directly proportional to the sodium content in the body. Sodium balance disorders, leads to many abnormal physiological functioning. Cypermethrin might have interacts with Na^+-K^+ ATPase, at its sodium sensitive site, emphasizing its toxicological and physiological significance [26]. Sodium concentration decreases significantly ($p < 0.01$) in all treated groups when compared to control in brain tissue while non-significantly in liver and heart tissues. In cypermethrin treated group, sodium increases in contrast to selenium treated group where it decreases. In combined treatment groups, the values remain similar to control.

The potassium concentration decreases as compared to control in cypermethrin treated rats. While there was no effect of selenium alone treatment on brain potassium concentration. In heart, potassium concentration decreases and in liver it increases significantly as compared to control group. High levels of Na in all treatment groups and low K levels suggests abnormal cardiovascular functions. Abnormal levels of Na and K play roles in the development of arrhythmias and related cardiovascular problems. Low K levels in the heart might have altered repolarization as was indicated by

the conditions of the rats that showed tremors during the treatment. In kidney, the potassium concentration increases in all treated groups.

The changes observed in trace minerals concentration in some tissues after cypermethrin treatment demonstrate the distribution of these bio-elements. Changes in bio-element metabolism can also result from cypermethrin influence on nutritional status. One should therefore take into consideration diminished intake of these elements in this type of study.

5. Conclusion

This study provides information as regards levels of electrolytes and trace elements, in case of cypermethrin toxicity and effects of the selenium co-administration in modulating its toxicity. Selenium co-treatment provided protection against cypermethrin toxicity to some extent. Further research is needed to investigate the mechanism underlying the effects of cypermethrin on electrolytes and trace minerals of the body.

Compliance with ethical standards

Acknowledgments

I would like to acknowledge Dr. Mohammad Shahab, Vice Chancellor, Shaheed Benazir Bhutto University, Sheringal Upper Dir, Pakistan and Higher Education Commission of Pakistan (MPhil leading to PhD Scholarship, Batch IV) for their support in this study.

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

All animal handling and subsequent killings were done according to the guidelines provided by the ethics committee of the Department of Zoology, Quaid-i-Azam University, Islamabad.

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