Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

# Bispyribac Sodium Induced Oxidative Stress and Hepatotoxicity in the Female Rats.

Afyaa sabah nasir1 and Ammarbadry unise2
1,2 University of Kufa/Faculty of Science/Department of Ecology/Iraq
Afyaa.nasir@uokufa.edu.iq

Abstract:
Bispyribac-sodium (a herbicide in rice fields). We explore the cytotoxic impact of bispyribac sodium in pale skinned person female rodents that intubated orally with 40 and 80 mg/kg of bispyribac sodium for thirty days. It was discovered that bispyribac herbicide caused critical decline in the body weight acquire proportion of pale skinned person rodents. Also, bispyribac sodium indicated huge decrement in the Hb, RBCs, PCV and raised level of WBCs. Conversely, bispyribac herbicide expanded huge degrees of AST, ALT and ALP in compare with control group. Additionally the outcomes demonstrated critical expansion in MDA level and huge decline in SODand GPX levels. Inconclusion, the utilized of bispyribac sodium for quite a while have an unsafe impacts in all the body organs coming about because of collection on it.

## Introduction

Pesticides considered as heterogeneous synthetics utilized for controlling of plant illnesses (vermin or weeds) to improve the efficiency of farming and yield (1). As herbicides are the absolute most utilized pesticides around the world, sub-deadly fixation location can go about as delicate early alert instruments to show their essence and can uphold for administrative appraisals and checking to be not hurt to oceanic life (2).

Herbicides comprise over 60% of pesticides that utilized in farming. Most herbicides have low mammalian harmfulness because of all herbicides that has dangerous impact on human or creatures has been dismissed (3). Bispyribac (sodium 2, 6-bis [(4, 6-dimethoxy-2-pyrimidinyl) oxy] benzoate) had a place with a pyrimidinyl thiobenzoate herbicide is a post emanant herbicide as indicated by Health Canada Pest Management Regulatory Agency and utilized for the most part to control weeds in rice development(4,5).

Hiroyuki detailed that bispyribac-sodium at a portion of 20,000 ppm as well as 50,000 ppm in a four-week concentrate in pale skinned person rodents, diminished body weight and feed utilization, on necropsy dilatation of the cecum with the expansion of bile channel and expansion in the degree of complete cholesterol, GPT, GOT, and ALP exercises (6). In a sub-constant investigation completed by the California Environmental Protection Agency, (2001) found that at portion level 1538 mg/kg/day for 13 weeks on female rodents expanded relative liver, kidney and spleen weight with tiny bury and intralobular bile pipe multiplication and lymphocytosis in urinary bladder and distinctive

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

body organs (7). The point of this investigation was to assess the biochemical boundary changes, histopathological changes and hematological boundaries of business bispyribac-sodium poisonousness in pale skinned person rodents (8).

The enzymatic cancer prevention agent framework remembers a few compounds for various cell compartments. Among the significant catalysts are superoxide dismutase (SOD)and ascorbate peroxidase (APX), which together advance the end of responsive oxygen species.

In the non-enzymatic framework, which comprises of a low atomic weight middle person, the features are ascorbate, diminished glutathione, carotenoids and phenolic mixes, which are integrated by plants because of stress. This system secures the trustworthiness of the films against the impacts of ROS, empowering better execution of specific species in unfavorable ecological conditions (9).

Realizing how plants safeguard themselves and carry on in light of different unfavorable conditions and upsetting circumstances is the initial step to grow more safe harvest assortments, in this way expanding the quality and subsequently plants yield. There are a few substances engaged with the enlistment of plant safeguard reaction against these negative impacts that have the right to be considered and better perceived (10).

**Experimental animals:**

Using nine female rats (*Rattus norvegicus* ) weighting 200-250 gm were obtained from the animals house in the faculty of science/university of kufa. the animals were kept under standard environment condition for one week (temperature 25-28 C° and 12 hr light-dark cycle) and allowed access to standard laboratory diet and water for acclimation. Bispyribac sodium was purchase from local market after the animals were divided into three groups each group contain three animals: group one received orally bispyribac sodium at dose 40 mg/kg , group two received orally bispyribac sodium at dose 80 mg/kg and the last group as control group received distal water and standard diet for thirty days.

**Blood Collection**

At the end of experiment. Each animal wasanaesthetized by the mixture of xylazine 0.1ml and ketamine 0.5 ml and they werescarified (11). Heart cut was finished with a 5ml expendable syringe and 2-5 ml blood wasdrawn delicately and gradually. Every bloodtest was separated into 2 sections. The initialsegment (around 0.5 ml) was set in a tubecontaining EDTA (22mg/ml) as anticoagulantand blended altogether, then utilized for theassurance of hematological investigation by aprogrammed auto analyzer.

The rest of the blood was put in test tubecontaining gel and left for 30 minutes in roomtemperature and used to get serum through centrifugation at 3000 rpm for 15 minutes toseparate serum and put in epindroff tubeswhich kept at (- 20) in a cooler for assurancebiochemical examination.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

**Hematological Analysis**

The hematological parameters were performed on EDTA blood using Ruby (Abbott., U.S.A), Ruby is hematology analyzer to perform red blood corpuscles (RBC), white blood cell (WBCs), hemoglobin (HB)and packed cell volume (PCV) on EDTA (12).

**Determination of Serum Transaminases Activity– Kit**

ALT & AST activity were determine by colorimetric method according to the biolabo kit,france and ALP (13) according to biomerieux kit (14).

**Determination of antioxidant enzymes and lipid peroxidation level in serum**

Measurement of SOD, GPX and MDA activity by ELISA Kit (Elabscience, U.S.A.) (www.elabscience.com, 2016).

**Statistical Analysis**

Data were presented as means ± S.E. and statistically analyzed using (ANOVA) test followed by least significant difference (L.S.D.) analyses at 0.05% probability of levels. Using computerized SPSS program (15).

**The results**

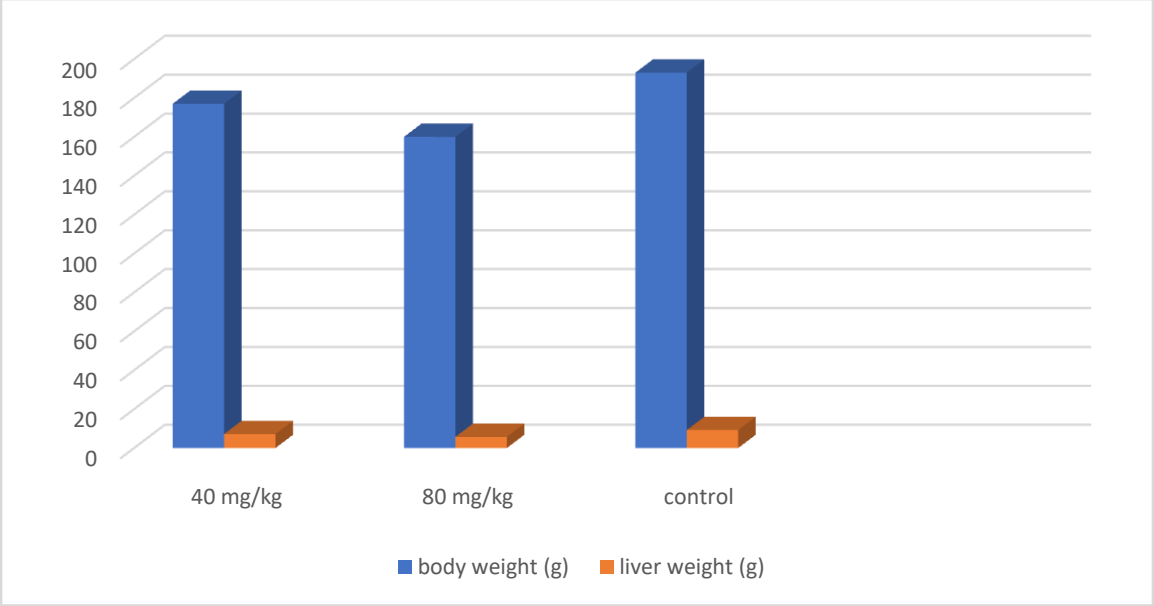


Figure (1) effect of bispyribac sodium on the body weight and liver weight for 30 days in the female rats.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

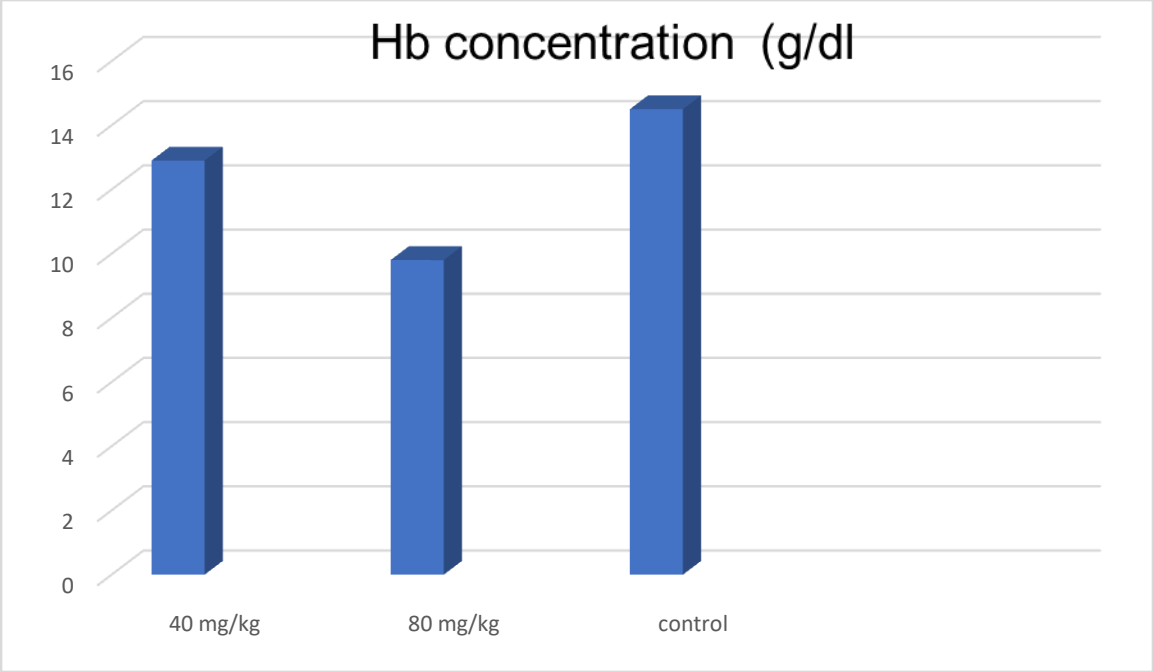


Figure (2) effect of bispyribac sodium on the level of hemoglobin concentration for 30 days in the female rats.

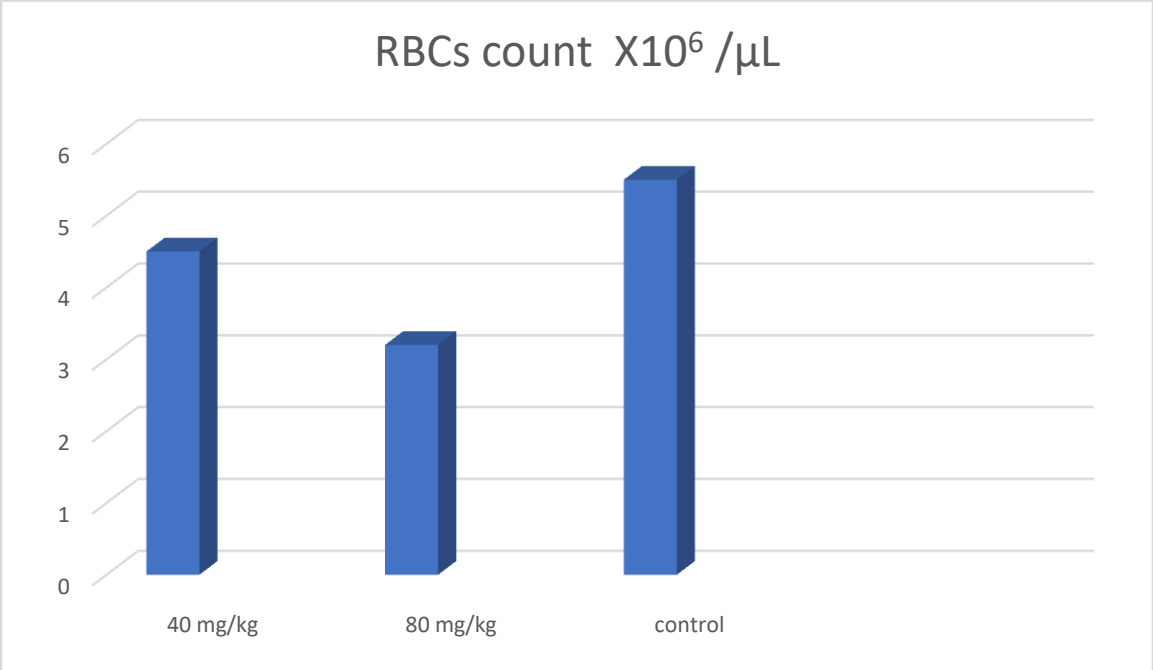


Figure (3) effect of bispyribac sodium in the red blood corpuscles for 30 days in the female rats.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

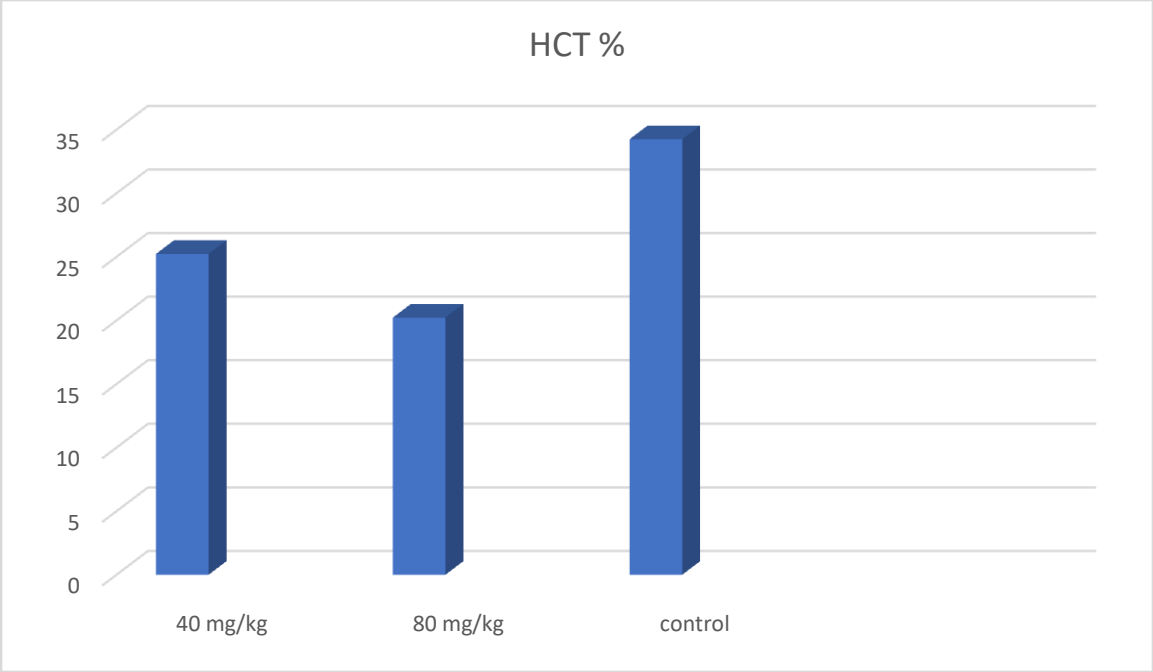


Figure (4) effect of bispyribac sodium in the packed cell volume for 30 days in the female rats.

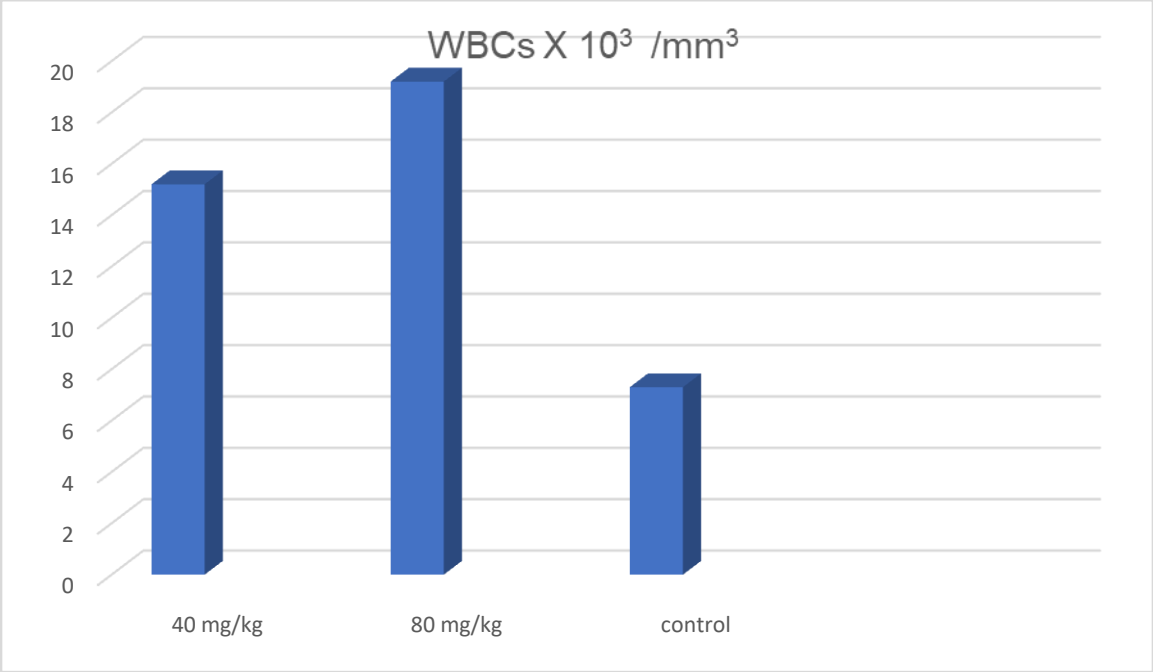


Figure (5) effect of bispyribac sodium in the white blood cells count for 30 days in the female rats.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

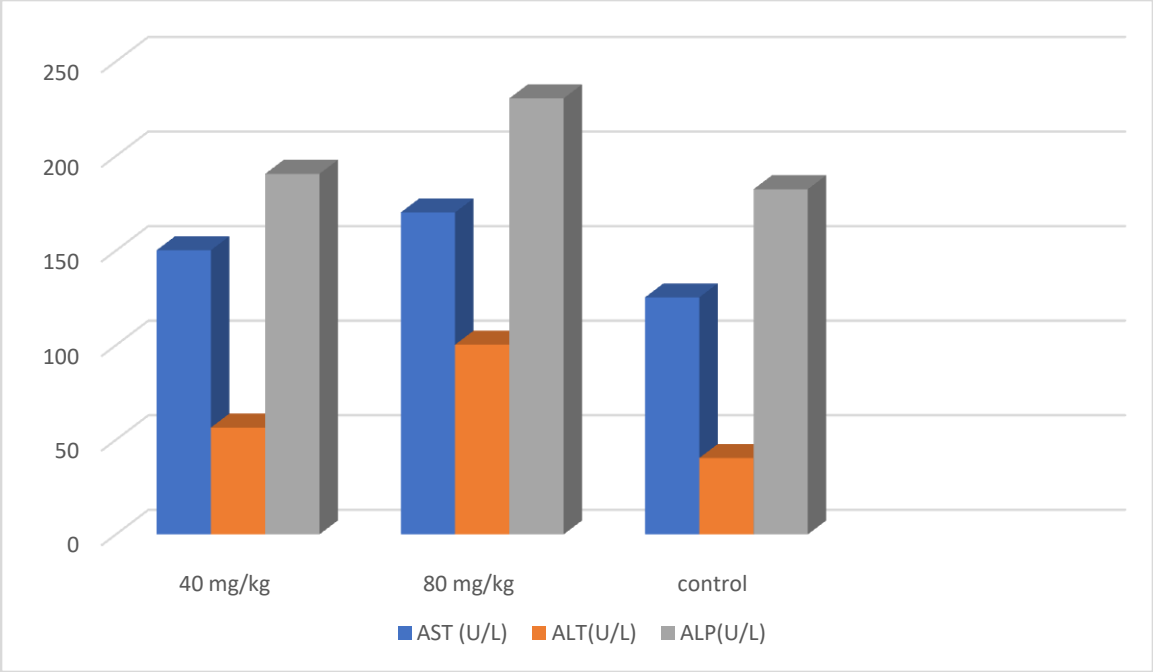


Figure (6) effect of bispyribac sodium in the levels of liver enzymes for 30 days in the female rats.

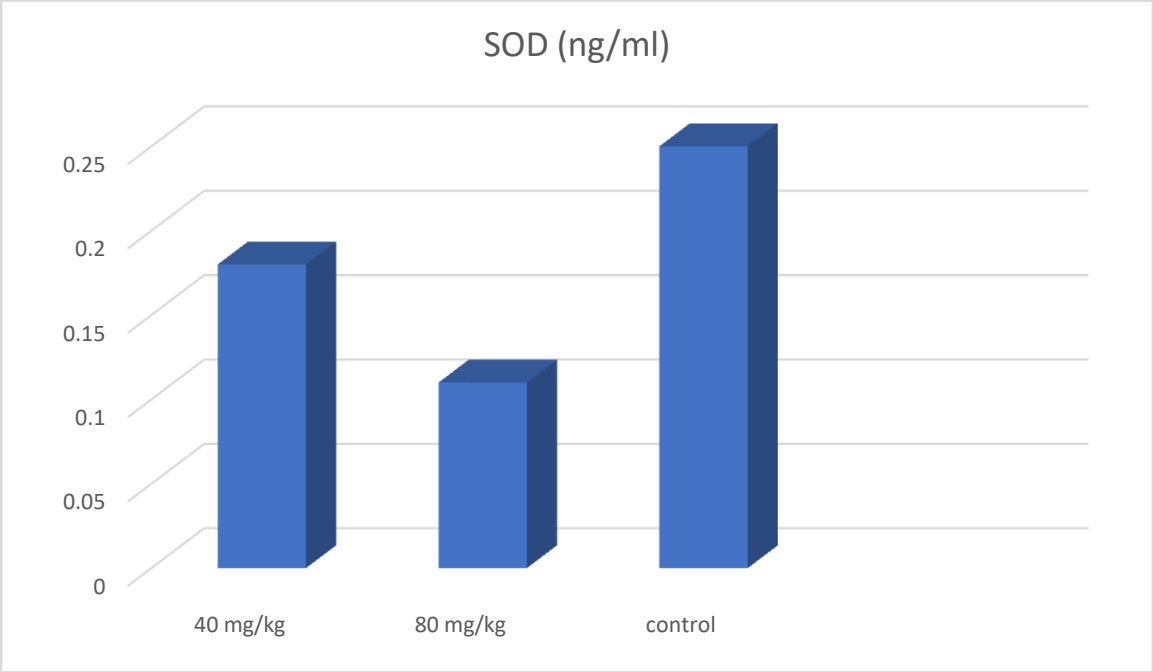


Figure (7) effect of bispyribac sodium in the level of SOD for 30 days in the female rats.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

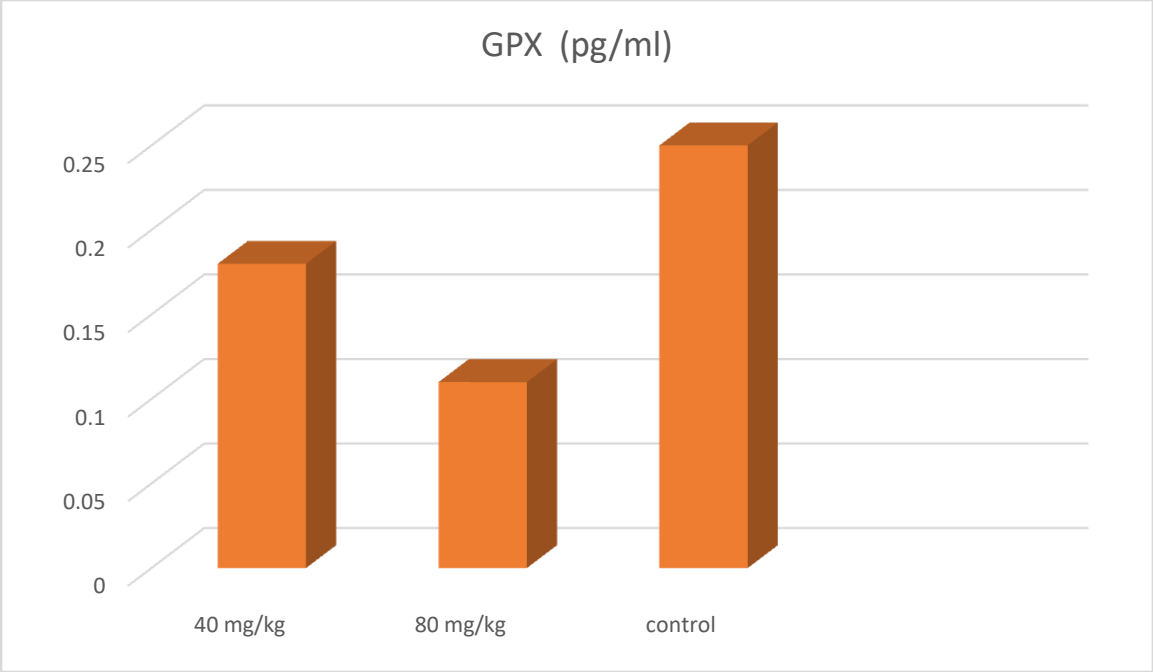


Figure (8) effect of bispyribac sodium in the level of GPX for 30 days in the female rats.

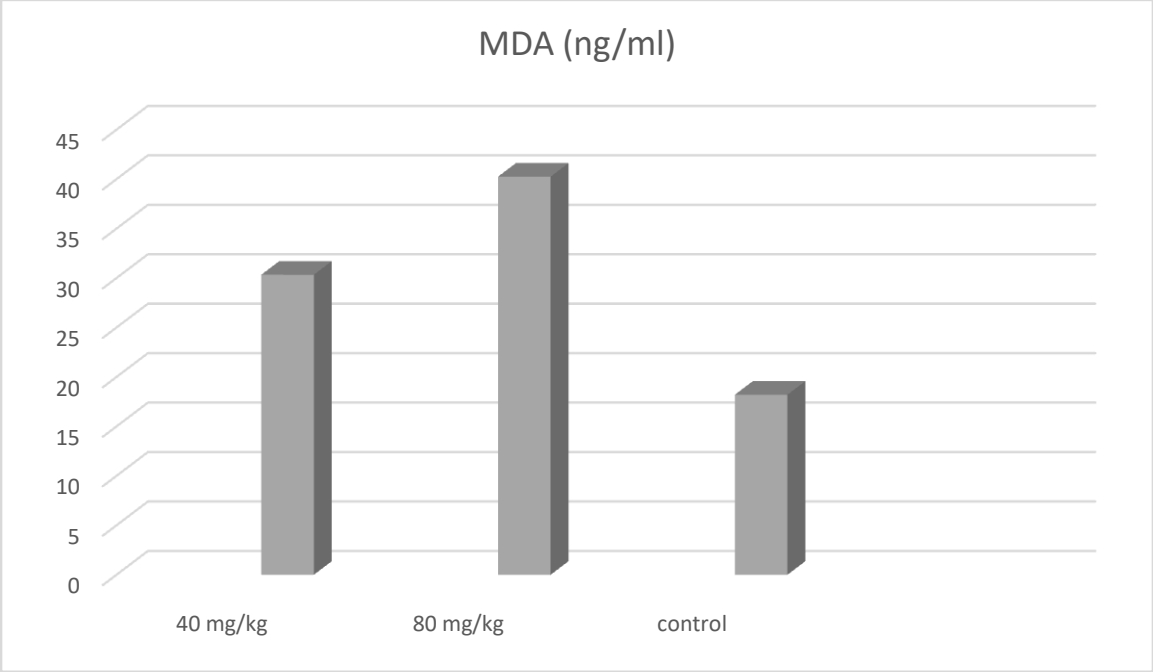


Figure (9) effect of bispyribac sodium in the level of lipid peroxidation MDA for 30 days in the female rats

**Discussion:**

**Body weight gain % of bispyribacsodium**

There was an uncommon diminishing in body weight acquire % in treated gatherings with bispyribac sodium at portion 40 mg/kg and 80 mg/kg individually in contrast control esteem that ascribed concurring with Glusczak et al. (16) suggested that the utilization of

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

energy to detoxify mixes and modification in protein and sugar digestion, thus less energy from food was accessible for advancement of development likewise decline in food utilization and such outcomes concur with Hiroyuki who detailed that female rodents at portion level 0, 100, 500, 20000 and 50000 ppm indications of lessening body weight and feed utilization and on necropsy, dilatation of cecum with histopathological bile conduit multiplication has been noticed additionally (17).

**Hematological finding for bispyribac sodium**

There was criticalness decline ($p<0.05$) altogether erythrocytic count, HGB, PCVand significant increment ($p<0.05$) in white blood cells in regard to control esteems yet there was huge expansion altogether and differential leukocytic include in treated gatherings in examination with the benchmark group where as indicated by Witeska (18) White platelet influenced by an assortment of natural and physiological factors particularly openness to poison and such outcomes concur with California Environmental Protection Agency, that at portion level 1538 mg/kg/day for multi week on female rodents causing increment in relative liver, kidney and spleen weight with infinitesimal entomb and intralobular bile channel multiplication and lymphocytosis in urinary bladder and diverse body organs (19).

**Biochemical changes**

All portions of bispyribac sodium demonstrated a huge expansion in AST, ALT and ALP esteems that considered by Daabees et al. (20). To be symptomatic to liver sicknesses and mirror the hepatotoxicity that thus lead to liver compounds freedom in the blood, and such outcomes concur with Hiroyuki who revealed that in multi week study completed in female rodents controlled orally bispyribac sodium at portion level 0, 100, 500, 20000 and 50000 ppm increment in the centralization of AST, ALT and ALP action of rodents getting 20,000 ppm or potentially 50,000 ppm than control gatherings ; additionally such outcomes affirmed by the histopathological change in the current examination where Liver indicated intralobular fibroblastic expansion with clog of the hepatic sinusoid and hyperplasia of bile ductulus (21).

All dosages of Bispyribac sodium indicated critical reduction in complete protein, egg whites, high thickness lipoprotein and huge expansion in the absolute cholesterol, fatty substance, low thickness lipoprotein, extremely low thickness lipoprotein levels in regard to control esteem that ascribed by Zaahkook et al. (22) to liver illness and aggravation in digestion of protein, sugars and lipid likewise as per Gawarammana et al. acetoacetate synthase hindered by bispyribac may repress expanded chain amino acids bio amalgamation as leucine in human that prompts metabolic issues (23).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

**Antioxidants**

Results of lipid peroxidation may prompt change in natural membrans, in this way these progressions bring about genuine cell injury. An expansion was seen in the arrangement of MDA in the hepatocytes of rodents which were presented to bispyribac sodium . It is recommended that, responsive oxygen species (ROS) assume a basic part in the gathering of neutrophils in tissues after ischemia, though initiated neutrophils are likewise an expected hotspot for ROS (24).

Life forms may have an endogenous defensive cancer prevention agent protect framework against the harms of free oxygen extremists. Turf, CAT and GPX are enzymatic cancer prevention agents that catalyze detoxification responses of harmful oxygen species. The referenced harms might be restricted by non-enzymatic cancer prevention agents, for example, nutrient A, E and C, melatonin, glutathione and so forth Grass, CAT and GPx can give a direct shield by cleaning the hydrogen peroxide that is one of the main hydroxyl revolutionaries that own a possibly receptive structure (25).

The decline in the serum SOD and CAT exercises are potentially a normal outcome that happens because of lipid peroxyl extremists and from an inactivation of their obliteration items. There is a propensity that, expanded MDA levels and diminished SOD and CAT exercises would well help this speculation. The expansion in protein oxidation levels and lipid peroxides is concentrated in numerous people with a realized liver infection initiated by openness to hepato-harmful specialists (26).

GPX movement of the bispyribac sodium bunches were found altogether low when contrasted and the benchmark group However, the reduction checked in the GPX action of the bispyribac sodium gatherings. can result from a lessening in the GSH levels. In like manner, it was accounted for that, a huge lessening was seen in the GSH substance of the liver in mice, which were infused with bispyribac sodium gathering (27).

**In conclusion:**

Bispyribac sodium has a harmful effects on the living organisms as plants, animals and human when used for a long time.

**References:**

1-Bolognesi C (2003) Genotoxicity of pesticides: a review of human biomonitoring studies. Mutat Res 543: 251-272.

2-Hasenbein S, Peralta J, Lawler SP, Connon RE (2017) Environmentally relevant concentrations of herbicides impact non-target species at multiple sublethal endpoints. Sci Total Environ 607-608: 733-743.

3-Amlia JS (2011) Herbicides: The Face and the Reverse of the Coin. An in vitro Approach to the Toxicity of Herbicides in Non-Target Organisms. In: Amlia JS, Maria FAS, Romeu AV, Francisco PP, Joaquim AFV (eds.) Herbicides and Environment, Environmental Sciences, Croatia, pp: 3-45.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

4-Geovane BR, Sérgio LOM, Maria Angélica O, Renato Z, Valderi Luiz D, et al. (2015). Imazethapyr and imazapic, bispyribac-sodium and penoxsulam: Zooplankton and dissipation in subtropical rice paddy water, Sci Total Environ 514: 68-76.

5-Health Canada Pest Management Regulatory Agency (2008) Registration Decision Bispyribac-sodium.

6-Australian Pesticides and Veterinary Medicines Authority (2011) On the evaluation of the new active bispyribac sodium in the product nominee® herbicide.

7-California Environmental Protection Agency (2001) Data Review Summary for Bispyribac; p. 10.

8-Blokhina O.B. et al.(2003). Antioxidants, oxidative damage and oxygen deprivation stress: a review. **Ann Bot.** ;91:179-94.

9- Mohamed Fathy1 & Ibrahim A. Mohamed1 & Ahmed I. A. Farghal1 & Sobhy A. H. Temerak1 & Alaa El-Din H. Sayed. (2019). Hemotoxic effects of some herbicides on juvenile of Nile tilapia *Oreochromis niloticus*Environmental Science and Pollution Research, p:1-9.

10-Marchezan, M.G. Avila, L.A. Schaedler, C.E. Amarante, L. Scherner, A. and Schreiber, F.(2017).Biochemical alterations of weeds in response to stress caused by herbicides and total plantsubmersion,Planta Daninha 2017; v35. p.p.: 1-11.

11-Kavakli H, Koca C, Alici O (2011) Antioxidant effects of curcumuin in spinal cord injury in rats. Turkish J. of trauma and emergency surgery, 14-18.

**12-Mathieleers, I.;** Lsabel, G.; Fadila, S. and Rick, G. (2012). Abbott apromise for life. Com, Case book, 1-91.

13-Tietz, N. Clinical guide to laboratory test 4th Ed., 1999, pp. 1074-1077.

14-**Belfieda, A.** and golberg, D. (1971). Revised assay for serum phenyl phosphatase activity using 4-amino-antipyrine enzyme, 12: 561-573.

15-Al-Rawi, K. Entrance to the Statistics. Second edition. Faculty of Agriculture and Forestry, University of Mosul. 2000.

16-Glusczak L, dos Santos MD, Crestani M, Braga da Fonseca M, de Araújo Pedron F, et al. (2006) Effect of glyphosate herbicide on acetylcholinesterase activity and metabolic and hematological parameters in piava (Leporinus obtusidens). Ecotoxicol Environ Saf 65: 237-241.

17-Hiroyuki Inoue (1991) KIH-2023 Technical: Subchronic Toxicity Study in Rats, Biosafety Research Center, Foods, Drugs and Pesticides; 582-2, Iwata-gun Shizuoka-ken Japan.

18-Witeska M (2005) Stress in fish - hematological and immunological effects of heavy metals. Electron J Ichthyol 1: 35-41.

19-California Environmental Protection Agency (2001) Data Review Summary for Bispyribac; p. 10.

20-Daabees AY, El-Damiaty NA, Soliman SA, El-Toweissy MY (1992) Comparative action of three synthetic pesticides on serum, liver, brain of the freshwater fish, Clarias lazera. J Egypt Ger Soc Zool 9: 105-109.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 273 - 283
Received 05 May 2021; Accepted 01 June 2021.

21- **Sanaa, M. Abdulrhman, Nahas, A.A. and Reem, M. Ziada**. (2020). **Pregnancy Outcome in Female Rats Exposed to Bispyribac Sodium and Ameliorative Effect of *Nigella Sativa* Oil. Egypt. Acad. J. Biolog. Sci., 12(2): 97-108.**

22-Zaahkook SA, Helal EG, Fahmy N, Al-Shinnawy MS, El-Ghany AB (2009) Physiological study about imidacloprid toxicity and the role of vitamin"C" as a protective agent on Japanese Quails. Egypt J Hospital Med 34: 183-197.

23-Bandara GI, Darren MR, Fahim M, Michael RS, Gregory M, et al. (2010) Acute human self-poisoning with bispyribac-containing herbicide Nominee®: A prospective observational study. Clin Toxicol (Phila) 48: 198-202.

24-Glusczak L, dos Santos MD, Crestani M, Braga da Fonseca M, de Araújo Pedron F, et al. (2006) Effect of glyphosate herbicide on acetylcholinesterase activity and metabolic and hematological parameters in piava (Leporinus obtusidens). Ecotoxicol Environ Saf 65: 237-241.

25-Liu XM, Shao JZ, Xiang LX, Chen XY (2006) Cytotoxic effects and apoptosis induction of atrazine in a grass carp (Ctenopharyngodon idellus) cell line. Environ Toxicol. 21: 80-89.

26-Daniel Camiletti-Moiron, Virginia Arianna Aparicio, Elena Nebot, Gerardo Medina, and Rosario Martinez, (2015). High-protein diet induces oxidative stress in rat brain: protective action of high-intensity exercise against lipid peroxidation. Nutr. Hosp. 2015;31(2):866-874.

27-Vijay Singh a, *, Mangi L. Jat b, Zahoor A. Ganie c, Bhagirath S. Chauhan d, and Raj K. Gupta. (2016). Herbicide options for effective weed management in dry direct seeded rice under scented rice-wheat rotation of western Indo-Gangetic Plains. Crop Protection 81 : pp. 168e176.