



Impact of Cypermethrin on Some Biochemical Parameters in Rat

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Abstract

Forty adult albino rats were used in this research. They were randomly divided into four groups. The first group served as control group. The other groups were subdivided into three groups according to the concentration of cypermethrin. Three concentrations of cypermethrin were applied (7.5, 15 and 30 mg/kg body weight). All treated doses were given orally every two days and the doses were continued for 30 days. This work included study the changes in the levels of some serum biochemical indices for liver and kidney functions. The findings of this study showed that cypermethrin induced a significant decrease ($P < 0.05$) in blood total protein, albumin and globulin, and a significant increase ($P < 0.05$) in the concentrations of aspartate transaminase, alanine transaminase, alkaline phosphatase, in addition to urea and creatinine. The current study suggests that cypermethrin has a potential toxicity in rats as a model for mammals. Also, the negative changes that observed in biochemical values were gradually increased with increasing concentrations of cypermethrin used in this study.

Key words: cypermethrin; pyrethroid pesticide; biochemical parameters; rats.

Introduction

The use of pesticides is an important method for elimination of harmful animals and plants in order to increase agricultural production, and also used in public health to eradicate disease-carrying organisms for human and animal (FAO, 2005). The annual consumption of pesticides was estimated by approximately 2 million tons worldwide (Uggini *et al.*, 2010). The pyrethroids (synthetic forms of pyrethrins) are the main class of pesticides used worldwide, especially in the United States of America, due to high activity, low toxicity to mammals and fast biodegradation in the environment after use (Ahmad *et al.*, 2009).

Cypermethrin (a type II pyrethroid compound) was manufactured for the first time in 1974 and was marketed in

1977 (WHO, 1989). It is widely used in agriculture, especially in the last two decades, because of the strong effectiveness of this pesticide against a wide range of harmful organisms. The systemic effects of cypermethrin almost targeted to the nervous system by inhibition of acetylcholinesterase (Eaton *et al.*, 2008). The other mechanism is the oxidative stress resulting from exposure to this pesticide (Idris *et al.*, 2012).

Pyrethroid pesticides, including cypermethrin, are one of the most pollutants in the ecosystems. Generally, the cypermethrin-induced toxicity has been reviewed in several

experimental and clinical reports (WHO, 1989; Bretveld *et al.*, 2006; USEPA, 2009; Idris *et al.*, 2012; Singh *et al.*, 2012). Recently, cypermethrin and other pyrethroid compounds are the most widely used in Iraq. Application of pesticides in agricultural activities and over fishing in the south of Iraq represent the potential threat for many aquatic organisms (Yasser and Naser, 2010). For this reason, the aim of this study was to investigate the impact of cypermethrin on some biochemical parameters for liver and kidneys of rats.

Materials and Methods

Preparation of cypermethrin concentrations

Cypermethrin (10 %) [(RS)-cyano-(3-phenoxyphenyl) methyl-(RS)-cis-trans-3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropane carboxylate] sample was obtained from one pesticide stores in Al-Najaf province during the year 2014. The concentrations of cypermethrin were calculated according to the body weight of animals.

Experimental animals

Forty adult female albino rats (*Rattus rattus*) were purchased from Faculty of Pharmacy / University of Karbala-Iraq, were used for this study. The present study was conducted at the animal house of Faculty of Veterinary Medicine / University of Kufa-Iraq. Healthy rats weighing between 215-288 gm were used in this experiment. The animals were maintained in an air-conditioned room in individual stainless steel cages at 22-25 °C throughout the study. The animals received standard pellet feed and water *ad libitum*. None of the rats had any clinically evident infection.

Experimental design

The study protocol was approved by the ethical committee of the Department of Biology- Faculty of

Science - University of Kufa. The rats were acclimated with the laboratory conditions for a period of two weeks before initiation of the experiments.

The mature female rats were randomly distributed into four groups (10 rats each). Three oral concentrations of cypermethrin (7.5, 15, 30 mg/kg body weight), dissolved in corn oil, were investigated. The orally concentrations of cypermethrin were determined according to Fang *et al.* (2013). The control group received only the same volume of corn oil. All treated doses were given orally every two days.

Sample collection

At the end of the experimental period (one month), all rats were anesthetized, using a mixture of ketamine and xylazine i.m., and then they were sacrificed (Schiller and McNamara, 1999). The hemato-biochemical analysis was performed on blood obtained from the experimental and control rats. The blood sample was obtained from animal through heart puncture by using a 5 ml disposable medical syringe. For biochemical tests, the blood was placed in tubes without anticoagulant and centrifuged at 3000 rpm for 10 minutes. The blood serum was separated, transferred into Eppendorf tubes and kept in a refrigerator at -20 °C until the time of analysis (Silici *et al.*, 2009).

Biochemical analysis

The levels of biochemical indices in blood serum that include total protein, albumin, globulin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), urea and creatinine were measured by the spectrophotometer at specific wave lengths according to the protocol of kits supplied by Cypress diagnostics, Belgium.

Statistical analysis

Analysis of data for present study was performed by using Statistical Package for the Social Sciences (SPSS, version 20). The findings were expressed as (mean ± standard error). One way analysis of variance (ANOVA) followed by least significant difference (LSD) was used for the statistical comparison between control and treated groups. Statistical significance

was accepted at P<0.05 values(Steel and Torrie, 1981)

Results and discussion

Blood proteins

Treatment with cypermethrin resulted in a significant decrease (P<0.05) in blood plasma proteins (total protein, albumin and globulin) of all cypermethrin treated groups in rats in comparing with control group as shown in table 1.

Table 1: Effect of cypermethrin on biochemical indices in blood serum in albino rats after 30 day.

| | Control group | Cypermethrin 7.5mg/kg | Cypermethrin 15mg/kg | Cypermethrin 30mg/kg |
|----------------------|----------------------|------------------------------|-----------------------------|-----------------------------|
| Total protein (g/dl) | 8.8 ± 0.21 | *7.5 ± 0.03 | *7.2 ± 0.04 | *6.3 ± 0.10 |
| Albumin(g/dl) | 4.9 ± 0.06 | *4.5 ± 0.02 | *4.3 ± 0.02 | *3.7± 0.17 |
| Globulin(g/dl) | 3.9 ± 0.18 | *3.0 ± 0.04 | *2.9 ± 0.06 | *2.6 ± 0.24 |
| AST (IU/L) | 39 ± 0.76 | *44 ± 0.33 | *47 ± 0.30 | *57 ± 2.24 |
| ALT(IU/L) | 21 ± 0.49 | *27 ± 0.49 | *31 ± 0.33 | *39 ± 0.70 |
| ALP(IU/L) | 44± 1.31 | *64 ± 1.38 | *82 ± 0.88 | *130 ± 6.59 |
| Urea (mg/dl) | 50 ± 0.73 | *55± 0.56 | *60± 1.17 | *76 ± 2.24 |
| Creatinine(mg/dl) | 1.6 ± 0.09 | *2.0± 0.03 | *2.6 ± 0.05 | *2.9 ± 0.04 |

- Data are expressed as mean ± standard error.

-*: Significantly different from control group.

- One-way ANOVA with LSD test at P<0.05.

In this study, a significant decline in serum proteins in all cypermethrin-treated groups was observed. These results are in agreement with those of Khan *et al.* (2009) on goats and Nishaletal. (2012) on mice. Yousefetal. (2003) reported that the decline in plasma protein was mainly due to the decrease in albumin rather than globulin fraction. In another study, Rivarola and Balegno (1991) suggested that the reduction in plasma protein, particularly albumin, in animals treated with pesticides could be attributed to changes in protein and free amino acid metabolism and their synthesis in the liver. Also, the protein depression in the blood was also reported to be mainly due to excessive

loss through nephrosis (Rahmanetal., 1990)

In recent study, it has been proposed that the decrease in serum proteins could be attributed in part to the damaging effect of cypermethrin on liver cells (Nishaletal., 2012). Additionally, the decrease in total protein and globulin might be due to the pathological changes with altered enzymatic activity and impaired protein synthesis by the liver through the production of ROS during the metabolism of cypermethrin (Kale *et al.*, 1999).

Serum transaminases and alkaline phosphatase

There was a significant increase (P<0.05) in the levels of aspartate

transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) in all cypermethrin treated groups in rats in comparison with control group (Table 1).

Based on current knowledge, serum AST, ALT and ALP levels are biomarkers for hepatic diseases. The increase in the activities of these enzymes in serum is indicative for liver damage and thus causes alteration in liver function (Sankar *et al.*, 2012). So, the estimation of various enzyme activities like AST and ALT were carried out because they represent the functional status of liver (Grewal *et al.*, 2009). Furthermore, the increase in ALP is assessed to indicate the damage of various organs such as heart, lungs and kidneys (Hoffmann *et al.*, 1999). As it's known, these compounds are released into the circulation after cellular damage (Friedman *et al.*, 1996).

The activities of enzymes in blood serum can also be used as a relevant stress indicator (Velisek *et al.*, 2006). The administration of cypermethrin has been shown to produce oxidative stress by generating ROS and reducing the antioxidant defense systems (Atessahin *et al.*, 2005). Thus, it may be proposed that cypermethrin-induced oxidative stress may account for the degenerative changes in various organs such as liver, lungs, heart and kidneys (Grewal *et al.*, 2009). Briefly, the high serum concentrations of AST, ALT and ALP are considered to be an index of organ damage. Thus, the increased in the activity of these enzymes, as observed in the present study, are probably due to the cypermethrin-induced pathological alterations of the liver, and kidney tissues.

Urea and creatinine

Results in the present study indicated that treatment with cypermethrin caused a significant increase ($P < 0.05$)

in the concentrations of serum urea and creatinine in all cypermethrin treated rats in comparison with the control animals as shown in table 1.

The elevation of serum urea and creatinine is considered as a significant marker of renal dysfunction. Elevated blood urea is correlated either with an increased protein catabolism in the mammalian body or from a more efficient conversion of ammonia to urea as a result of increased synthesis of enzyme involved in urea production (Rodwell, 1979).

Additionally, the increase in blood urea and creatinine induced by pesticides was correlated closely with histopathological changes in the kidney, and these changes caused disturbance in the transport system of biochemical constituents in the kidney (Janardhan *et al.*, 1988). Also, elevated creatinine is correlated with an increased protein catabolism, as creatinine is the end product of protein catabolism (Grewal *et al.*, 2009).

In conclusion, the results of the present study clearly showed marked disturbances in biochemical parameters of vital organs such as liver and kidneys in various levels. This study showed that cypermethrin has accumulative dose-dependent toxic effects and may be one of the environmental factors that affect mammalian animals. Consequently, The mechanisms of cypermethrin intoxication requires further investigations.

References

Ahmad, L.; Khan, A.; Khan, M. Z. and Hussain, I. (2009). Cypermethrin induced anemia in male rabbits. *Pakistan Vet. J.*, 29(4): 191-195.

Atessahin, A.; Yilmaz, S.; Karahan, I. and Tasmedir, P. B. (2005). The effects of vitamin E and selenium on cypermethrin induced oxidative stress in rats. *Turk. J. Vet. Anim. Sci.*, 29:385-91.

- Bretveld, R. W.; Thomas, C. M. G.; Scheepers, P. T. J.; Zielhuis, G. A. and Roeleveld, N. (2006).** Pesticide exposure: the hormonal function of the female reproductive system disrupted. *Reproductive Biology and Endocrinology*, 4(30):1477-7827.
- Eaton, D. L.; Daroff, R. B.; Autrup, H.; Costa, L. G.; Coyle, J.; Mckhann, G.; Mobley, W. C.; Nadel, L.; Nubert, D; Schukte-Hermann, R.; Peter, S. and Spencer, P. S. (2008).** Review of the toxicology of chlorpyrifos with emphasis on human exposure and neurodevelopment. *Crit. Rev. Toxicol. S.*, 2:1-125.
- Fang, L. Y.; Chen, P.; Xia, H. J.; Jing, L. and Chun, X. L. (2013).** Effects of cypermethrin on male reproductive system in adult rats. *Biomed. Environ. Sci.*, 26(3):201-208.
- Food and Agriculture Organization (FAO) (2005).** International Code of Conduct on the Distribution and Use of Pesticides. Rome, Italy.
- Friedman, L. S.; Martin, P. and Munoz, S. J. (1996).** Liver function tests and the objective evaluation of the patient with liver disease, in: Zakin, D. and Boyer, T. D. (Eds.), *Hepatology: A Textbook of Liver Disease*, 3rded., WB Saunders, Philadelphia, pp.791-833.
- Grewal, G.; Verma, P. K.; Dhar, V. and Srivastava, A. K. (2009).** Toxicity of subacute oral administration of cypermethrin in rats with special reference to histopathological changes. *Int. J. Green Pharm.*, 3:293-299.
- Hoffmann, W. W.; Graham, E. S.; Baldwin, B. H.; Wickenden, C. and Tennant, B. C. (1999).** Clinical enzymology. In: Loeb WF, Quimby FW, editors. In: *Clinical chemistry of laboratory animals*. Philadelphia, PA: WB Saunders Co., p. 399-454.
- Idris, S. B.; Ambali, S. F. and Ayo, J. O. (2012).** Cytotoxicity of chlorpyrifos and cypermethrin: The ameliorative effects of antioxidants. *African Journal of Biotechnology*, 11(99): 16461-16467.
- Janardhan, A.; Rao, A. B. and Sisodia, P. (1988).** Short-term toxicity of methyl benzimidazolecarbamate in dogs. *Bull. Environ. Contam. Toxicol.*, 41:704-711.
- Kale, M.; Rathore, N.; John, S. and Bhatnagar, D. (1999).** Lipid peroxidative damage on pyrethroid exposure and alterations in antioxidant status in rat erythrocytes: a possible involvement of reactive oxygen species. *Toxicol.Lett.*, 105:197-205.
- Khan, A.; Faridi, H. A. M.; Ali, M.; Khan, M. Z.; Siddique, M.; Hussain, I. and Ahmad, M. (2009).** Effects of cypermethrin on clinico-hemato-biochemical and pathological parameters in male Dwarf goats (*Capra hircus*). *Exp. Toxicol. Pathol.*, 61(2):151-160.
- Nishal, K. P.; Manjusha, C.; Sahu, I. and Sirisha, D. (2012).** Protective effect of leucoverin on cypermethrin-induced toxicity in mice. *J.Bio.Innov.*, 1(2): 33-40.
- Rahman, M. F.; Siddiqui, M. K. J.; Mahboob, M. and Mustafa, M. (1990).** Hematological and hepatotoxic effects of isoprocarb in chicken. *J. Appl. Toxicol.*, 10:187-192.
- rivarola, V.. and Balegno, H. F. (1991).** Effect of 2,4-dichloro phenxyacetic acid on polyaminesynthesis in Chinese hamster ovary cells. *Toxicology*, 56:151-157.
- Rodwell, E. W. (1979).** Review of physiological chemistry. 17thed.

California: *Lange Medical Publications*, P.401-4.

Sankar, Palanisamy; Telang, A. G. and Manimaran, A. (2012). Protective effect of curcumin on cypermethrin-induced oxidative stress in Wistar rats. *Experimental and Toxicologic Pathology*, 64:487-493.

Schiller, N. K. and McNamara, D. B. (1999). Balloon catheter vascular injury of the alloxan- induced diabetic rabbit: The role of insulin-like growth factor-1. *Molecular and Cellular Biochemistry*, 202:159-167.

Silici, S.; Ekmekcioglu, O.; Eraslan, G. and Demirtas, A. (2009).Antioxidative Effect of royal jelly in cisplatin-induced testes damage. *J.Urology.*, 74(3):545-551.

Singh, Anand Kumar;Tiwari, ManindraNath; Prakash, Om andSingh, MahendraPratap (2012). A Current Review of Cypermethrin-Induced Neurotoxicity and Nigrostriatal Dopaminergic Neurodegeneration. *Curr.Neuropharmacol.*, 10(1): 64-71.

Steel, R. G. D. andTorrie, J. H. (1981). Principle and Procedure of Statistics. A Biometrical Approach, 2nd ed., McGraw-Hill Book Company, New York, USA.

Uggini, G. K.; Patel, P. V. and Balakrishnan, S. (2010).Embryotoxic

and teratogenic effects of pesticides in chick embryos: a comparative study using two commercial formulations. *Environ. Toxicol.*, 27 (3):166-174.

United States Environmental Protection Agency (USEPA) (2009). A Review of the Relationship Between Pyrethrins, Pyrethroid Exposure and Asthma and Allergies.

Velisek, J.; Wlasow, T.; Gomulka, P.; Svobodova, Z.; Dobsikova, R.; Novotny, L. and Dudzik, M. (2006). Effects of cypermethrin on rainbow trout (*Oncorhynchusmykiss*). *Vet Med.*, 51: 469-476.

World Health Organization (WHO) (1989). Cypermethrin. Environmental Health Criteria 82. International Programme on Chemical Safety, Geneva, Switzerland.

Yasser, A. G. and Naser, M. D. (2010). Acute toxicity of cypermethrin to Benni fish *Barbussharpeyi* (Günther, 1874). *ANU. J. Nat. Sci.*,1(1):107-111.

Yousef, M. I.; El-Deerdash, F. M. K.; Kamel, I. and Al-Salhen, K. S. (2003a). Changes in some haematological and biochemical indices of rabbits induced by isoflavones and cypermethrin. *Toxicology*, 189:223-234.