WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 14, 603-613. Research Article ISSN 2277– 7105

DIMETHOATE INDUCED ALTERATION IN SERUM BIOCHEMICAL PARAMETERS IN *RATTUS RATTUS*

Yaqoob Lone[1-2], Abhilasha Chaurasia*[2], Muzaffar Ahmad Bhat[3] and Rayees Ahmad Naik[2] and Raj Kumar Koiri[2]

[1]Laboratory of Endocrinology, Bioscience Department, Barkatullah University, Bhopal, (M. P.) India.

[2]Department of Zoology, Dr. Harisingh Gour Central University, Sagar, Madhya Pradesh – 470003, India.

[3]Department of Applied Aquaculture and Zoology, Barkatullah University, Bhopal, (M. P.) India.

Article Received on
05 Sep. 2017,
Revised on 26 Sep. 2017,
Accepted on 17 Oct. 2017
DOI: 10.20959/wjpr201714-9934

***Corresponding Author**
Dr. Abhilasha Chaurasia
Department of Zoology, Dr. Harisingh Gour Central University, Sagar, Madhya Pradesh – 470003, India.

ABSTRACT

Dimethoate is an organophosphorus insecticide used for the control of a wide range of insects, including mites and houseflies on a variety of vegetables, fruits, fields and forestry crops. The aim of the present study was to evaluate the toxicity of orally administered dimethoate in Wistar albino rats, based on the biochemical findings in the serum. The animals of the exposed groups were orally administered 1mg/kg/alternate day dimethoate (30 EC, 98.4% pure) for 15 and 30 days respectively under controlled laboratory conditions. At the end of the experiment, body weight, glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), acid phosphatase (ACP), creatinine and urea levels were determined. Results showed that there were decreases in body weights of exposed rats while the level of sGOT, sGPT, ALP, ACP, creatinine and urea in serum were significantly increased in both 15 and 30 days exposed rats. The present study indicates that dimethoate induces changes in biochemical parameters of liver and kidney of exposed rats inducing hepatotoxicity and nephrotoxicity.

KEYWORDS: Dimethoate, Biochemical Parameters, Rats.

INTRODUCTION

In recent years, the excessive and indiscriminate use of pesticides causes severe effect on environment and human beings. Pesticides have been used in agriculture fields to increase the production of food by eradicating harmful insects and disease vectors.[1] Organophosphorus (OP) compounds are most favoured insecticides due to their high insecticidal activity, moderate toxicity and low environmental persistence. They are widely used in medicine, agriculture and industry.[2] However, the uncontrolled use and methods of application over urban and agricultural areas have caused severe environmental pollution.[3] Toxicity of organophosphorus pesticides results in harmful effects on the kidney, liver, immune system, nervous system and reproductive system.[4-8]

Dimethoate (DM) (O, O-dimethyl-S(N-methyl carbomethyl) phosphorodithioate), an important organophosphorus pesticide is frequently used in agriculture against a wide range of insects and mites to protect crops.[9] While, its use on large scale may pose a various adverse health effects due to its persistence in crops, soil and water.[10] The DM residues and its analog are also present in foods stuffs, including cow's milk.[11] Intoxication with DM induced oxidative stress and cellular injury, which leads to free radical production and lipid peroxidation. Dimethoate inhibits the acetylcholinesterase (AChE) activity in the target tissues results in accumulation of acetylcholine which prevents the smooth functioning of nerve transmission leads to convulsions and death.[12] Dimethoate toxicity modulates the immune system[13] and also induces hyperglycemia on rat pancreas following acute, subchronic and chronic exposure.[14-16] Earlier studies have shown that acute, subchronic and chronic exposure to dimethoate induces the oxidative stress and alters the histology of liver and brain in rats.[17-20] Liver being the primary organ for xenobiotic metabolism, its toxicity is considered as end point in the evaluation of the effect of a particular xenobiotic. Histopathological and clinical chemistry estimations are frequently used methods for detecting organ-specific effects induced by chemical exposure.[21-22] Despite extensive use of dimethoate in crop protection and in controlling vectors, information on its health effects is still scarce. The present work has been done to assess the serum biochemical parameters of rats exposed to formulation grade of dimethoate (30 EC, 98.4% pure), to provide further information on the pesticide toxicity.

MATERIAL AND METHODS

Chemicals: Dimethoate (30% Rogor EC) which had been used for the experiment are purchased from SM chemicals, M.P. Nagar Bhopal. Sodium hydroxide and copper sulphate was obtained from Thermo Fisher Scientific India Pvt. Ltd and Ranbaxy Laboratories Ltd, India respectively. Rests of the chemicals used were purchased from Central Drug House (P) Ltd, New Delhi.

Animals: Adult Wistar rats weighing 125 ± 5 gm were housed in the laboratory facility of Bioscience department, Barkatullah University, Bhopal, (M.P.) at standard laboratory conditions with the supply of water ad libitum.

Dose: The effective dose of 1mg/kg/alternate days of dimethoate was administered via oral route, for 15 and 30 days respectively.

Experimental design: Rats were randomly divided into 3 groups with 4 rats in each group. The second group of mice known as 15 days group was treated orally with 1mg/kg/alternate days of dimethoate for 15 days and the third group known as 30 days group was treated orally with 1mg/kg/alternate days of dimethoate for 30 days. Simultaneously normal control group rats were also treated with same volume of normal saline.

Body weight: Body weight of rats was recorded at an interval of 3 days starting from the day of treatment with the help of a laboratory weighing balance.

Preparation of samples for biochemical studies: After the treatment was over, 4 rats from each group were sacrificed by cervical dislocation and serum was collected as reported earlier.[23] Blood collected in unheparinized tubes was allowed to clot at room temperature (22 ^{o}C), followed by centrifugation at 1500Xg for 15 min.

Biochemical assay: Glutamic oxaloacetic transamianse (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), acid phosphatase (ACP), creatinine and urea levels were determined spectrophotometrically using commercial diagnostics kits (Siemens Ltd, India).

Statistical analysis: Experimental data were expressed as mean ± SD. Student's t test was used to verify the level of significance between the control and treated groups and $p < 0.05$ was considered significant.

RESULTS

Body weight

The body weight gain in control rat was 5 grams when compared with that of the initial body weight. A significant decrease in the body weight gain was observed in all dimethoate treated rat (table 1) when compared with those of controls.

Table 1: Effect of dimethoate on body weight of rats after 15 and 30 days treatment. The values represent mean ± SD where n=4. ***p<0.001 (normal control versus treated group).

Body weight (gms)			
Days	**Control**	**15 days treatment**	**30 days treatment**
0	103.35±1.457	104.3±2.003	103.5±1.323
15	105.2±1.504	96.1±1.119***	
30	108.42±2.109		85±1.162 ***

Biochemical indicators of liver function

Oral administration of dimethoate caused abnormal liver and kidney functions in treated rats. Liver specific enzymes such as glutamic oxaloacetic transamianse, glutamic pyruvic transaminase, alkaline phosphatase, acid phosphatase and also creatinine and urea level were increased significantly in serum treated rats($p<0.001$).

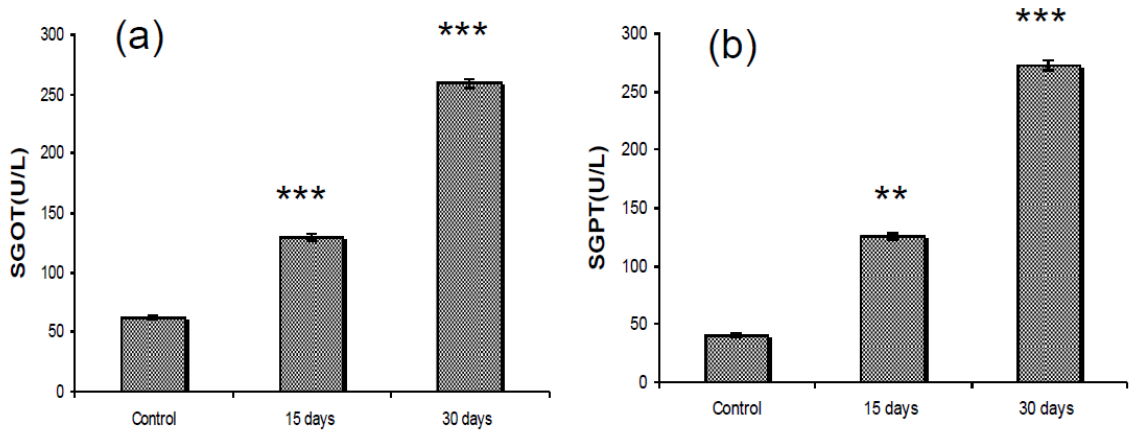

Fig. 1: Effect of dimethoate on (a) sGOT, and (b) sGPT of rats after 15 and 30 days treatment. The values represent mean ± SD where n=4. **p<0.01, ***p<0.001 (normal control versus treated group).

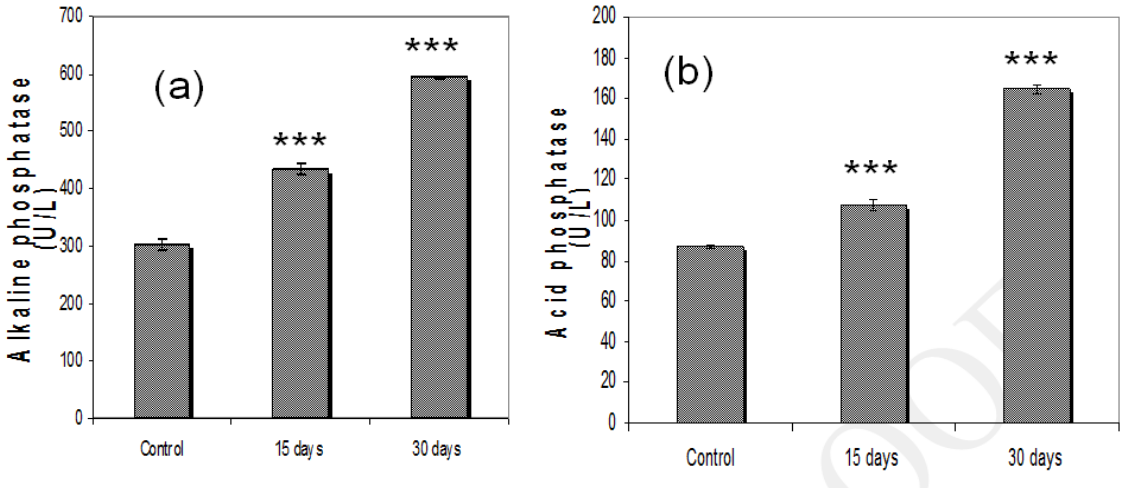

Fig. 2: Effect of dimethoate on (a) alkaline phosphatase and (b) acid phosphatase in serum of rats after 15 and 30 days treatment. The values represent mean ± SD where n=4. ***p<0.001 (normal control versus treated group).

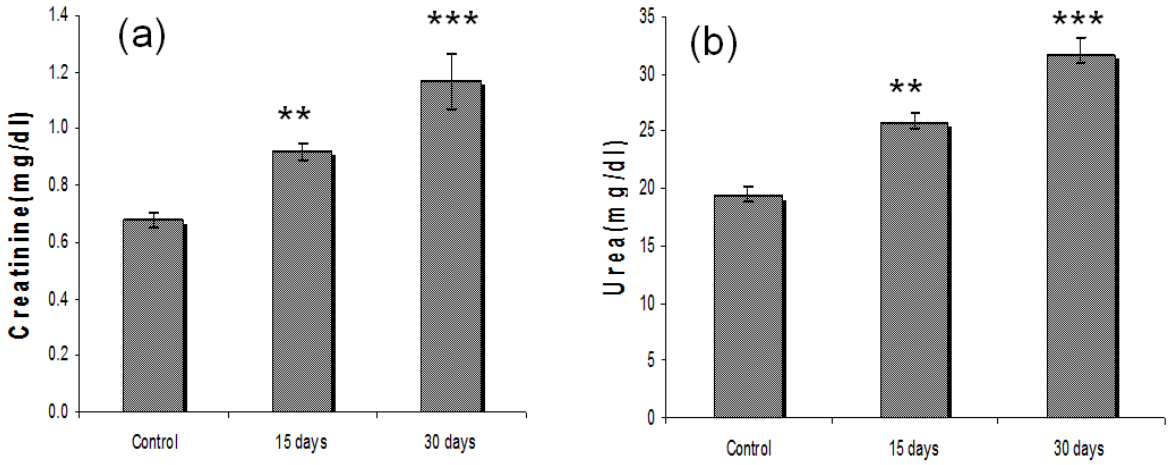

Fig. 3 : Effect of dimethoate on levels of (a) creatinine and (b) urea in serum of rats after 15 and 30 days treatment. The values represent mean ± SD where n=4. **p<0.01, ***p<0.001 (normal control versus treated group).

DISCUSSION

The extensive use of different pesticides for several decades in agriculture and controlling the disease vectors, has led to severe effects in many non-target species including human beings.[10, 24-25] The current study was carried out to explore the hepatic toxicity of dimethoate, (1mg/kg b.w./alternate days) in rats following 15 and 30 days exposure. The present study revealed that dimethoate administration induced toxicity in rats as observed by weight loss and other biochemical parameters. The reason for weight loss might be due to protein declination which could be due to variation in electrolyte balance leading to water

loss in tissue.[26] Moreover, the reduced intake of feed may show protein catabolism, thereby contributing to observed kidney injury[27] as evident by enhanced level of creatinine and urea in the serum.

The liver is at great risk of injury, as it is involved in the transformation of environmental xeno- biotics which induces hepatotoxicity. Oral administration of dimethoate to rats induced a significant hepatic damage, as observed from the alteration of hepatospecific enzyme activities. Altered cell membrane permeability of liver cells can lead to enhanced enzyme activity in plasma.[28] The transaminases are involved in metabolism of aminoacid and an increase in the level of these enzymes indicates tissue damage or toxic effects in liver[29-30] In the present study the rise in transaminases levels in the liver of rats might be due to hepatotoxicity alterations in cell permeability and leakage of lysosomal enzymes induce increase in release of enzymes.[29-33] GOT and GPT enzymes act as an important link between protein and carbohydrate metabolism supplying source of keto acids for gluconeogenesis and Kreb's cycle. Shrivastava et al.,[31] have also reported that the transaminases levels were increased significantly in kidney, plasma, liver, heart, lung, brain, muscle and intestine of rat treated with dichlorvos and suggested that this alteration might be due to increased permeability of plasma membrane or cellular damage. Similar reports of increased level of these enzymes in the tissues and plasma have also been reported in different species of animals given different doses of insecticides.[32-33] Our results are in agreement withSunder and Rao[34] who reported that administration of mancozeb to rats for 90 days caused significant increase in the serum GOT and GPT. Acid and alkaline phosphatase are lysosomal enzymes commonly found in most tissues of the body generally located on secretory and absorptive surface of cells as membrane bound enzymes splits the phosphoric acid from phosphoric esters. ACP hydrolysis the ester linkage of phosphate esters at acidic pH helps in autolysis of the degenerated cells.[35] Alkaline phosphatase splits various phosphorous esters at an alkaline pH, involved in carbohydrate metabolism, protein synthesis, growth and differentiation, secretion activity, synthesis of certain enzymes and transport to phosphorylated intermediates across the cell membranes.[36-37] Enhanced level of ALP in serum is clinically important as it suggests increased osteoblastic activity and hepatobilliary diseases.[38] Increase of ACP level in the serum may indicate prostate cancer and hyper parathroidsim.[39]Kackar et al.,[40] have also reported that oral administration of fungicide mancozeb atdifferent doses caused alteration in hepatic enzymes, such as GOT and GPT and whereas ALP was increased. The elevated activity of GOT, GPT, ALP and ACP indicates a

compensatory mechanism by the dimethoate affected tissue which needs extra energy for its maintenance. Our results are in agreement with other researchers which reported that the exposure to dimethoate and other pesticides induced severe biochemical and physiological disturbances in experimental mice, buffalo calves, cockerels, rabbits, poultry, goatsand rats.[41-47]

Creatinine is an amino acid produced as a waste product of creatine, which acts as an important energy storage in muscle metabolism. Creatinine clearance calculated from creatinine concentrations in serum is used to determine the glomerular filtration rate of the kidneys. Urea is formed in the liver as a waste product during protein metabolism and is carried to the kidneys where it is filtered out of the blood into urine. Urea and creatinine level in blood rises when there is kidney impairment which prevents the kidneys from filtering urea and creatinine out of the blood. Our results also suggested significant increase in urea and creatinine level in serum after dimethoate exposures for 15 and 30 days. These results suggested that dimethoate induced hepatic injury and also indicate that kidneys may suffer to clear the waste products and toxins from the blood.[48-51] Our results are in agreement with results of Lone et al.,[52] who reported that microcystin lr treated mice increasese the level of urea in serum as compared to control mice leads to nephrotoxicity. Similiar results have been observed by Chauhan et al.,[53] who reported that rats treated with different doses of cyclophosphamide for 15, 30 and 60 days increases the urea and creatinine level in different tissue.

CONCLUSION

The present study indicates that dimethoate induces changes in biochemical parameters of liver and kidney of exposed rats inducing hepatotoxicity and nephrotoxicity. This study suggests that dimethoate exposure might cause harmful effects to non-target organisms, including humans. The above results emphasize us to conclude that an appropriate use of environment friendly microbial pesticides should be promoted for pest management program.

CONFLICT OF INTEREST

The authors declare no conflict of interest with respect to this article.

ACKNOWLEDGMENTS

Yaqoob Lone is thankful to the Department of Bioscience, Barkatullah University Bhopal, for providing infrastructural facilities and financial support.

REFERENCE

1. Prakasam A, Sethupathy S, Lalitha S. Plasma and RBCs antioxidant status in occupational male pesticide sprayers. Clin. Chim. Acta, 2001; 310: 107–112.
2. Storm JE, Karl KR, Doull J. Occupational exposure limits for 30 organopho- sphate pestcides based on inhibition of red cell acetylcholinesterase. Toxicology, 2000; 150: 1–29.
3. Al-Saleh IA. Pesticides: a review article. J. Environ. Toxicol. Oncol. 1994; 13: 151–161.
4. Kossmann S, Magner-Krezel Z, Sobieraj R, Szwed Z. The essesment of nephrotoxic effect based on the determination of the activity of some selected enzymes in urine. Przegel Lek, 1997; 54: 707–11.
5. Nagymajtenyi L, Schulz H, Pappa A, Desi I. Developmental neurotoxicological effects of lead and dimethoate in animal experiments. Neurotoxicology, 1998; 19: 617–22.
6. Rawlings NC, Cook SJ, Waldbiling D. Effects of the pesticides carbofuran, chlorpyrifos, dimethoate, lindane, triallate, trifluralin, 2,4-D and pentachlorophenol on the metabolic endocrine and reproductive endocrine system in ewes. J Toxicol Environ Health, 1998; 54: 21–36.
7. Gomes J, Dawodu AH, Lloyd O, Revitt DM, Anilal SV. Hepatic injury and disturbed amino acid metabolism in mice following prolonged exposure to organophosphorus pesticides. Hum Exp Toxicol, 1999; 18: 33–7.
8. Aly NM, El-Gend KS. Effect of dimethoate on the immune system of female mice. J Environ Sci Health, 2000; 35: 77–86.
9. Hayes WJ, Laws ER. (Eds.), Academic Press Inc., New York. 1991.
10. WHO/PCS. Pesticides residues in foods. 1996 evaluations. Part II, Toxicological, Geneva. Publication no. WHO/PCS/ 97.1.1997, 1996.
11. Srivastava MK, Raizada RB. Developmental effect of technical dimethoate in rats: maternal and fetal toxicity evaluation. Indian J. Exp Biol., 1996; 34: 329–333.
12. Jayaratnam J, Maroni M. Organophosphorus compounds, Toxicology, 1994; 91: 15–27.
13. Institoris L, Siroki O, Desi I, Undeger U. Immunotoxicological examination of repeated dose combined exposure by dimethoate and two heavy metals in rats. Hum Exp Toxicol, 1999; 18(2): 88–94.
14. Hagar HH, Fahmy AH. A biochemical, histochemical and ultrastructural evaluation of the effect of dimethoate intoxication on rat pancreas. Toxicol Lett, 2002; 133: 161–70.
15. Kamath V, Rajini PS. Altered glucose homeostasis and oxidative impairment in pancreas of rats subjected to dimethoate intoxication. Toxicology, 2007; 231: 137–46.

16. Kamath V, Joshi AKR, Rajini PS. Dimethoate induced biochemical perturbations in rat pancreas and its attenuation by cashew nut skin extract. Pestic Biochem Phys, 2008; 90: 58–65.
17. Sharma Y, Bashir S, Irshad M, Gupta SD, Dogra TD. Effects of acute dimethoate administration on antioxidant status of liver and brain of experimental rats. Toxicology, 2005a; 206: 49–57.
18. Sharma Y, Bashir S, Irshad M, Nagc TC, Dogra TD. Dimethoate-induced effects on antioxidant status of liver and brain of rats following subchronic exposure. Toxicology, 2005b; 215: 173–81.
19. Sayim F. Histopathological effects of dimethoate on testes of rats. Bull Environ Contam Toxicol, 2007; 78: 479–84.
20. Lone MY, Baba BA, Raj P, Shrivastava VK, Bhide M. Haematological and Hepatopathological Changes Induced by Dimethoate in Rattus rattus Indo American Journal of Pharmaceutical Research, 2013; 3(6).
21. Travlos GS, Morris RW, Elwell MR, Duke A, Rosenblum S, Thompson MB. Frequency and relationship of clinical chemistry and liver and kidney histopathology findings in 13-week toxicity studies in rats. Toxicology, 1996; 107: 17–29.
22. Crissman JW, Goodman DG, Hildebrandt PK, Maronpot RR, Prater DA, Riley JH, et al. Best practice guideline:toxicologic histopathology. Toxicol Pathol, 2004; 32: 126–31.
23. Lone Y, Bhide M, Koiri RK. Amelioratory effect of coenzyme Q10 on potential human carcinogen Microcystin-LR induced toxicity in mice Food and Chemical Toxicology, 2017; 102: 176-185.
24. Chantelli-Forti G, Paolini M, Hrelia P. Multiple end point procedure to evaluate risk from pesticides. Environ Health Perspect, 1993; 101: 15–20.
25. Chaudhuri K, Selvaraj S, Pal AK. Studies on the genotoxicity of endosulfan in bacterial systems. Mutat Res., 1999; 439: 63–7.
26. Wong PYD, Au CL, Ngai HK. Electrolyte and water transport in rat epididymis, its possible role in sperm maturation. Int J Androl Suppl., 1978; 2: 608-628.
27. Tessari EN, Oliveira CA, Cardoso AL, Ledoux DR and Rottinghaus GE. Effects of aflatoxin B1 and fumonisin B1 on body weight, antibody titres and histology of broiler chicks. Br Poult Sci., 2006; 47(3): 357-364.
28. Plaa GL. Toxic response of the liver In: Klaassen C.D., Amdur M.O., Doull, J. (eds) Casarett and Doull'stoxicology, the basic science of poisons, 3rd edn. MacMillan Publishing Company, New York, 1986; 310-329.

29. Klassen CP,Plaa GL.Relative effects of various chlorinated hydrocarbons on liver and kidney function in mice. Toxicol. & Appl. Pharmacol., 1966; 9: 139.
30. Worblewski F, La Due JS. Serum glutamic oxaloacetic transaminase activity as index of liver cell injury. A preliminary report. Ann. Inter. Medicine, 1955; 43: 345.
31. 31. Shrivastava AK, Raina R, Choudhary RK,Malik TK. The acute toxicity and Bioehcmial alterations in rats after single oral exposure to dichlorvos. Pesticides, 1989; 2: 35-40.
32. Snow DH, Watson AD. The acute toxicity of dichlorvos in the dog. Aust. Vet. J., 1973; 49: 113 119.
33. Enan EE. Comparative biochemical effects of three aliphatic organophosphorus insecticides on white rats. Intrnl. Pest control, 1983; 25: 42-44.
34. Sundar SR, Rao MV. Hepatotoxicity of a combined fungicide (metalaxyl + mancozeb) in wistar rats – A biochemical assessment. Ind. J. Environ. Toxicol., 1998; 8(1): 19-21.
35. DeDuvev C, Presman BG, Gianetto G, Wattiau R, Appelmans F. Intra cellular distribution pattern of enzymes in rat liver tissue. Biochem J., 1955; 60: 604-617.
36. Goldfisher SE, Esser E, Novikof AB. Use of histological and histochemical assessment in the prognosis of the effects of aquatic pollutants (ed.) D.E.Hinton, M.W.Kendall and B.B.Silver. Sect. 528, ASTM, Philadelphia, 1964; 194-208.
37. Vijayavel K, Balasubramanian MP. Fluctuation of biochemical constituents and markers enzymes as a consequence of naphthalene toxicity in the edible estuarine crab Scylla serrata. Eco. Env. Safe, 2006; 63: 141-7.
38. Baron DN, Wicher JT, Lee KE. A New Short Textbook of Chemical Pathology. ELBS 5th Edition, 1994; 151-156.
39. Nordenson NG. Acid phosphatase. Health atozconal, 2002.
40. Kackar R, Shrivastava MK, Raizada RB. Assessment of toxicological effects of mancozeb in male rats after chronic exposure. Ind. J. Expt. Biol., 1999; 37: 553-559.
41. Mohssen M. Biochemical and histopathological changes in serum creatinine and kidney induced by inhalation of Thimet (phorate) in male Swiss albino mouse, Mus musculus. Environmental Research, 2001; 87(1): 31–36.
42. Singh G, Sharma LD, Ahmad AH, Singh SP. Fenvalerate induced dermal toxicity in buffalo calves. Journal of Applied Animal Research, 1999; 16(2): 205–210.
43. Singh SP, Sharma LD, Singh SP, Ahmad AH. Haematobiochemical profiles in cockerels following prolong feeding of fenvalerate. Indian Journal of Agronomy, 2003; 8(2): 141–145.

44. Yousef MI, El-Demerdash FM, Kamel KI, Al-Salhen KS. Changes in some hematological and biochemical indices of rabbits induced by isoflavones and cypermethrin. Toxicology, 2003; 189(3): 223–234.
45. Jayasree U, Gopala Reddy A, Reddy KS, Kalakumar B. Study on the mechanism of toxicity of deltamethrin in poultry. Indian Journal of Toxicology, 2003; 10(2): 111–114.
46. Kaur H, Srivastava AK, Garg SK, Prakash D. Subacute oral toxicity of chlorpyriphos in goats with particular reference to blood biochemical and pathomorpholigical alteration. Indian Journal of Toxicology, 2000; 7(2): 83–90.
47. Attia AA, Nasr HM. Dimethoate-induced changes in biochemical parameters of experimental rat serum and its neutralization by black seed (Nigella sativa L.) oil. Slovak Journal of Animal Science, 2009; 42(2): 87–94.
48. Lynch NR, Salomon JC and Turner KJ. Evolutionary Development of IgE and the role of Analphylacti Types Reaction in Resistance to solid Tumours. Can Immunol Immunother, 1969; 4: 223-228.
49. Dalela RC, Rani S, Kumar V and Verma SR. In vivo heamatological alteration in fresh watre teleost Mystu vittalus following subacute exposure to pepticide and their combination. J Enviran Biol., 1981; 2(2): 79-86.
50. El-Nekeety AA, El-Kholy W, Abbas NF, Ebaid A, Amra HA and Abdel Wahhab MA. Efficacy of royal jelly against the oxidative stress of fumonisin in rats. Toxicon, 2007; 50: 256-269.
51. Abdel-Fattah SH, Sanad MM, Safaa, M A and Ragaa FG. The protective effect of white ginseng against biochemical and pathological changes induced by aflatoxins in rats. J Am Sci., 2010; 6(12): 461-472.
52. Lone Y, Koiri RK and Bhide M. Nitrate Enhances Microcystin-LR Induced Toxicity in Mice. Austin J Mol & Cell Biol., 2015; 2(1): 1006.
53. Chouhan S, Ahmad B, Chauhan R, ShrivastavaVK.Ameliorative role of ascorbic acid against hepatotoxicity induced by chemotherapeutic drug cyclophosphamide, in male albino rat, Rattus norvegicus Int. J. of Bio.l & Pharm. Res., 2014; 5(11): 830-842.