EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 3
124-128
Year: 2020

SUB-LETHAL TOXICITY OF LAMBDA-CYHALOTHRIN ON REPRODUCTIVE BIOMARKERS OF FEMALE WISTAR RATS

***Iheanacho J.U.I., Onyeka P.I.K., Okafor A. I., Udujih, H. I. and Okoroigbo F. I.**

Physiology Unit, Department of Animal and Environmental Biology, Faculty of Science, Imo State University Owerri, P.M.B. 2000 Owerri, Nigeria.

***Corresponding Author: Dr. Iheanacho J.U.I.**
Physiology Unit, Department of Animal and Environmental Biology, Faculty of Science, Imo State University Owerri, P.M.B. 2000 Owerri, Nigeria.

Article Received on 12/01/2020 **Article Revised on 02/02/2020** **Article Accepted on 22/02/2020**

ABSTRACT
A study on Sub-lethal Toxicity of Lambda-Cyhalothrin on reproductive biomarkers of female Wistar rats were carried out using approved protocols by institutional animal ethics committee and guide lines of National Research Council for care and maintenance of animals. Three concentrations 0.2%, 0.4% and 0.8% of sub-lethal solutions were prepared and administered to three treatment groups of female Wistar rats through feed. At the end of treatment period, blood samples were collected for reproductive hormonal analysis. The results showed that Wistar rats in the treatment groups had a significant dose dependent decrease in serum estrogen, FSH and LH levels while progesterone had a non-significant dose dependent decrease across treated rats. It is therefore necessary to create public awareness on the possible toxic effects of Lambda-Cyhalothrin. Also, further studies should be conducted on its exposure and risks to humans.

KEYWORDS: Lambda-Cyhalothrin, reproductive biomarkers, female Wistar rats.

INTRODUCTION
Pesticides are used in agriculture and public health to control insects, weeds, animals, and arthropod vectors of diseases. The Food and Agriculture Organization of the United Nations (FAO) defined a pesticide as 'any substance or mixture of substances intended for preventing, destroying or controlling any pest, including vectors of human or animal disease, unwanted species of plants or animals causing harm or otherwise interfering with the production, processing, storage, transport, or marketing of food, agricultural commodities, wood, wood products or animal feedstuffs, or which may be administered to animals for the control of insects, mites/spider mites or other pests in or on their bodies' (Bretveld *et al*., 2006).

Currently, pyrethroids are preferred over other classes of pesticides due to their high effectiveness, low toxicity to non-target organisms and biodegradability. Long-term exposure to pesticides can harm animal and human life and can disturb the normal physiological functions of different organs in the body which consequently lead to death. (He, *et al.,* 2008; Mostafalon and Abdollahi, 2012). Pesticides constitute the most widespread xenobiotics due to their ubiquitous use in all aspects of human endeavors. Pesticide residues are often reported in food and drinks and known to gain entry into the human and animal body through the consumption of such. The public who use pesticides or get exposed with them must understand the high toxicity and potential health hazards associated with these pesticides. Lambda cyhalothrin is one of the important pyrethroid pesticides used by farmers for controlling pest in Imo State.

According to Fetoui, *et al*., (2008) Lambda cyhalothrin pesticide is a synthetic pesticide and acaricide used to control a wide range of pests in different applications. Lambda cyhalothrin is a stomach or contact pesticide (Velmurugan, *et al*., 2007). It shows adulticidial, ovicidial and larvicidal activity against insects belonging to Lepidoptera, Hemiptera, Diptera and Coleoptera (Bao, *et al.,* 2007). It is effective against vectors of diseases like flies, mosquitoes, cockroach and ticks (Kidd and James, 1991; Oros and Werner, 2005). Lambda cyhalothrin have also shown some level of toxicity to mammalians though considered less toxic compared to other pesticides (Atamanalp, *et al.,* 2002; Ratnasooriya, *et al.,* 2003; Anadon, *et al.,* 2006).

The toxicity of pyrethroid pesticides to mammalian animals, animals exposed to them exhibited changes in their physiological activities beside other pathological features. Therefore, using pyrethroid containing products will exposed humans and animals to the toxicants (Dahamna, *et al.,* 2009). According to El-Demerdash, 2007; Fetoui, *et al.,* 2010 and Abdallah, *et al.,* 2012 lambda cyhalothrin, a third generation type-II synthetic pyrethroid used due to its rapid metabolism and

excretion is prone to create health hazards. Several reports confirmed the toxicity of lambda cyhalothrin exposure on female and male reproductive system of mammals (Oshoke, *et al.*, 2016). Therefore, the purpose of this study was to investigate whether lambda cyhalothrin poses on reproductive biomarkers toxicity to female Wistar rats sub-lethally exposed, since lambda cyhalothrin pesticide commonly use domestically and in agriculture.

MATERIALS AND METHODS

This research was ethically approved by the appropriate authority and the guide line of National Research Council (NRC, 2011) were followed for care and maintenance of animals.

Animals

Mature healthy Wistar rats (*Rattus norvergicus)*, thirty six (24 female and 12 male) in number weighing between 160-185g were used. They were procured from the Animal House of the Department of physiology, University of Port Harcourt, River State Nigeria.

After three weeks of acclimatization before the commencement of the treatment at normal room temperature. The female rats were randomly divided into four groups, group 1 served as control group while 2 to 4 groups were the treatment groups and were paired 2 female per 1 male for fertilization to occur which was confirmed by a vagina smear test carried out each morning, confirmation of spermatozoa was considered day 1 of gestation.

The animals were housed in labeled plastic cages covered with wire gauze under standardized animal conditions, fed with pelleted food (Vita feeds) twice daily with each rat consuming estimated feed weight of 30g per day and drinking water *ad libitum.*

Lambda cyhalothrin Preparation

Three concentrations 0.2%, 0.4% and 0.8% of sub-lethal solution were prepared by diluting the commercially available Lambda Cyhalothrin liquid in distilled water (DW). The protocols were approved by institutional animal ethics committee and guide lines of National Research Council for care and maintenance of animals.

Lambda Cyhalothrin administration

The solution was administered to the female Wistar rats only through feed by mixing 15ml of different prepared concentration of lambda cyhalothrin accordingly to 15g of feed twice a day throughout the period of gestation and 21 days after parturition. The first day of administration was considered day 1 of treatment.

Blood sampling

At the end of treatment period, each animal was anesthetized by chloroform and blood sample collected through cardiac puncture. Heparinized bottle containing blood were then centrifuged at 3000 rpm during 20min and obtained serum was conserved at -80^{o}C. Serum progesterone, Estrogen, LH and FSH level were measured at 450nm by spectrophotometry.

Statistical analysis

Data obtained was expressed as Mean ± Standard Deviation and analyzed using the SPSS package 20.0. One-way Analysis of Variance (ANOVA) was used. Values at $p<0.05$ was regarded as significant in comparison with appropriate controls.

RESULTS

Reproductive hormones

Wistar rats sub-lethally exposed to lambda cyhalothrin with respect to progesterone levels showed a non-significant dose dependent decrease in treated groups. Estrogen levels significantly decreased ($p<0.05$) in rats treated with lambda cyhalothrin. FSH and LH levels showed a significant dose dependent decrease in lambda cyhalothrin treated rats compared to untreated (control) group. (See Table 1).

Table 1: Serum levels of Progesterone, Estrogen, LH and FSH on female rats after treatment with different doses of Lambda-cyhalothrin.

Groups	Progesterone(ng/ml)	Estrogen(pg/ml)	LH(mIU/ml)	FSH(mIU/ml)
Control (0.0%)	10.10 ± 0.34	62.25 ± 2.06	2.28 ± 0.39	2.80 ± 0.31
Treatment 1 (0.2%)	8.74 ± 0.35	59.45 ± 0.20	2.00 ± 0.20	1.80 ± 0.21
Treatment 2 (0.4%)	8.95 ± 0.29	59.00 ± 0.27	1.40 ± 0.27	1.56 ± 0.17
Treatment 3 (0.8%)	9.63 ± 0.27	58.10 ± 0.69	1.29 ± 0.21	1.43 ± 0.21

Values are expressed as means ± SD; n = 6 for each treatment group.

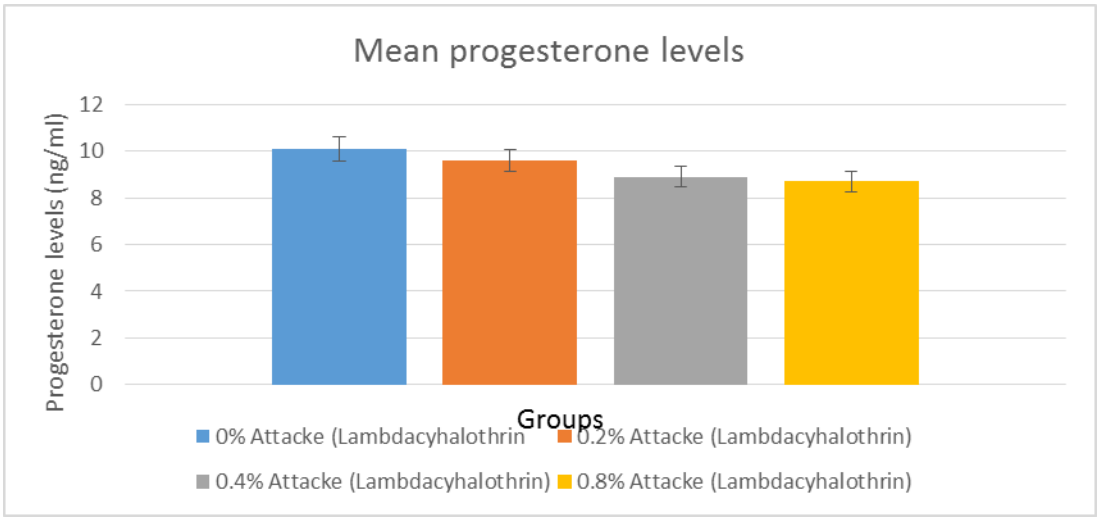

Figure 1: Effect of Lambda-cyhalothrin on progesterone level.

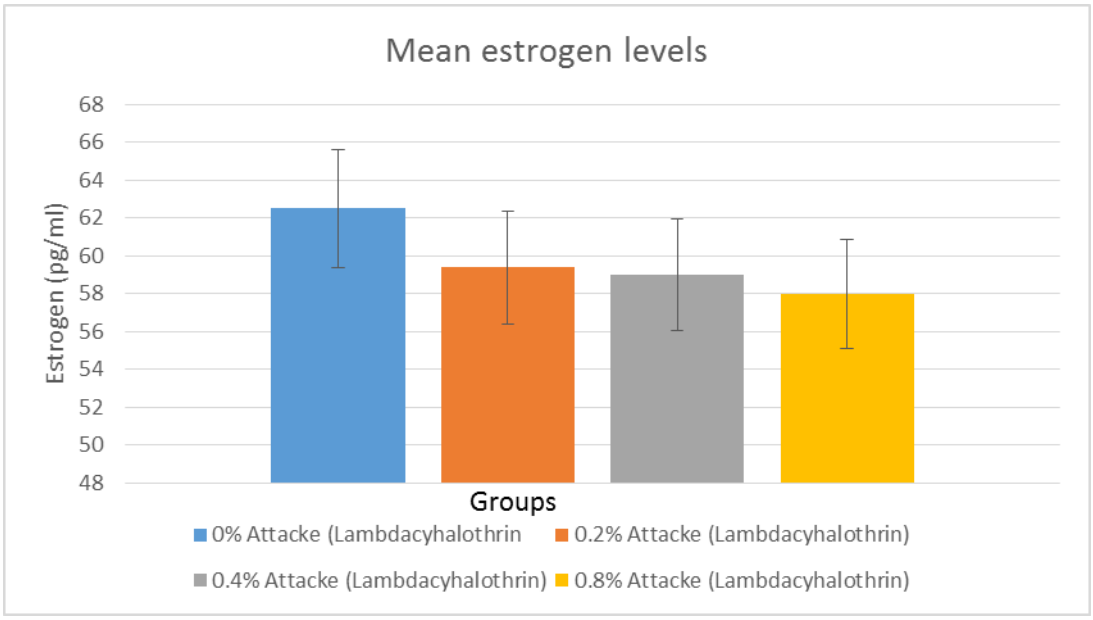

Figure 2: Effect of Lambda-cyhalothrin on estrogen level.

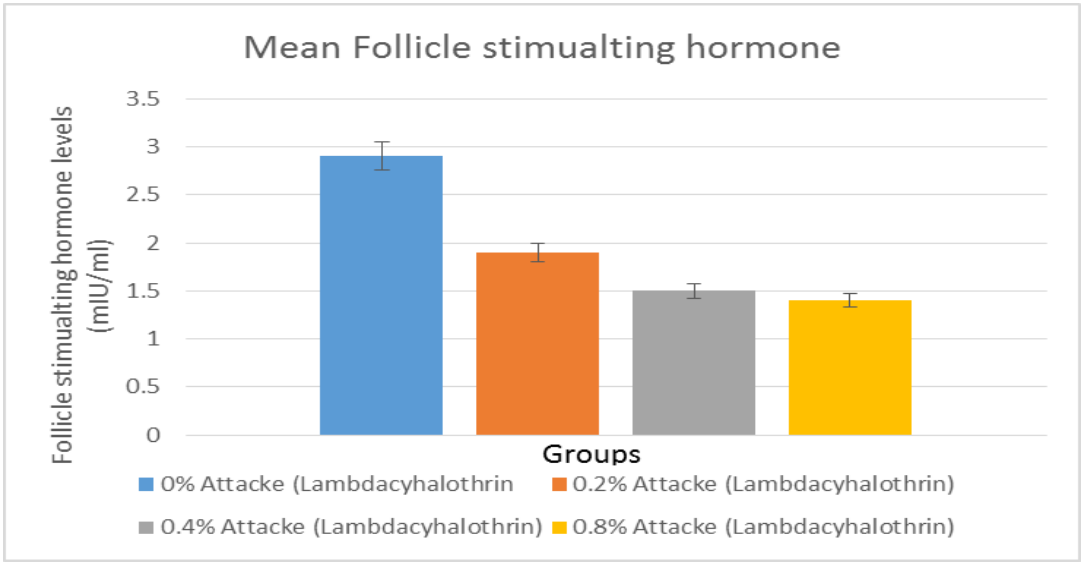

Figure 3: Effect of Lambda-cyhalothrin on Follicle stimulating hormone level.

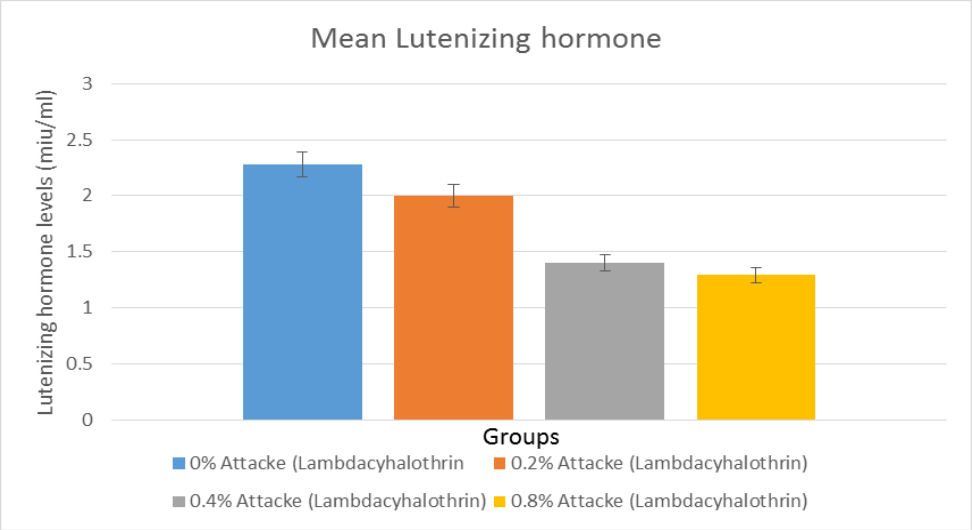

Figure 4: Effect of Lambda-cyhalothrin on Lutenizing hormone level.

DISCUSSION

In the present study lambda cyhalothrin exposure at different concentration 0.2%, 0.4% and 0.8% induced physiological stress in the female Wistar rats. Reproductive biomarkers in females are responsible for the regulation of reproductive functions and characteristics. These biomarkers, estrogen and progesterone are produced in the ovaries under the stimulation of LH and FSH from the anterior pituitary through a feedback mechanism. Some xenobiotics such as pesticides that interrupt reproductive biomarkers synthesis, secretion or function are referred as endocrine disruptors (Wissem, *et al.*, 2011). Lambda cyhalothrin are known to act as endocrine disruptors as they can interact competitively with androgen receptors and sex hormones binding globulin (SHBG) triggering disruption on the endocrine system or by mimicking the effect of the female hormone estrogen (Eil and Nisula, 1990). Endocrine disrupting toxicants may interfere with the synthesis, transport, metabolism and excretion of hormones, thereby decreasing the concentration of natural hormones (Wissem, *et al.*, 2011).

The result from this study noted a non-significant dose dependent decrease in serum progesterone level. There was a significant dose dependent decrease in serum estrogen, FSH and LH levels. In agreement with the report of this study Obinna and Kagbo, 2017 study showed that treatment of female Albino rats with Beta cypermethrin recorded a non-significant decrease in serum LH, FSH and estrogen levels and a non-significant increase in serum progesterone levels.

The sub-lethal exposure of the rats to lambda cyhalothrin a type II pyrethroid, may be responsible for the decrease in the estrogen serum level since pyrethroid pesticides have affinity for androgen or estrogen receptors. According to Hall (2011), one of the routes in the synthesis of estrogen in the ovaries is the conversion of androgens (testosterone and androstenedione) into estrogens by enzyme aromatase in the granulose cells activity regulated by FSH (Trif, *et al.*, 2010). This is in line with study which reported that the decrease in estrogen level could be the cause of decrease of FSH serum level as a result of chromium exposure which reduced the aromatase in the granulosa cells and androgen transformation into estrogen. Administration of spondiasmembin to non-pregnant female rats resulted to estrogen inhibition (Asuquo, *et al.*, 2013). The decrease in the estrogen serum level in this study invariably affected other hormones. Example the decrease LH interrupts corpus luteum and thereby resulted to decrease serum progesterone levels.

In a two-generational study by Suter, *et al.*, (1990) on rats showed no adverse effect on the reproductive hormones or birth defects with pesticide (imidacloprid) following exposure before and during mating, gestation and lactation which is not consistent with the result of the present study.

CONCLUSION

The current study of lambda-cyhalothrin exposure of three different concentrations to female Wistar rats deliberately affected their reproductive biomarkers (Estrogen, Progesterone, FSH and LH) in a dose dependent manner. This investigation demonstrate that lambda cyhalothrin is an endocrine disruptor and a threat to life. Thus, exposure of animals, humans, plants and the environment to widely xenobiotic chemicals like lambda cyhalothrin may lead to insidious alteration in reproductive biomarkers.

REFERENCES

1. Abdallah, F., Fetoui, H. Fakhfakh, F. and Keskes, L. (2012): Caffeic acid and quercetin protect erythrocytes against the oxidative stress and the genotoxiceffects of lambda-cyhalothrin in Vitro. *Hum. Exp. Toxicol*, 31(1): 92-100.
2. Anadon, A., Martinez, M., Martinez, M.A., Diaz, M.J. and Martinez-Larranaga, M.R. (2006):

Toxicokinetics of lambda-cyhalothrin in rats. *Toxicol. Lett*., 1: 165(1): 47-56.
3. Atamanalp, M., Kelep, M.S., Haluloulu, H.U. and Aras, M.S. (2002): The effects of cypermethrin (a synthetic pyrethroid) on spme biochemical parameters (Ca, P, Na and TP) of rainbow trout (*Oncorhynchusmykiss). Turk. J. Vet. Ani. Sci.,* 26: 1157-1160.
4. Asuquo, O.R., Oko, O.O.K., Brownson, E.S., Umoetuk, G.B. and Utin, I.S. (2013): Effects of ethanolic leaf extract of *Spondiasmombin*on the pituitary-gonadal axis of female wistar rats. *Asian Pacific Journal of Reproduction*, 2(3): 169-173.
5. Bao, G.G., Wang, M.H. William, L.C., Dao, J.C. and Zheng, J.S. (2007): Risk assessment of cyhalothrin on aquatic organisms in paddy field in China. *Reg. Toxicol. Pharmacol*, 48: 69-74.
6. 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? *Reprod. Biol. Endocrinol*, 4: 30.
7. Dahamna, S., Harzallah, D., Guemache, A. and Sekfali, N. (2009): Toxicopathological effects in rats induced by Lambda-cyhalothrin. *Comm. Agr. Appl. Bio. Sci.*, 74(1): 143-148.
8. El-Demerdash, F.M. (2007): Lambda-cyhalothrin induced changes in oxidative stress biomarkers in rabbit erythrocytes and allevation effect of some antioxidants. *Toxicol. In-Vitro*., 21: 392-397.
9. Eli, C. and Nisula, B.C. (1990): The binding properties of pyrethroids to human skin fibroblast androgen receptors and to sex hormone binding globulin. *J. Steroid Biochem*, 35(3-4): 409-414.
10. Fetoui, H., Garoui el M. Makni-Ayadi, F. and Zeghal, N. (2008): Oxidative stress induced by lambda-cyhalothrin in rat erythrocytes and brain: Attenuation by vitamin C. Environ. *Toxicol. Pharmacol*, 26(2): 225-31.
11. Fetoui, H., Makni, M. and Garoui, M. (2010): Toxic effects of lambda-cyhalothrin, a synthetic pyrethroid pesticide, on the rat kidney: Involvement of oxidative stress and protective role of ascorbic acid. Experimental and *Toxicologic Pathology*, 62(6): 593-599.
12. Hall, J.E. (2011): Female physiology before pregnancy and female hormones. *In: Guyton and Hall textbook of medical Physiology 12th Ed. Philadelphia: Saunders Elsevier*, 987-1002.
13. He, L.M., Troiano, J. Wang, A. and Goh, K. (2008): Environmental Chemistry, Ecotoxicity, and Fate of Lambda Cyhalothrin. *Review of Environmental Contamination and Toxicology.*
14. Kidd, H. and James, D.R. (1991): The agrochemicals handbook, 3rd edition. *Royal society of Chemistry Information Services, Cambridge, UK.*
15. Mostafalou, S. and Abdollahi, M. (2012): Concerns of environmental persistence of pesticides and human chronic diseases. *Clin. Exp. Pharmacol*, (3): 1000-108.
16. Oros, D.R. and Werner, I. (2005): Pyrethroid insecticide: An analysis of use pattern, distribution, potential toxicity and fate in the sacramento. San Joaquin Delta and Central Valley. White paper for the interagency ecological program. SFEI contribution 415. *San Francisco Estuary Institut, Oakland, CA.*
17. Obinna, V.C. and Kagbo, H.D. (2017): Endocrine effect of Beta Cypermethrin on Female Albino Rats. *Journal of Advances in Medicine and Medical Research*, 23(3): 1-7.
18. Oshoke, F.I, Fadina, O.O and Fayinminnu, O.O. (2016): Sub-chronic toxicity study of synthetic Pyrethroids (lambda-cyhalothrin) on reproductive organs of male wistar rats. *International Journal of Advance Agricultural Research*, 4: 38-45.
19. Ratnasooriya, W.D., Ratnayake, S.S. and Jayatunga, Y.N. (2003): Effects of Icon, a pyrethroid insecticide on early pregnancy of rats. *Hum. Exp. Toxicol*, 23(10): 47-56.
20. Suter, P., Biedermann, K., Luetkemeier, H., Wilson, J. and Terrier, C. (1990): NTN 33893 technical. Multiple generation study in rats. *RCC, Research and Consulting Company AG. Itingen, Switzerland*. Study No. 100647. Vol. 51950-0019.
21. Trif, A., Snejana, P., Dumitrescu, E. and Muselin, F. (2010): Dynamics of female sexual hormones after six months exposure to potassium dichromate (Cr Vi). *Lucrări Stiinlifice Medicină Veterinară*, 14(2).
22. National Research Council (2011): Guide for the care and use of laboratory animals 8th Ed. *The National Academies Press Washington, D.C.*
23. Wissem, Mnif, Aziza, Ibn Hadj Hassine, Aicha Bouaziz, Ahgleb Bartegi and Olivier Thomas (2011): Effect of endocrine disruptor pesticides: A review. *International Journal of Environmental Research and Public Health*, 8(6): 2265-2303.
24. Velmurugan, B., Selvanayagam, M., Cengiz, E.I. and Unlu, E. (2007): Histopathology of lambda cyhalothrin on tissues (gill, kidney, liver and intestine) of Cirrhinusmrigala. *Environment Toxicology Pharmacology*, 24: 286-291.