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Protective Effects of Some Antioxidants on Mosquito Repellent (Bioallethrin)-Induced Toxicity in Infant Rats

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ABSTRACT

The aim of the present study was to investigate the potential toxic effects of bioallethrin-based Mosquito-Repellents (MR) in non-adult rats as well as to ascertain whether the antioxidant substances such as Vitamin C and Vitamin E + Selenium have any roles in preventing such toxic effects or not. 100 rat pups were divided into four study groups (each group consists of 25 rat pups) as Group I (control), Group II (bioallethrin), Group III (Vit C+ bioallethrin) and Group IV (Vit E+selenium+bioallethrin). The animals in Group II, III, IV were exposed to the vapor of heated tablets including 4.2% bioallethrin 8 hours/day for a period of ninety days in a room with a volume of 23 m^3. Vit C was added at a concentration of 500 mg/L to the fresh drinking water of animals in Group III. Vit E+Selenium combination was administered intraperitonally to the animals in Group IV once weekly at a dose of 50 mg/kg. According to the results, it was determined that antioxidants, particularly combination of Vitamin E+selenium administration, may be beneficial at preventing toxic effects of bioalletrin in rat pups. As a conclusion, when bioallethrin based- MR is used, Vit E+Selenium combination can be advised to prevent the effects of bioallethrin.

Keywords : Mosquito repellent, Bioallethrin, Toxicity, Vitamin C, Vitamin E, Selenium

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INTRODUCTION

Currently, pyrethroid-based mosquito repellents are commonly used against the mosquito in home, because these products exhibit high efficiency and have a low risk of accumulation in environment. It is well known that these insecticides, which are accepted as safe for human health and environment; lead to some changes in organism as a consequence of long-term use. If the indoor air is refreshed continuously, acute toxic effects are not observed. However, these products have chronic toxic effects on nervous system, immune system, endocrine system, reproductive system and liver, especially in children. According to the studies conducted with pyrethroids, permanent changes linked with pyrethroids in behaviors and biochemical structure comprising learning ability [1], motor activity [2], sexual behaviours [3], muscarinic receptor binding density [4] and permeability of blood-brain barrier [5] in infants were reported. Pyrethroids can cause lesions in cholinergic system and deficiency in learning and memory abilities [6]. Lipid peroxidation (LPO) has been reported to be among the intoxication mechanisms caused by pesticide exposure [7].

In this study, we aimed to detect the minimum probable toxic effects of the mosquito-repellents in non-adults by means of neuropharmacological, biochemical, hematological and histopthological methods as well as to ascertain whether the antioxidant substances such as Vit C and Vit E+Selenium combination have any roles in preventing this kind toxic effects or not.

MATERIALS AND METHOD

Material

Experimental animals used in this study were obtained from Laboratory Animal Unit at Faculty of Medicine, University of Yuzuncu Yil /Turkey (Ethical approval number: 2006/004). Bioallethrin-based mosquito-repellent mat (Spira Mat®, Sedat Tahir Ltd. Inc, Turkey) and mosquito-repellent tablet heater device (Raid®, Turkey) was bought from a local hypermarket (Turkey). Vit C (L-ascorbic acid, purity +99%) was obtained from Sigma Aldrich, Germany, Vit E+selenium (Eselen®, 20 mL vial) was provided from Vetas, Turkey. The commercial kits for SOD (Ransod kits®) and GPx (Ransel kits®) assay were from Randox Company, United Kingdom, and catalase kits (Calbiochem®) were provided by Merck Millipore, Germany.

Methods

100 rat pups were divided into four groups (each group consists of 25 rats) as Group I (control), Group II (bioallethrin), Group III (vitamin C + bioallethrin) and Group IV (vitamin E+selenium + bioallethrin). The animals in Group II, III, IV were exposed to the vapor of heated tablets

(including 4.2% bioallethrin) 8 hours/day for a period of ninety days in a room with a volume of 23 m^3. Vitamin C was added at a concentration of 500 mg/lt to the fresh drinking water of animals in Group III [8]. Vitamin E+selenium combination was administered intraperitonally to the animals in Group IV once weekly at a dose of 50 mg/kg [9]. Initially, neuropharmacological tests were performed on the rats on 30th, 45th, 60th, 75th and 90th days of the experiment. A day after finishing these tests, 5 rats were randomly selected from each group and were anesthesized, blood was drawn intracardiacally, and the biochemical and hematological examinations were carried out. Moreover, the 90 days old rat pups were euthenasied following the obtain of blood samples. After all the liver, spleen and brain samples were isolated and examined histopatologically.

Analyses of mosquito repellent tablets

Gas chromatography (Schimadzu GC-17A, Japan) analysis of tablets were performed at Faculty of Veterinary Medicine, University of Ondokuz Mayis, Turkey.

Neuropharmacological tests

These tests were performed using Motor Activity Cage Device (LSI Letica LE 8811, Comelia, Spain) and Rotarod Device (Degisim, Turkey). The duration of tests for each rat was determined to be 5 minutes. The number of rapid and slow movements and total number of movements were recorded. Defecation number was also counted. To avoid the probable variations of rats' movements, after each measurement the cage was wiped off with 10% ethyl alcohol and was dried with a cotton towel. The factors that may have an negative impact on the motions of the rats such as sound, movement and light was tried to be minimalized as possible. Experimental animals were transferred to the rotarod test, after the open field test. In rotarod test, the rotational speed was settled to 20 rpm/200 sec. In order to habitate the rats to the test, all rats were run on the rotarod before the precise measurements and the device was operated for 200 seconds until the animals can run without falling down. To evaluate the rotarod function performance after administration of bioallethrin and antioxidant, the rats were placed onto the rotarod apparatus and rotation process was initiated. The time from start to the moment of falling down was automatically recorded by the device. This assessment was performed twice in one hour intervals. According to the results of two rotarod tests, the phenomenons, in which the rats that were not able to maintain balance for 200 seconds and thus fell down, were considered as an indicator of damage of locomotor system.

Biochemical tests

MDA measurements were performed according to the method based TBA reaction described by Akkus [10], intra-erythrocyte GSH levels were measured according to the method by Beutler et al. [11], GPx enzyme activity measurements were performed according to the method by Paglia and Valentine [12], SOD enzyme activity measurements were performed according to the method by Woolliams et al. [13], and CAT enzyme activity measurements were performed according to the method developed by Wheeler et al. [14] by using UV spectrophotometer (Schimadzu UV-mini 1240, Japan).

Hematological tests

The analysis of the 5 parameters in the blood panel was performed in Physiology Department Laboratory at Faculty of Veterinary Medicine with an automatic blood count device operating based on impedance method (Beckman Coulter AcT 5diff AL, USA).

Histopathological tests

The animals were euthanized on the 90th day. Liver, spleen and brain specimens were taken and placed in 10% formaldehyde and fixed in paraffin; then 4 µm sections were stained with hematoxylin and eosin, and evaluated under an Olympus optical microscope.

Statistical analyses

Statistical evaluations were carried out utilizing MEANS and GLM (General Linear Model) procedures of SAS (1998) statistical software. One-way variance analysis (ANOVA) method was used for statistical analysis. The data was shown as mean ± standard deviation. Post-hoc Duncan's was further applied in order to detect significant differences in groups with statistical significance. $P<0.05$ value was considered as statistically significant.

RESULTS AND DISCUSSION

Each tablet was containing 4.2% bioalletrin according to the results of analysis of mosquito repellent tablets.

As shown in Table 1, inhalation of bioalletrin caused a statistically significant increase in locomotor and general movement activity on the 75th and 90th days in Group II and Group III, according to the open field test. In Group II and Group III, a statistically significant increase in defecation rate was observed on the 60th day ($p <0.05$). According to results of Rotarod test, the difference was significant between Group II and the other groups on 30th, 45th, 75th, and 90th days, however; on the 60th day, only the difference between Group II and Group I was significant ($p <0.05$). In the Rotarod data of Group II, there was a significant decrease compared with Group I and the other groups.

Table 1: Neuropharmacological findings

Tests	Groups	30th day	45th day	60th day	75th day	90th day
	Group I	2946±76	1937±256	3582±840	2309±453	2866±620
Locomotor	Group II	2540±279	2516±550	4176±604	[a]4611±366	[a]4847±552
movement	Group III	2261±252	1814±307	3966±451	[a]4162±333	4348±795
	Group IV	2879±519	2013±577	3489±647	[bc]2650±487	3848±369
	Group I	903±61	633±72	818±120	570±58	529±53
Rearing	Group II	795±67	584±50	901±60	[a]879±97	[a]893±72
Movement	Group III	968±91	611±116	996±81	[a]865±79	[a]908±115
	Group IV	864±171	577±122	804±69	[bc]512±98	[a]813±58
	Group I	3849±130	2571±325	4400±904	2878±507	3395±657
General	Group II	3335±307	3100±568	5077±657	[a]5490±453	[a]5740±584
Movement	Group III	3229±334	2425±405	4963±468	[a]5028±408	5256±876
	Group IV	3743±656	2591±683	4292±697	[bc]3162±575	4661±379
	Group I	1.54±0.33	1.64±0.28	1.72±0.33	1.15±0.15	2.063±0.37
Defecation	Group II	1.78±0.33	2.17±0.15	[a]2.65±0.22	1.75±0.19	2.37±0.38
frequency	Group III	1.73±0.32	2.16±0.37	[a]2.73±0.36	1.88±0.41	2.30±0.16
	Group IV	1.48±0.23	2.03±0.35	[bc]1.25±0.25	1.49±0.30	1.78±0.33
	Group I	200±0	194±6.50	176±15.4	189±6.74	200±0
Rotarod	Group II	[a]125±23.2	[a]58±27.51	[a]92±36.6	[a]122±31.9	[a]154±22.6
findings	Group III	[b]195±5.30	[b]167±20.03	149±24.1	[b]190±10	[b]194±6
	Group IV	[b]186±8.84	[b]182±18.2	162±24.1	[b]193±7.5	[b]192±7.6

a: $p<0.05$ (Comparison with Group I)

b: $p<0.05$ (Comparison with Group II)

c: $p<0.05$ (Comparison with Group III)

According to the results obtained from biochemical exams, there was a statistically significant increase in MDA, SOD and catalase activity of Group II and Group III compared with Group I and Group IV on the 90th days. As GSH levels reduced on 45th, 60th, 75 and 90th days in the Group II, it reduced on the 75th and 90th days in the Group III. The GPx enzyme activity of Group IV was higher than the other groups. Furthermore, there was no statistically significant decrease in the GPx enzyme activity of Group II, compared with the control group (Table 2).

Table 2: Biochemical findings

Data	Groups	30th day	45th day	60th day	75th day	90th day
	Group I	1.68±0.004	1.67±0.008	1.69±0.003	1.71±0.010	1.72±0.008
MDA	Group II	[a]1.87±0.02	[a]1.88±0.013	[a]1.89±0.03	[a]1.93±0.03	[a]1.91±0.02
(nmol/ml)	Group III	[ab]1.79±0.01	[ab]1.78±0.02	[ab]1.80±0.012	[ab]1.83±0.05	[ab]1.80±0.02
	Group IV	[bc]1.72±0.02	[ab]1.74±0.02	[bc]1.73±0.01	[b]1.75±0.012	[bc]1.74±0.012
	Group I	54±1.92	52±2.90	50±1.98	60±1.17	58±2.01
GSH	Group II	45±2.22	[a]42±3.30	[a]37±2.00	[a]44±1.63	[a]42±2.43
(nmol/ml)	Group III	49±2.47	45±2.49	[b]46±3.08	[a]51±3.56	[ab]52±2.46
	Group IV	[b]56±4.31	[b]54±3.51	[b]51±1.64	[b]58±3.23	[bc]59±1.43
GPx	Group I	4.49±0.90	6.06±0.37	5.45±0.32	6.49±0.92	6.33±0.27
enzyme	Group II	3.39±0.22	4.54±0.81	4.52±0.59	4.95±0.57	5.02±0.63

activity	Group III	4.87±0.22	4.84±0.48	5.69±0.45	5.96±0.88	6.29±0.16
(U/ml)	Group IV	[b]5.50±0.34	[bc]6.90±0.40	[abc]7.95±0.51	[bc]8.22±0.39	[b]7.44±0.78
SOD	Group I	219.8±0.22	220.9±0.89	219.3±1.04	221.8±0.58	221.9±0.67
enzyme	Group II	[a]242.0±0.73	[a]245.7±1.22	[a]244.4±1.14	[a]244.6±1.22	[a]243.2±2.42
activity	Group III	[ab]229.1±2.01	[ab]228.2±1.63	[ab]227.9±1.44	[ab]231.8±1.85	[ab]228.6±2.03
(U/ml)	Group IV	[bc]219.9±0.25	[bc]219.7±0.61	[bc]219.5±0.71	[bc]220.1±0.53	[bc]220.3±0.38
CAT	Group I	1.68±0.13	1.70±0.16	2.18±0.19	2.48±0.22	2.22±0.18
enzyme	Group II	[a]3.34±0.25	[a]4.40±0.22	[a]3.92±0.14	[a]3.92±0.21	[a]3.64±0.38
activity	Group III	[ab]2.24±0.19	[a]3.56±0.51	[ab]3.22±0.19	[a]3.84±0.34	[b]2.88±0.26
(U/ml)	Group IV	[b]1.86±0.09	[abc]2.62±0.17	[bc]2.44±0.19	3.12±0.43	[b]2.42±0.15

a: p<0.05 (Comparison with Group I)

b: p<0.05 (Comparison with Group II)

c: p<0.05 (Comparison with Group III)

As shown in Table 3, the erythrocytes, leukocytes, haemoglobin and hematocrit data of Group II and Group III were higher than that of Group I. However, there was a decrease in the platelet number, and also an increase was detected in leukocyte levels in these groups, particularly in Group II.

Table 3:Hematological test results

Data	Groups	30th day	45th day	60th day	75th day	90th day
Erythrocyte	Group I	5.03±0.21	6.43±0.09	6.99±0.27	7.24±0.28	6.55±0.10
count (10^6	Group II	[a]5.93±0.22	[a]8.10±0.25	[a]8.20±0.22	[a]8.82±0.35	[a]8.43±0.18
/μL)	Group III	5.74±0.29	[ab]6.95±0.10	[b]7.00±0.18	[a]8.71±0.34	[a]7.70±0.38
	Group IV	5.40±0.26	[b]6.78±0.15	7.51±0.22	[abc]6.22±0.15	[b]7.34±0.39
Hemoglobin	Group I	9.94±0.34	12.42±0.31	13.70±0.44	13.99±0.39	13.36±0.14
count (g/dL)	Group II	11.23±0.64	[a]13.83±0.48	14.46±0.40	15.25±0.54	[a]14.95±0.31
	Group III	11.26±0.46	13.08±0.23	13.36±0.24	[a]16.19±0.62	[a]15.26±0.67
	Group IV	11.15±0.64	[b]12.73±0.23	13.43±0.66	[bc]12.68±0.30	[bc]13.43±0.57
	Group I	30.6±1.2	37.1±0.9	41±1.4	42.2±1.2	36.4±1
Hematocrit	Group II	34.9±2	[a]42.3±1.1	43.6±1.3	46.3±1.7	[a]44.5±1.1
count (%)	Group III	34.3±1.4	[b]39.3±0.6	[b]39.6±0.8	[a]48.3±1.9	[a]44.3±2
	Group IV	32.3±1.6	[b]38.6±0.7	40.3±1.6	[abc]36.5±1.1	[bc]39.6±1.9
Platelet count	Group I	681±36	648±23	722±42	550±39	756±41
(10^3/μL)	Group II	684±30	634±42	660±26	[a]663±17	[a]640±37
	Group III	568±95	834±52	604±61	[a]637±34	[a]609±39
	Group IV	515±124	[c]575±102	587±125	632±18	[a]587±27
	Group I	2.52±0.24	3.42±0.16	4.24±0.42	4.03±0.50	1.86±0.66
Leukocyte	Group II	[a]3.72±0.10	5.47±3.60	7.22±0.72	[a]9.43±1.32	[a]6.40±1.72
count (10^3/μL)	Group III	[b]2.84±0.19	5.45±0.57	5.63±1.00	[b]5.44±0.67	[a]5.24±0.52
	Group IV	[b]2.43±0.29	4.74±0.29	7.53±3.55	[b]4.14±0.38	[b]3.41±0.47

a: p<0.05 (Comparison with Group I)

b: p<0.05 (Comparison with Group II)

c: p<0.05 (Comparison with Group III)

Histopathological evaluation revealed some changes and degenerations in brain tissues (Figure 1, 2, 3 and 4) and liver tissues (Figure 5 and 6)

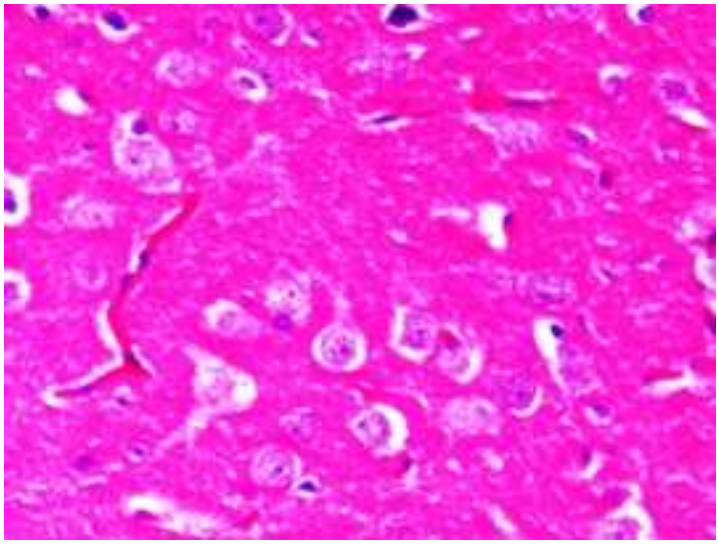

Figure 1:Thalamus H&E, x800 (Group I)

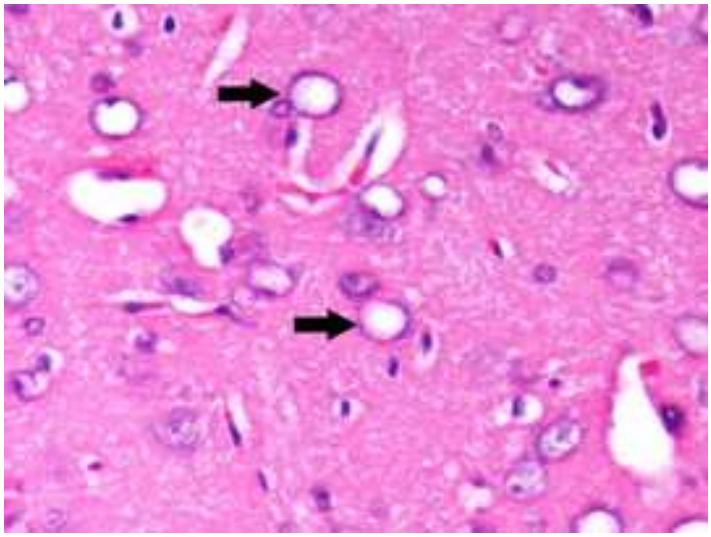

Figure 2: Thalamus, nuclear swelling (arrow), H&E, x800 (Group II)

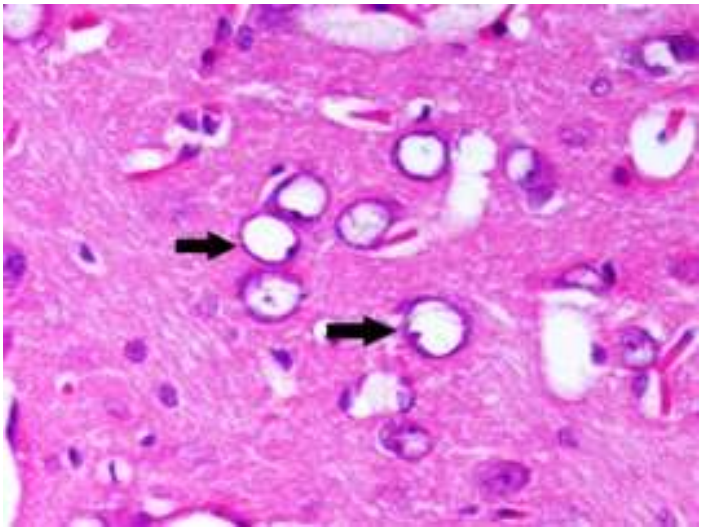

Figure 3: Thalamus, nuclear swelling (arrow), H&E, x800 (Group III)

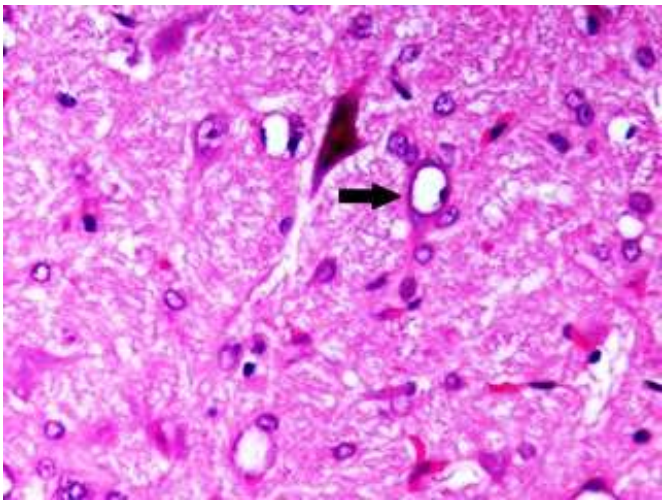

Figure 4: Thalamus, nuclear swelling (arrow), H&E, x800 (Group IV)

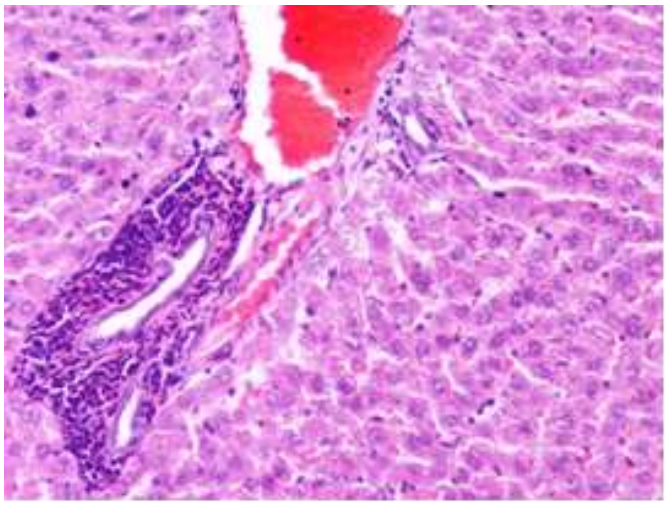

Figure 5: Increased Kuppfer cell count in portal space and degeneration, H&E, x400 (Group II)

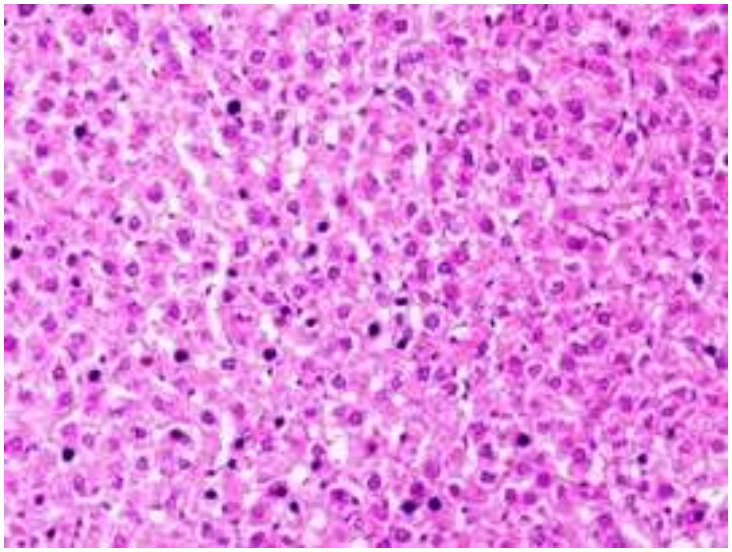

Figure 6: Degenerative alterations, H&E, x200 (Group IV)

According to a study conducted by Nasuti et al. [15], an increase in the locomotor activity of the neonatal rats exposed to low-dose pyrethroid on 30th day after the birth was observed. There was an observed increase in the rearing activity at the rats which were exposed to cypermethrine, as well. The impacts of deltamethrine on physical, reflex and behavioral development were examined in a study by Lazarini et al.[3], and an increase in the frequency of rearing movements and in stratial DOPAC levels were detected in male rat pups on the 21th day.

Hussain et al.[16] have reported that deltamethrine caused a significant increase in locomotor activity. The increase in motor movements determined on 75th and 90th days in Bioallethrin Group and Vit C + Bioallethrin Group could be caused by the brain damage and oxidative stress induced by bioallethrin which was also histopathologically detected. The alterations in locomotor movements show a resemblance to the movement alterations reported in other studies.

In the bioallethrin group, open field test of animals has shown a hyperactivity, the case of the restlessness on the rotarod device indicates a lack of attention. Also a reduced motor coordination has occured in these animals. The hyperactivity detected by the open field tests and the attention deficit detected by the rotarod test were similar to the symptoms of the hyperactivity/attention deficit disorder (ADHD) seen in children. Elevated dopamine metabolism has been suggested in ADHD [17]. In USA, a research was carried out with pyrethroids as a risk factor for ADHD in children between 6 and 15 ages.

In this study, the international health and nutritional committee was consulted for parent's opinions on ADHD, whose children suffer from ADHD. The level of 3-pheoxybenzoic acid, which is a metabolite of pyrethroid pesticides, in urine was investigated as a measure of

exposure. The parents with detectable levels of pyrethroid metabolite in their urine, have noticed that their children exhibit signs of ADHD. This number was twice more than those, whose children were diagnosed with ADHD by an expert [18]. Manna et al. [19] have reported that deltamethrine does decrease the motor coordination. Moreover, the rats that were exposed to deltamethrine [20], and to alpha cypermethrine [21], has shown a decrease in their motor coordination in the rotarod test.

Despite the fact that we are not able to explain the exact reason of how combination of Vit E + selenium application prevents behavioral changes caused by bioallethrin, it can be thought that the strong antioxidant properties of these combination is associated with the prevention of damage in the brain tissue induced by free radicals. Pecticides exhibit their toxic effects via oxidative stress mediated mechanism which leads to cell damage [22]. In this study, the high MDA levels detected in bioallethrin group is an indicator of oxidative stress inducing effect of bioallethrin. While Vit C partly prevented the oxidative stress induced by bioallethrin, it was almost completely prevented by Vit E+ selenium. In recent years, many structural changes and biochemical disorders were detected in erythrocytes following the exposure of pyrethroids such as cypermethrin [23], fenvalerate [24]. In this study, the increase in MDA levels in erythrocytes as a result of bioallethrine application were in conformity with those reported by Nasuti et al. 25 and Prasanthi et al. [26] who detected the oxidative damage induced by pyrethroids that can easily pass through the cell membrane due to the properties like high lipid solubility and the lack of α-cyano group.

In this research, the reason of decrease in the GPx activity in bioallethrin group might have elevated the levels of superoxide radicals and decreased GSH amount. Because the excessive increase of superoxide radicals causes a decrease in GPx enzyme activity. Moreover, the reason of increased GPx activity in the group treated with Vit E + selenium combination; may be the addition of selenium which forms an important part of GPx enzyme. The addition of selenium is known to increase the radical scavanger GPx enzyme activity, significantly [27]. The increased GPx activity detected in the group treated with Vit E + selenium combination; can provide a better protection of cells against H_2O_2

It has been reported that cypermethrin and fenvalerate causes an increase in LPO, and this elevation induces an increase in the activity of antioxidant enzymes such as SOD and CAT. Moreover, a decrease in the GSH levels in erythrocytes was determined [28]. Maiti et al. [29] have reported increased levels of free radicals and increased activity of SOD and CAT enzymes in mices treated with fenvalerate. Gabinelli et al. [30] have reported increased levels of LPO and

decreased activity of GPx enzyme in mices treated with cypermethrine. Manna et al. 19 examined the short-term toxicity of deltamethrin in rats and as a consequence, they have detected a reduction in the activity of CAT and SOD enzymes and a decrease in GSH levels. High-dose cypermethrin and permethrin has been reported to cause a significant increase in activity of LPO, CAT and SOD enzymes; however caused a decrease in activity of GPx enzyme [25]. In a study by Gupta et al. [31], rat pups were exposed to the allethrin containing mosquito-repelling vapor 18 hours a day for 8 days and they have reported decreased GSH levels in brain tissue and increased LPO levels in brain, liver and kidney tissue. In this research, the obtained results from biochemical tests are in agreement with the results reported in the studies by Kale et al. [28], Maiti et al. [29], Gabbianelli et al. [30], Nasuti et al. [25], Prasanthi et al. [26], and Gupta et al. [31].

In this study, erythrocytes, hemoglobin and hematocrit levels were higher in the group treated with Vit C + bioallethrin combination than the control group. These results exhibit compliance with those obtained by Haratym-Maj [32], Garba et al. [33]. Al-Damegh [34] has reported an increase in the levels of total RBC, WBC, lymphocytes and hemoglobin in rat blood exposed to the electric mosquito-repellent liquid (prallethrin 1.6 %)

The case of elevation of erythrocytes, hemoglobin and hematocritin levels might be due to the release of an excess amount of erythrocytes in the blood circulation as a result of stimulating erythrocyte formation by hematopoietic system induced by bioallethrin. The decreased platelet amount is similar to the results obtained in a research carried out by Sayım et al. [35]. An elevated level of leukocytes was detected in the group treated with Vit C and bioallethrin combination; the increase was more significant in the group treated with bioallethrin. The elevated leukocyte levels were attributed to physiological response occurred in the body of living-being to toxic substances [36]. Therefore, increased leukocyte amounts can be associated with an immune mechanism evolved by the living-being in order to defense against bioallethrine toxicity.

According to the histopathological examination of the brains of the rats especially in bioallethrin group, basophilic neurons, hydropic nuclear swelling and nuclear margination were determined. Furthermore, an increase of the number of Kupffer cells was detected along with mononuclear cell infiltration and formation of splenic germinal centers. It was observed that these lesions formed in brain, liver and spleen were decreased with the selenium application. According to the literature survey, we did not encounter so many studies carried out to examine the histopathological effects of bioallethrin or pyrethroids on the brain except for one study. Srivastava et al. [37] have reported that allethrin-based liquid MR had no significant pathological changes in liver, brain, kidney and gonads.

In this study, chronic toxic effects of bioallethrin which has been considered as safe for mammals; was determined according to neuropharmacological, biochemical, hematological and histopathological evaluations obtained from the rats exposed to bioallethrin inhalation for 3 months; and also applications of Vit E+selenium combinations and Vit C were determined to demonstrate protective effects against the toxicity of bioallethrin. The effect of Vit C was found to be weaker than Vit E and selenium combination. Vit E is the only fat-soluble and chain-braking antioxidant which is present in plasma and erytrocytes of humans [38]. As for Vit C, it is water-soluble and is slower in scavenging peroxyl radicals than Vit E [39]. Vit E, which inhibits formation of free radicals [40], can effectively minimize the LPO in biological systems [41].

Song and Narahashi [42] determined that Vit E selectively blocks the sodium channels modified by pyrethroids in a dose dependent manner without effecting the normal sodium channels. It has been reported that in pyrethroid intoxication, the effect of the Vit E may proceed an antioxidant effect and cell membrane stabilising effect of this substance. Selenium is also necessary for activity of Vit E. Selenium and Vit E behave in a way that supporting each other [43].

CONCLUSION

As a result, the bioallethrin containing mosquito-repellents, which are commonly used because of being considered as safe to protect from mosquitos; have toxic effects in non-adults. Vit E+Selenium combination can play an important role in alleviating these toxic effects. It can be concluded that this study may provide a fundamental basis for the future studies and might provide a significant contribution to the practice.

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