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The Protective Role of Vitamins E, A, D3 against the Toxicity Induced by Lambdacyhalothrin Pesticide in Testosterone Hormone and the Testes of Laboratory Male Rat

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ABSTRACT
The use of pyrethroids in the treatment of plant infection and its effect on the environment and human has been got great attention. The present study aimed to evaluate the protective role of vitamin combination against the testicular damage. Methods twenty seven Adult male rats were used in this study. They treated with 5µg. Lambdacyhalothrin solution Animals The animal treated daily for fourteen days, The number of spermatogonia, primary and secondary spermatocyte were counted for 20 semniferous tubule for each treated and control group. Conclusion the result showed that the section of testes in treated animal with Lambdacyhalothrin appeared reduction in the spermatogenesis process and there. While the testes of animal treated with vitamin combination and with Lambda cyhalothrin it Shows un affected tubules which was contain all stages of germ cells There is significant decreasing p< 0.05 in testosterone level in the group treated with Lambdacyhalothrin compared with control and the group treated with vitamin combination. Results were explained that vitamins combination had protective role against the toxicity of lymcyhalothrin. They indicate that vitamin may reduce the decrease of testosterone level

Keywords: lambdacyalothyrin, antitoxic effect, vitamin E.A D3 tesetes.

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INTRODUCTION
The use of insecticide for plant infection treatment has been received a great attention due to their negative impacts on the environment and human. One of these insecticides is the pyrethroids lambdacyhalothrin which include the characteristic group of pyrethrin-like compound with a better distinctive performance which is used globally[1-5] .Pyrethroids are synthetic analogues of pyrethrins I, the naturally occurring insecticides extracted from the dried flowers of Chrysanthemum cinerariaefolium [4-7]. Pyrethroids can be grouped into two large categories [8,9]. The first Type (e.g. allethrin, permethrin) not have a cyano moiety. The second type of pyrethroids (e.g. deltamethrin, fenvalerate and cyhalothrin) with a group of cyano group. Pyrethroid insecticide is broadly used in the most recent two decades of many Arabic countries [2,10]. Unintended contact with pyrethroids caused by an advertent use. workers in the factories produced the previously mentioned insecticide in addition to farmers are in danger of contact [14].Recently the side effect of pyrethroid insecticides to human and animals has conventional attention in the current period. Animals which are exposed to these insecticides demonstrate alternative in their physiological activities and other pathological sign ,also they may affect the human reproductive organs or by indirect toxicity by intervention with the function of hormones [8,11].Several studies have shown that a different types of pesticides, can caused serious problems in both male and female animals, including infertility even when they used in low concentrations [11-15] Vitamin E is present in fatty Foods and, its lipophilic so it allows being stored within the fatty tissues[16].All the different homologues in varying proportions among the tocopherols, the alpha- and gamma-tocopherols are present in the serum and in the erythrocytes[7, 17-20].The function of vitamin E is the protects tissues from the oxidative stress. Vitamin E inhibits the production of reactive oxygen after the oxidation or formation of fats of free radical [21].Vitamin A is a group of lipophilic biomolecules which is important to complete many vital biological function. Vitamin A, may play a role as a hormone-like growth factor for epithelial tissue and many other cell in the human body [21]. vitamin A is utilized therapeutically for treatment of many cases such as dermatological disturbances, immunodeficiency, and leukemia, and in reduction of toxicity by increasing glutathione-S transferase (GST) enzyme activity [22-25].The other important vitamin is vitamin D3 The pharmacological properties of vitamin D3 have congregate much attention, especially in the previous decades due to the delineation of its exact molecular pharmacodynamics. A number of analogs are being produced to extend the utility of this metabolite to a diversity of non-classic conditions [4].So the present study aimed to focus on the role of the vitamin combinations against the toxicity of pyrithroid, pestcside, lymdhacylothrin in laboratory rats .

SUBJECTS AND METHODS
Laboratory animal
Twenty one Adult male Wistar rats each with 130- 150g weight and 12 weeks age were used in this study. The animals were maintained in the animal house of faculty pharmacy, university of kufa and were maintained in a controlled environment the room temperature was (22 ± 2 ◦C and with a 12 h light/dark cycle and water were available ad libitum. Lambdacyhalothrin solution was bought from local market 0.5ml diluted d by add it to 5 ml

of D.W. since each 0.1 ml contain 5mg of Lambda cyhalothrin was administered to each animal orally once daily by gastric gavage tube. Vitamins AD3E: Vitol-140 (Interchemie, Holland), contains vitamin A, D3 and E in oily solution were used for intra peritoneal injection. Each 1 ml of Vitol-140 contains 8000 IU of Vitamin A, 4000 IU of Vit D and 20 mg of Vitamin E. Each animal was given 0.4 ml of this vitamin daily

Experimental design

Animals were divided into three groups A, B and C control group each was consist of 7. Animals they treated daily for fourteen days AS the following -:

Group (A) treated with 0.4ml mixture solution (Lambda cyhalothrin) alone in a dose of 0.1 ml and 0.3ml of olive oil. The toxic solution was orally administered by gastric gavage tube once daily

Group (B) injected with 0.4 ml a combination of vitamins once daily intra peritoneally and treated with 0.4ml mixture of Lambda cyhalothrin and olive oil orally

Control group (C) treated with 0.4 ml of olive oil orally.

The level of testosterone hormone was measured using special Elisa kit for rat testosterone hormone measurements, cusabio company

Slide sections examinations

At the end of the treatment the animals were sacrificed and the testis were prepared for the process of sectioning using the microtom Five-micron thick sections with 5µ thick were obtained and stained with Haematoxyline and Eosin (H&E) stain .then examined by microscope. The number of spermatogonia, primary and secondary spermatocyte were counted for 20 semniferous tubule for each section in the treated and control groups [21, 26-29]

RESULTS

Histological sections examination

Result in fig. (1). showed unaffected spermatogenesis process in the seminiferous tubules and there were normal spermatogonia, primary and secondary spermatocytes and spermatid also unaffected interstitial tissue between the seminiferous tubules in the control group. While fig. (2) showed the testes tissue and spermatogenesis process of a treated animals with Lambda cyhalothrin were affected and there was congestion in blood vessels of the testicular tissues. The destruction in interstitial tissue will affect the developing germ cells and all spermatogenesis process. Interstitial tissue between the tubules showed edematous changes and atrophy in Leydig cells. While figure (3)showed the testes of the treated animal with vitamin combination and Lambda cyhalothrin it Shows normal seminiferous tubules and un affected spermatogenesis process with normal germ cells especially spermatozoa. It is also had interstitial tissue appear to be normal.

Result of hormonal assay

fig.(4) show significant decreasing in testosterone level in the group treated with Lambda cyhalothrin compared with control and the group treated with vitamin E combination this obvious from the destruction of the atrophy in the leydig cell which in turn may be explain the decreasing in testosterone level since leydig cell responsible for testosterone secretion

Semniferous tubule examination

As it appear from the fig. (5) there are no significant differences between the control group and the treated group in the mean number of spermatogonia Result in fig. (6)showed significant differences $p< 0.05$ in the mean number of primary spermatocyte in control compared with the treated group while the result also showed significant $p< 0.05$ differences between control and group (A) compared with the group (B).The result in figure (7) showed significant $p< 0.05$ in secondary spermatocyte between control and group A.

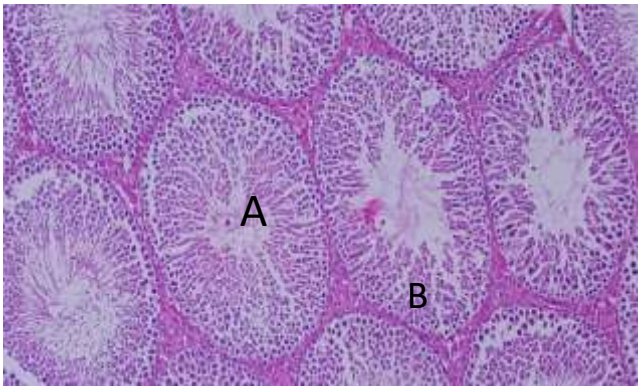

Fig 1: C.S. in the rat testes (A) showed the spermatogenesis stages spermatogonia ,primary spermatocyte, secondary spermatocyte and spermatide and (B) normal interstitial tissue in control group.

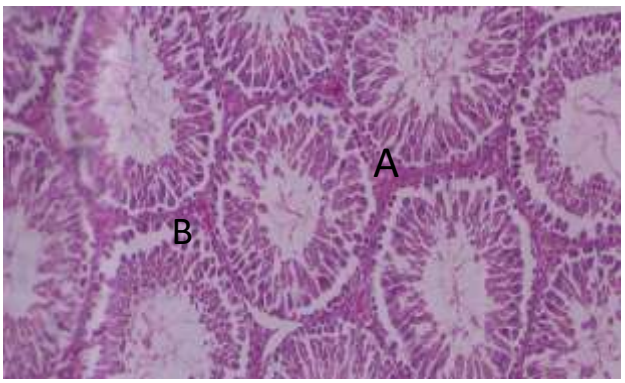

Fig 2: Showed C.s. in the testes of male rats treated with Lambda cyhalothrin (A) showing an affected primary germ cells but some tubules still containing spermatozoa. (B) Showed the presence of destructions in some tubules and atrophy in the interstitial leydig cells.

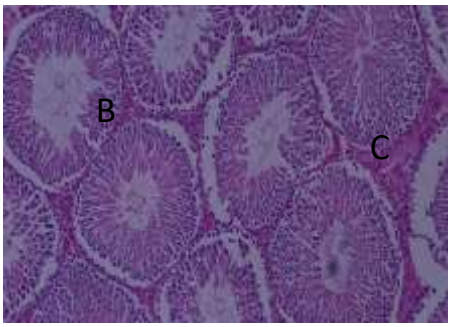

Figure 3: Showed C.s. in the testes of male rats treated with Lambda cyhalothrin and vitamin combinations showed normal spermatogenesis (A) and normal interstitial tissue between the somniferous tubules (B). Spermatozoa(C)

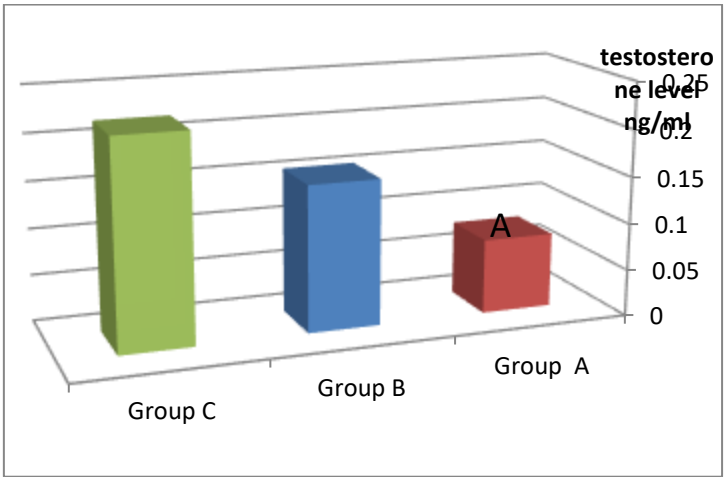

Fig 4: Effect of lymdacyalothyrine in testosterone level in male rats n=7

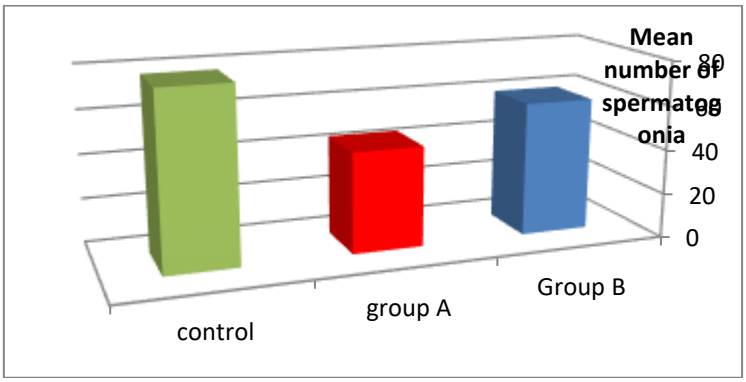

Fig 5: Effect of Lambda cyhalothrin in mean number of spermatogonia

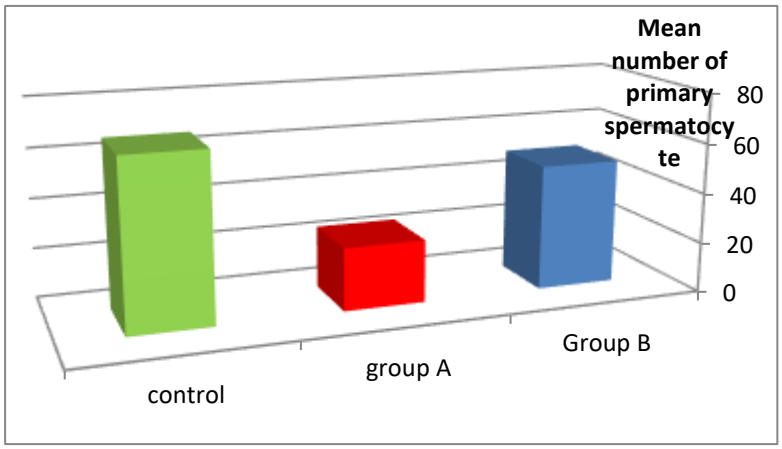

Fig 6: Effect of Lambda cyhalothrin in the mean number of primary spermatocyte

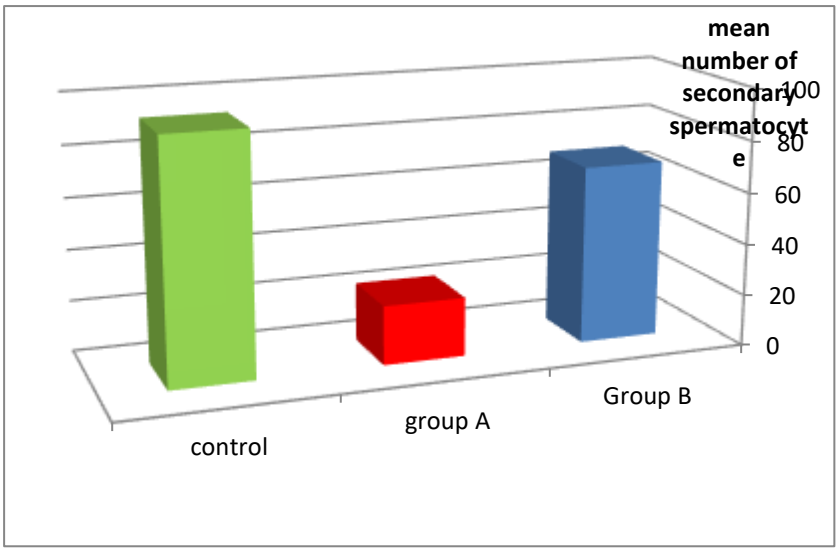

Fig 7: Effect of Lambda cyhalothrin in the mean number of secondary spermatocytes

DISCUSSION

The result in figs. (1,2,3) Showed alternation in testes tissue this may be due to the effect of the accumulation of Lambda cyhalothrin in this tissue prior study have indicate that pesticides, since it lipid-soluble nature, were mainly accumulated in the biological membrane especially in the phospholipids bi layers of And in the tissues which are rich in fat including body, skin, liver, kidney, ovaries and the parts of the central and peripheral nervous system [16,26]. Result agreed with many studies indicates that Lambdacyhalothrin has much histological effect. Many studies showed that tissue subjected to pollution by various pesticides and detailed adverse effects of environmental exposures, particularly pesticides on both male and female reproductive system [28-32].The effect of Lambdacyhalothrin in the testes is may be explained by its effect on the testicular tissue damage and this indicate by histological changes the decreasing in testosterone level.[4] The result in our study also indicate that there were a protective effect of vitamin E to reduce the toxicity .This is agree with many studies indicate the anti-oxidant effect of vitamin E which plays an important role in the intracellular protection mechanism. Since the absence of vitamin will caused the tissue damage were increasing because of its oxidative stress [17, 33]. Also Vitamin E reduce the release of reactive oxygen so that it efficiently avoid germ-cell injure and destruction [34-38]. Maret et.al 2011 (6) shows that treatment with vitamins C and E had a cooperative defensive effect on lipo peroxide production. The role of hormones in the regulation of spermatogenesis occurs through its effect on gonadotropins, steroids, and the interstitial tissue between the seminiferous tubules, which affected by luteinizing hormone (LH) from the pituitary gland and secret testosterone the male steroid hormone. Vitamin E may inhibit the decreasing of LH and FSH [15].Also vitamin E may inhibits the decrease of testosterone and spermatozoa number; and vitamin E decreased the damage of the testis structure tissue structure [34-36]. in addition to the vitamin E there is vitamin A which is required for fertility and normal spermatogenesis, and recently the mechanisms that drive RA regulation of germ cell development have begun to be understood [36-38]. Vitamin A may regulates germ cell differentiation and how it may lead to the generation of both the cycle of the somniferous epithelium [38].

REFERENCES

1. Agarwal, A., Gupta, S., Sekhon, L.,Shah, R. Redox considerations in female reproductive function and assisted reproduction: From molecular mechanisms

to health implications. Antioxid. Redox Signal. 2008, 10, 1375–1403 .

2. Assayed M.E, Khalaf A.A. Salem H.A. Protective effects of garlic extract and vitamin C against in vivo cypermethrin-inducedcytogenetic damage in rat bone-marrow, Mutat.Res., 2010, 702, 1–7.
3. Bolognesi, C., Genotoxicity of pesticides: A review ofhuman biomonitoring studies. Mutat. Res.Rev. Mutat. Res. 2003, 543, 251-272.
4. Brunton L L, Lazo JS, and Parker, KL, editors. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 11th Ed. New York, McGraw Hill,2006.
5. Michael J. R., Holly J. D., Megan D, Kenneth ;B. G., Brent :A. B., G. Gregory H., Robert G. C., and Stephen E. Always Vitamin E and C supplementation reduces oxidative stress, improves antioxidant enzymes and positive muscle work in chronically loaded muscles of aged rats .Exp Gerontol. 2010; 45(11): 882–895 .
6. Maret G. Trabera,c, and Jan F. Stevensa, Vitamins C and E. Beneficial effects from a mechanistic perspective free Radic Biol Med. 2011; 51(5): 1000–1013 .
7. Charlotte C., Lioara R. , Jocelyne D. , Emilie B., Adeline R. Sybil C. *etal*, Establishment of reference values ofα-tocopherol in plasma, red blood cells and adipose tissue in healthy children to improve the management of chylomicron retention disease, a rare genetic hypocholesterolemia . Orphanet Journal of Rare Diseases (2016) 11:114
8. Abdel-Tawab H.M. ,Samia,M.M.M. , and Natarajan Ch. Safety of Natural Insecticides: Toxic Effects on Experimental Animals. BioMed Research International.2018. 1-17.
9. DE Oliveira M., Da Rocha R.., Stertz L.and Fries Gr., Total and mitochondrial nitrosative stress, decreased brainderived neurotrophic factor (BDNF) levels and glutamate uptake, and evidence of endoplasmic reticulum stress inthe hippocampus of vitamin A-treated rats. Neurochem Res 2011,36,506-517.
10. Fisker, A.B.; Bale, C.; Rodrigues, A.; Balde, I.; Fernandes, M.; Jorgensen, M.J.; Danneskiold-Samsoe, N.; Hornshoj, L.; Rasmussen, J.; Christensen, E.D.; et al. High-Dose vitamin A with vaccination after 6 monthsof age: A randomized trial. Pediatrics 2014, 134, e739–e748 .
11. Garcia A. Occupational exposure to pesticides and congenital malformations: a review of mechanisms, methods, results. Amer. J. Indus.Med. 1998,33,232–240
12. Breckenridge C, Holden L, Sturgess N, Weiner M, Sheets L, Sargent D, et al. Evidence for a separate mechanism of toxicity for the Type I and the Type II pyrethroid insecticides. NeuroToxicology 2009 ; 30S:S17-31.
13. Muhammad Khalil A. K., Muhammad Z., Munazza P., Shagufta A., Chaman A., Khurram S. and Asmatullah ,A . Developmental defects induced by lambda cyhalothrin in mice o. J. Zool.2014. 29: (2).85-90.
14. Mostafalou S, Abdollahi M. Concerns of environmental persistence of pesticides and human chronic diseases. Clin. Exp. Pharmacol. 2012;2(3):1000—108.
15. Hai-ping, y. jan-ping ,x.,xian qing Z,Ying W. Effects of vitamin E on reproductive hormones and testis structure in chronic dioxin-treated miceJ .Toxilogical and industerial health 2012,28 ,152-161
16. Volodymyr I. Lushchaka , Tetiana M. Matviishyna , Viktor V. Husaka , Janet M. Storeyb Kenneth B. Storeyb . Pesticide toxicity: a mechanistic approach Canada excli journal 2018. 17:1101-1136 - Review article
17. Liu, P. Y. Feng, C. Dong, D. Liu, X. Wu, H. Wu, P. Lv and Y. Zhou, Study on therapeutic action of bone marrow derived mesenchymal stem cell combined with vitamin E against acute kidney injury in rats, Life Sciences 2013.92: 829-837
18. Meistrich, ML, Hess RA.. Assessment of spermatogenesis through staging of seminiferous tubules Methods Mol Biol. 2013. 92: 299-307 .
19. Soderlund DM, Clark JM, Sheets PL, Mullin LS, Piccirillo VJ, Sargent D, et al. Mechanisms of pyrethroid neurotoxicity: implications for cumalative risk assessment. Toxicology 2002. 171:3-59.
20. Hiroki N., Tomohiko W., Yoshimi T., Shoichi I.. Quantitative Analysis of the Cellular Composition in Seminiferous Tubules in Normal and Genetically Modified Infertile Mice Quantitative Analysis of the journal of histochemistry and cytochemistrty 2015 .63(2):99-113.
21. Olukole S.G., Obayemi TE. Histomorphometry of the testes and epididymis in the domesticated adult African great cane rat (Thryonomys swinderianus) Int J Morphol . 2010,28,1251–1254.
22. Pandey,A.K., George, K.C. and Peer Mohamed, M..Histopathological alterations induced in the liver of an estuarine mullet, Liza parsia by mercuric chloride and DDT.1996 Indian J. Fish, 43(3), 277-284.
23. Shojaei S/, H. and Abdollahi, M. Is there a link between human infertilities and exposure to pesticides? Int. J. Pharmacol. 20128.(8):708-710.
24. Ramadhan O.,and , Ian F. P. . The biological significance of vitamin A in humans: A review of nutritional aspects and clinical considerations. J. Science Jet. 2012, 1, 19
25. Maret G. T. and Jeffrey A. Vitamin E, Antioxidant and Nothing More. J Free Radic Biol Med. 2007 July 1; 43(1): 4–15 .
26. Soderlund , DM.,. Clark, JM., Sheets, LP., Mullin, LS., Piccirillo, D Sargent, VJ. et al. Mechanisms of pyrethroid neurotoxicity: implications for cumulative risk assessment. Toxicolog 2002,171, 3–59.
27. Agnieszka C. , Iga Hoły. , Inga D.Joanna B., Marcin W., Anna C. and Dorota O. Current Research on the Safety of Pyrethroids Used as Insecticides . 2018. Medicina, 54, 61

28. Tilak, K.S., Veeraiah, K. and Koteswara Rao, D.Histopathological changes observed in the gill, liver, brain and kidney of the Indian major carp Cirrhinus mrigala (Hamilton) exposed to chlorpyrifos. Poll. Res.2014, (1), 101-111
29. Naser Z. A. and Ezdihar A. H.2. Protective Effects of Vitamin A and Vitamin E Succinate agains 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-Induced Body Wasting, Hepatomegaly, Thymic Atrophy, Production of Reactive Oxygen Species and DNA Damage in C57BL/6J Mice C Basic & Clinical Pharmacology & Toxicology 2004, 95, 131–138.
30. Righi DA, Palermo-Neto J. Effects of type II pyrethroids cyhalothrin on peritoneal macrophage activity in rats. Toxicology 2005;212:98-106.
31. Zingg JM. Vitamin E: An overview of major research directions.Mol aspects med.2007,28,400-422.
32. Esmaeil Saddein, Tahereh Haghpanah, Seyed Noreddin Nematollahi-Mahani , Fatemeh Seyedi,3and Massood Ezzatabadipour. Preventative Effects of Vitamin E on Testicular Damage and Sperm Parameters in the First-Generation Mice Pups due to Pre- and Postnatal Mancozeb Exposure. Journal of Toxicology. 2019. 1- 12 pages
33. U. R. Acharya, M. Mishra, J. Patro, and M. K. Panda, Effect of vitamins C and E on spermatogenesis in mice exposed to cadmium," Reproductive Toxicology. 2008. 25, (.1) 84–88.
34. Theodosiou M., Laudet V., Schubert M. From carrot to clinic: an overview of the retinoic acid signaling pathway. Cell. Mol. Life Sci. 2010;67:1423–1445.
35. Tiemann, U. In vivo and in vitro effects of the organochlorine pesticides DDT, TCPM, methoxychlor, and lindane on the female reproductive tract of mammals: a review. Reprod. Toxicol. 2008. 25:(3) 316-326.
36. Cathryn A. Hogarth and Michael D. Griswold. The key role of vitamin A in spermatogenesis The Journal of Clinical Investigation.2010. 120: 4. 956-962.
37. Unni E., Rao M.R., Ganguly J. Histological & ultrastructural studies on the effect of vitamin A depletion & subsequent repletion with vitamin A on germ cells & Sertoli cells in rat testis. Indian J. Exp. Biol. 1983;21:180–192.
38. Nematollah Asadi , MAHMOUD BAHMANI, Arash Kheradmand, Mahmoud Rafieian-Kopaei The Impact of Oxidative Stress on Testicular Function and the Role of Antioxidants in Improving it: A Review. Journal of Clinical and Diagnostic Research. 2017.11:(5)1-5.