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ONLINE ISSN: 2992-5460
PRINT ISSN: 2992-6041

NEWPORT INTERNATIONAL JOURNAL OF RESEARCH IN MEDICAL SCIENCES (NIJRMS)

Volume 6 Issue 3 Page 9-17 2025

https://doi.org/10.59298/NIJRMS/2025/6.3.917

Histopathological Impact of Bisphenol A on the Brain, Liver, and Kidney of Wistar Rats *(Rattus norvegicus)*

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ABSTRACT

Bisphenol A (BPA), an endocrine-disrupting compound widely used in plastics, has raised significant toxicological concerns due to its potential impact on vital organs. This study investigates the histopathological impact of BPA exposure on the brain, liver, and kidney tissues of Wistar rats. Adult male Wistar rats were divided into control (C) and treatment groups of Low Dose Group (LD) (50mg/kg); Middle Dose Group (MD) (100mg/kg) and High Dose Group (HD) (200mg/kg), based on the dosage of BPA orally administered to the rats for 28 days. Histological analysis revealed degenerative and necrotic changes in hepatocytes, vacuolar degeneration in renal tubules, and neuronal degeneration in cortical regions of the brain. Both the control group and the 200 mg/kg BPA group displayed normal liver architecture, with hepatocytes organized in radial plates surrounding central veins and intact portal triads. In contrast, the 50 mg/kg and 100 mg/kg groups exhibited mild to moderate hepatocellular swelling, particularly in the periportal and mid-zonal regions. Kidney tissues from all experimental groups, including those exposed to BPA, appeared histologically normal with well-preserved glomeruli and renal tubules suggesting that the exposure levels and duration may have been insufficient to produce overt nephrotoxic effects, or that renal compensatory mechanisms were able to mitigate damage under the experimental conditions. Evidence of neuronal degeneration was found in the brains of rats exposed to 200 mg/kg BPA, characterized by shrunken and deeply stained (basophilic) neurons—features indicative of necrosis. These findings suggest that chronic BPA exposure induces multi-organ toxicity, highlighting the urgent need for stricter regulation of BPA-containing products.

Keywords: Bisphenol A, Histology, Brain, Liver, Kidney, Wistar rats, Endocrine disruptor

INTRODUCTION

The endocrine system is a network of glands and organs that produce secrete and store hormones. The endocrine system works with other systems to regulate the normal body healthy development all through life [1]. Bisphenol A (BPA) is a synthetic organic compound used in the production of polycarbonate plastics and epoxy resins, commonly found in food containers, water bottles, and dental sealants. As an endocrine disruptor, BPA mimics estrogen and interferes with hormonal signaling, leading to adverse health outcomes in both humans and experimental models. While BPA's endocrine-disrupting potential is well-documented, its specific effects on vital organs such as the brain, liver, and kidney are still being explored [2]. Bisphenol A can access the human body through skin, gastrointestinal tract and placenta and inevitably affect the entire system [3], [4], [2] and [5]. BPA can lead to renal tubule degeneration in the kidneys of rats and mice [6]. It can also lead to sexual dysfunction, heart disease, metabolic disorders, obesity, and enlargement of cerebral ventricles [7]. It can also affect the liver as the major organ for detoxification of waste toxins (xenobiotics) including BPA [7]. Recent publications reported that BPA effects are dependent on several factors like age, sex, exposure route, exposure time, and dose. The brain, as the central nervous system regulator, is highly vulnerable to oxidative and excitotoxic damage. The liver, a major detoxification site, and the kidney, responsible for excretion, are primary targets of xenobiotic-induced injury. This study evaluates the

ONLINE ISSN: 2992-5460
PRINT ISSN: 2992-6041

histological alterations in these organs following sub-chronic BPA exposure in Wistar rats [5]. The aim of this study is to examine the histopathological impact of BPA on the Brain, Liver, and Kidney of Wistar Rats *(Rattus norvegicus)*

MATERIALS AND METHODS

Ethical Considerations: Ethics committee approval (Protocol no: 2021/18-2) was obtained from Ebonyi State University Ethical Committee of Faculty of Health Science and Technology. All the experiment followed the guidelines provided and were in tandem with the global Institutional Animal Care and Use in which all procedures minimized animal suffering and use the 3Rs principle: Replacement, Reduction, and Refinement

Lethal Dose Toxicity (LD_{50}): Lethal Dose Toxicity (LD_{50}) test procedure for Bisphenol A was done following OECD test guidelines 423.

Experimental chemicals: The Bisphenol A 99% standard were purchased from Punkinosis chemical company Limited (House 21, 41 Crescent Gwarimpa, Abuja FCT). The powder was dissolved in corn oil and orally administered to non-anesthetized rats via gavage

Experimental Protocol

Experimental Animal: The wistar rats used from this research were purchased from Animal House, University of Nigeria, Nsukka. A total of 40 adult Wistar rats (20 males and 20 females), aged 8–10 weeks and weighing 80–200g. The rats were bred in animal house of Faculty of Health Science and Technology, Ebonyi State University Abakaliki, Nigeria and they were used in this study. All the rats were kept at a constant temperature of 24–26°C and in a 12-hr light/12-hr dark cycle.

Experimental Design and Grouping

The rats were randomly divided into the following groups:

- ✓ Control Group (C): No exposure to BPA
- ✓ Low-Dose Group (LD): 50 µg/kg body weight/day of BPA
- ✓ Middle-Dose Group (MD): 100 µg/kg body weight/day of BPA
- ✓ High-Dose Group (HD): 200 µg/kg body weight/day of BPA

Each group contained 5 males and 5 females. BPA was administered orally via gavage for a period of 21 days prior to mating to simulate chronic exposure. Treatments lasted for 28 consecutive days and the histological samples were collected immediately after the animal sacrifice. All experiments were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, 8th edition [8],

Histopathological Analysis of brain kidney and liver

Samples were carefully collected from the brain, kidney, and liver, ensuring minimal damage during the process. These tissues were immersed in formalin (a fixative solution, to preserve their structure and prevent degradation. After which the tissues were dehydrated by passing them through a series of increasing concentrations of alcohol to remove water. To make the tissues translucent, they were passed through xylene to make the tissue translucent and then embedded in paraffin wax, creating a solid block that can be sectioned. Sectioning was done by cutting thin slices (5-6 µm thick) from the paraffin block. This was followed by staining by using Hematoxylin and Eosin (H&E) technique. Hematoxylin stains cell nuclei blue/purple, while eosin stains the cytoplasm and extracellular matrix pink/red. Microscopic Examination was done by examining the stained tissue sections under a light microscope, typically to assess tissue morphology and identify any abnormalities or pathological changes. Histological analysis of the brain focused on identifying changes in neuronal structure, glial cells, and blood vessels, as well as the presence of any lesions, plaques, or abnormal protein deposits. Kidney analysis involves examining the glomeruli, tubules, and blood vessels to assess for signs of inflammation, necrosis, or structural damage. Liver analysis focuses on evaluating the hepatocytes, bile ducts, and blood vessels for signs of inflammation, fibrosis, necrosis, or other pathological changes.

RESULTS

Histological Analytical Results: The following diagrams were obtained from the histological analysis of the studies.

Control Group: Sections of the brain presented on this slide showed the normal cerebral histomorphology. Neurons (red arrow) Glial cells (black arrow) Blood capillaries (green arrow).Neuropil (N).HE x200.

Group C dozed with 200mg/kg: Sections of the brain presented on this slide showed neuronal necrosis. Affected neurons appear deeply basophilic and shrunken (red arrow).Normal neurons (blue arrow).Glial cells (black arrow), Blood capillaries (green arrow). Neuropil (N). HE x200.

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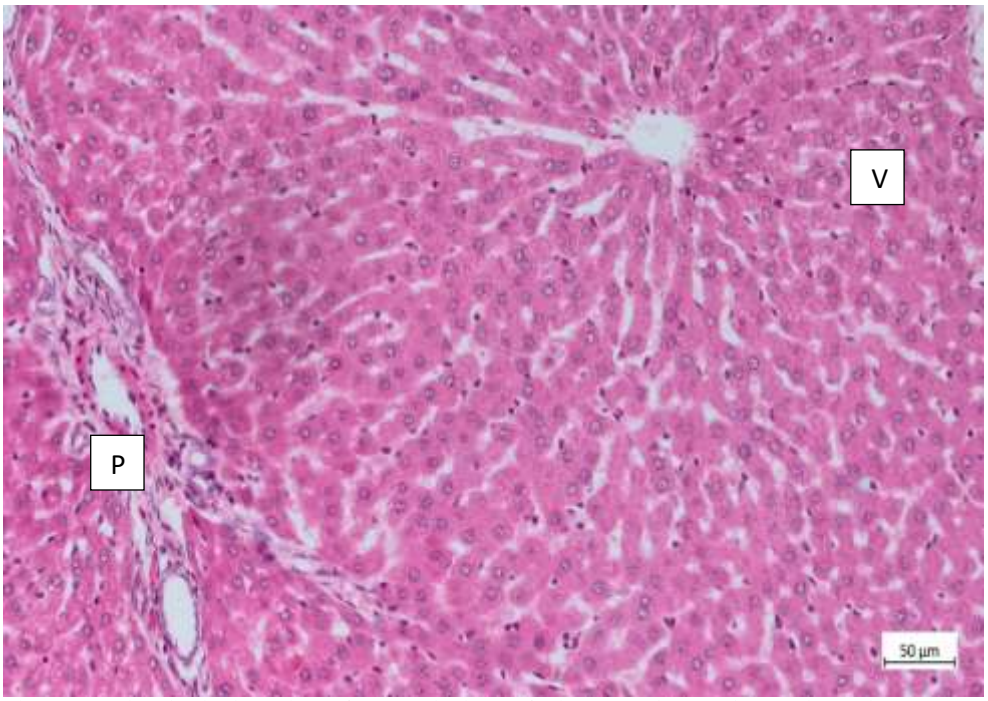
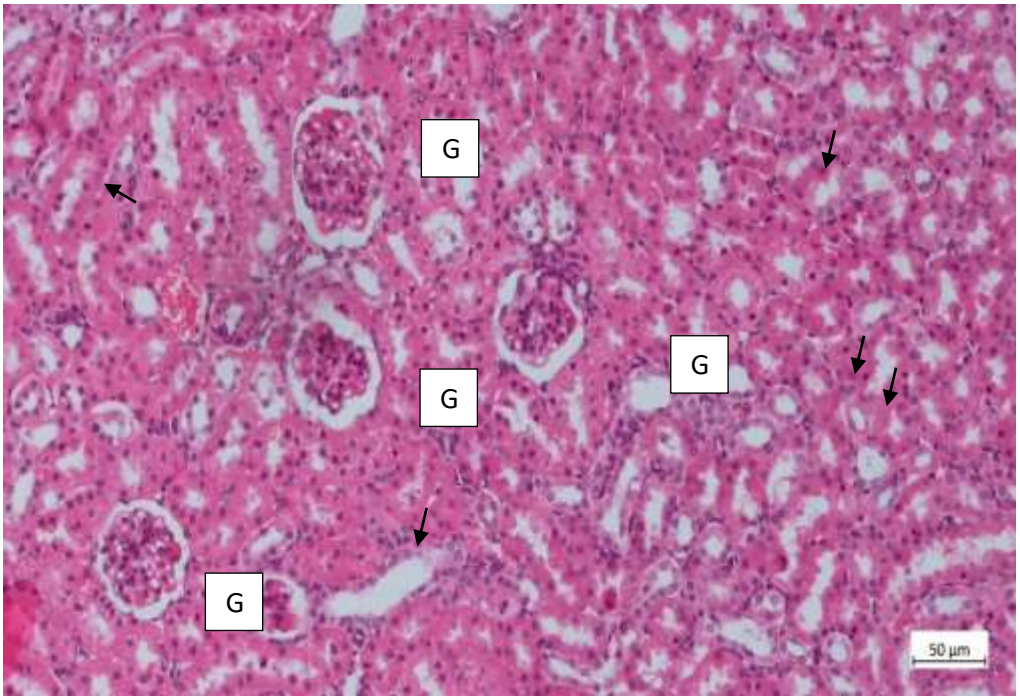


Sections of the liver presented on this slide showed the normal hepatic histomorphology. Normal hepatocytes were observed, arranged in interconnecting cords around the central veins (V). Normal structure of the portal triads (P) were also observed.

HE x200.

Figure 1: Histological section of Normal Liver of wistar rat (control experiment)



Sections of the kidney presented on this slide showed the normal renal histomorphology.

Glomeruli (G)

Renal tubules (arrow)

HE x200.

Figure 2: Histological section of Kidney of wistar rat (control experiment)

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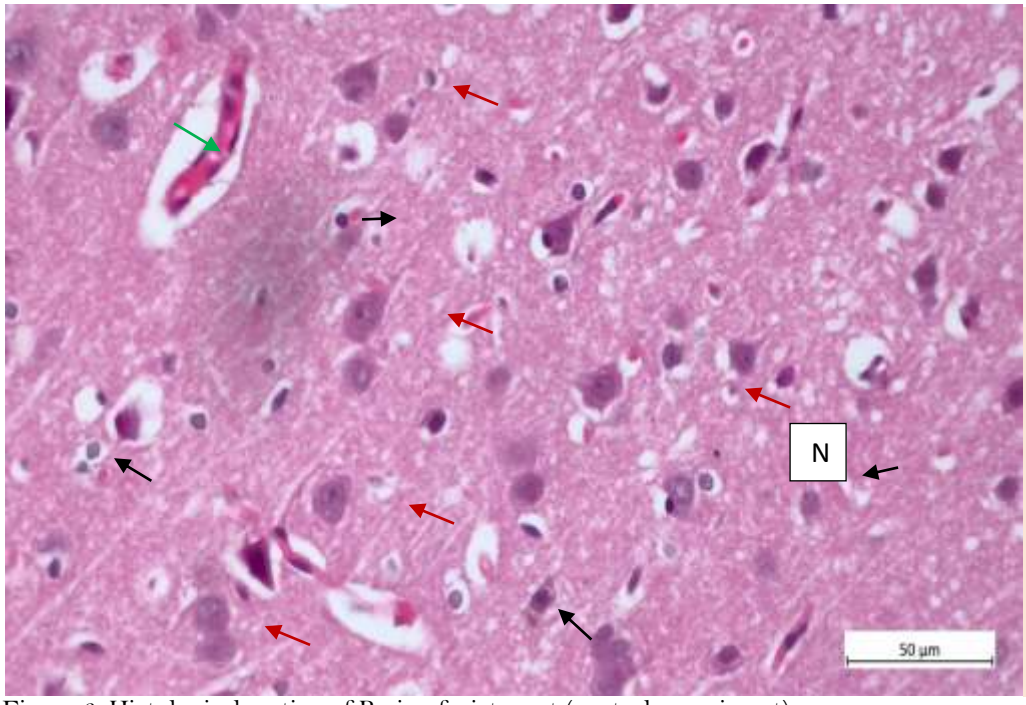


Sections of the brain presented on this slide showed the normal cerebral histomorphology.

Neurons (red arrow)

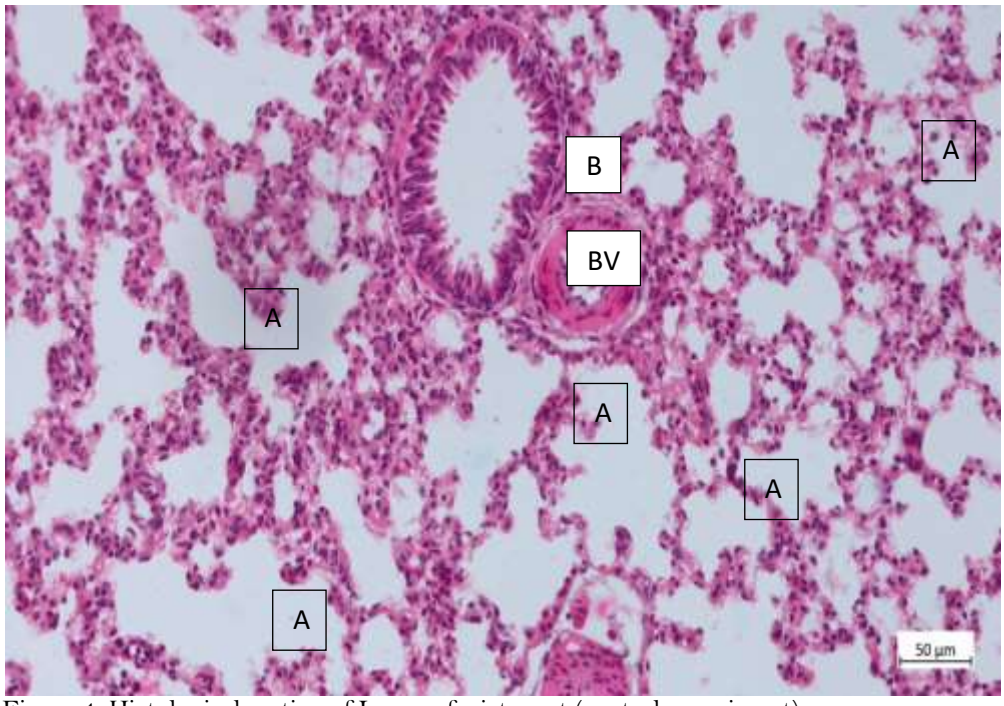
Glial cells (black arrow)

Blood capillaries (green arrow).

Neuropil (N).

HE x200.

Figure 3: Histological section of Brain of wistar rat (control experiment)



Sections of the lungs presented on this side showed the normal pulmonary histomorphology.

Alveoli (A)

Bronchiole (B)

A branch of the pulmonary artery (BV)

HE x200.

Figure 4: Histological section of Lungs of wistar rat (control experiment)

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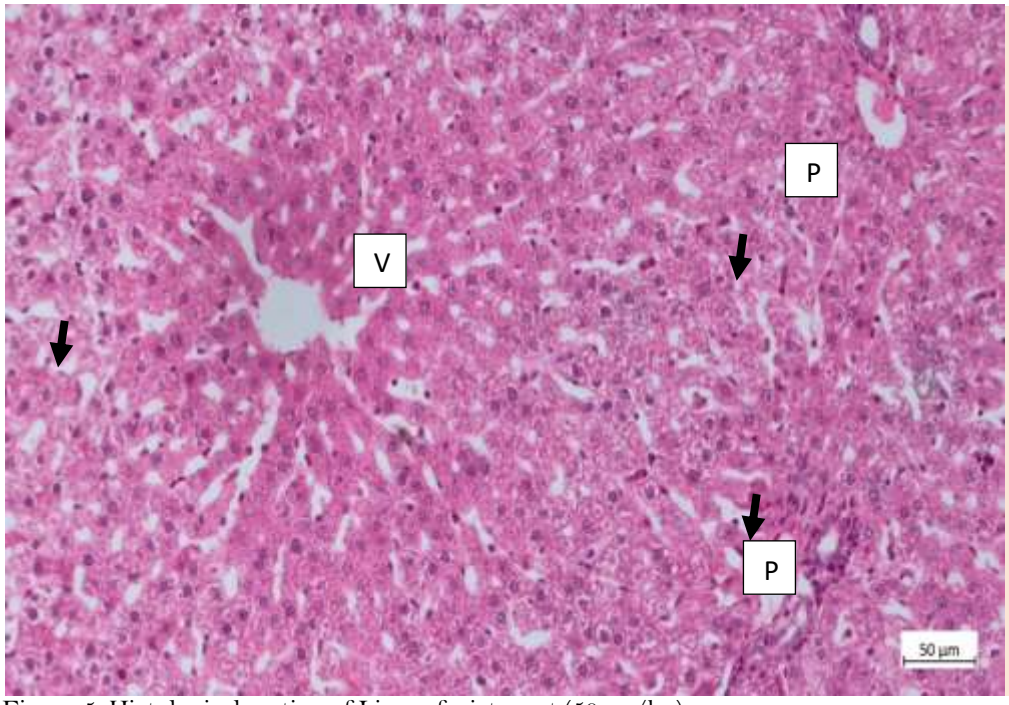


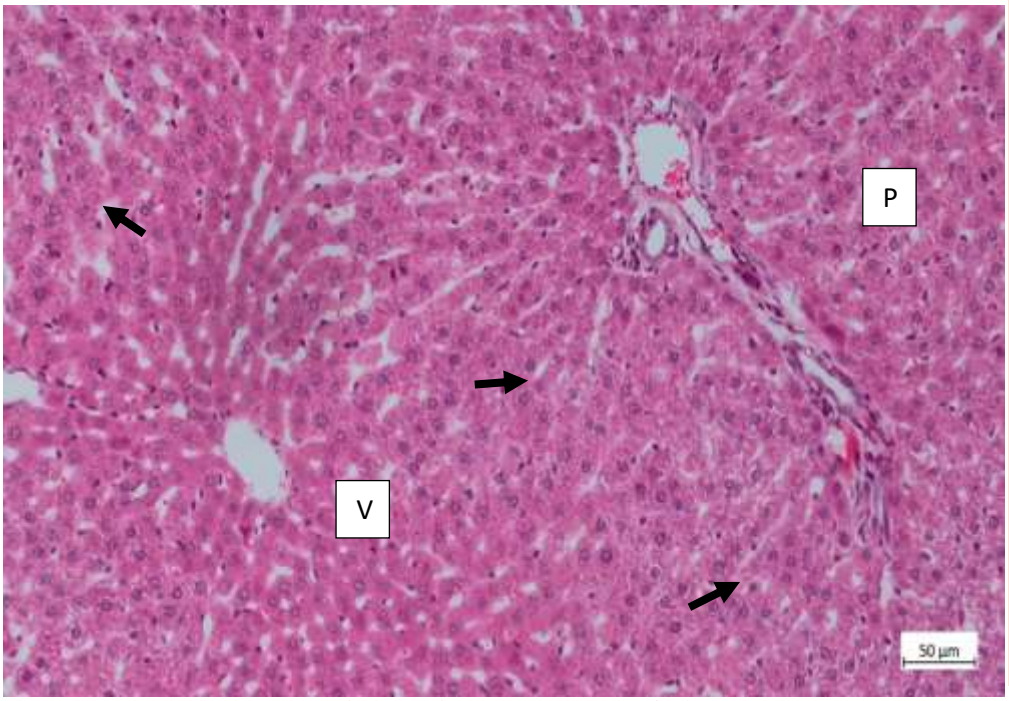
Sections of the liver presented in this group showed mild-to-moderate acute cellular swelling of the hepatocytes in the mid-zonal and periportal areas of the hepatic lobules. Affected cell appear somewhat swollen with cloudy cytoplasm (arrow).

Central vein (V)

Portal triad (P)

HE x200.

Figure 5: Histological section of Liver of wistar rat (50mg/kg)



Sections of the liver presented in this group showed mild acute cellular swelling of the hepatocytes in the mid-zonal and periportal areas of the hepatic lobules. Affected cell appear somewhat swollen with cloudy cytoplasm (arrow).

Central vein (V)

Portal triad (P)

HE x200.

Figure 6: Histological section of Liver of wistar rat (100mg/kg)

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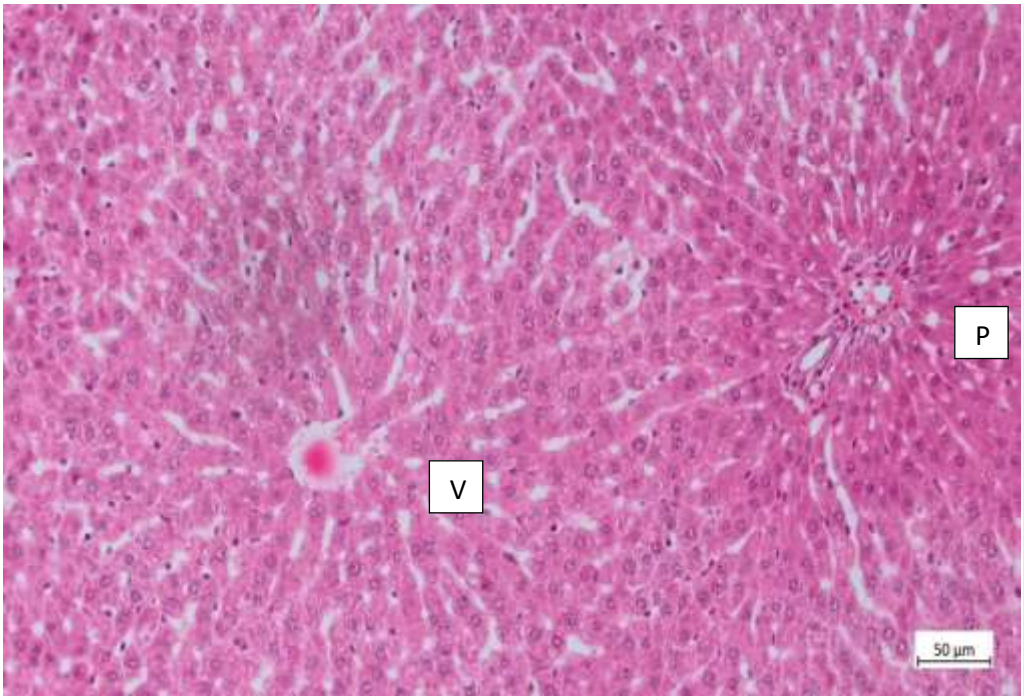


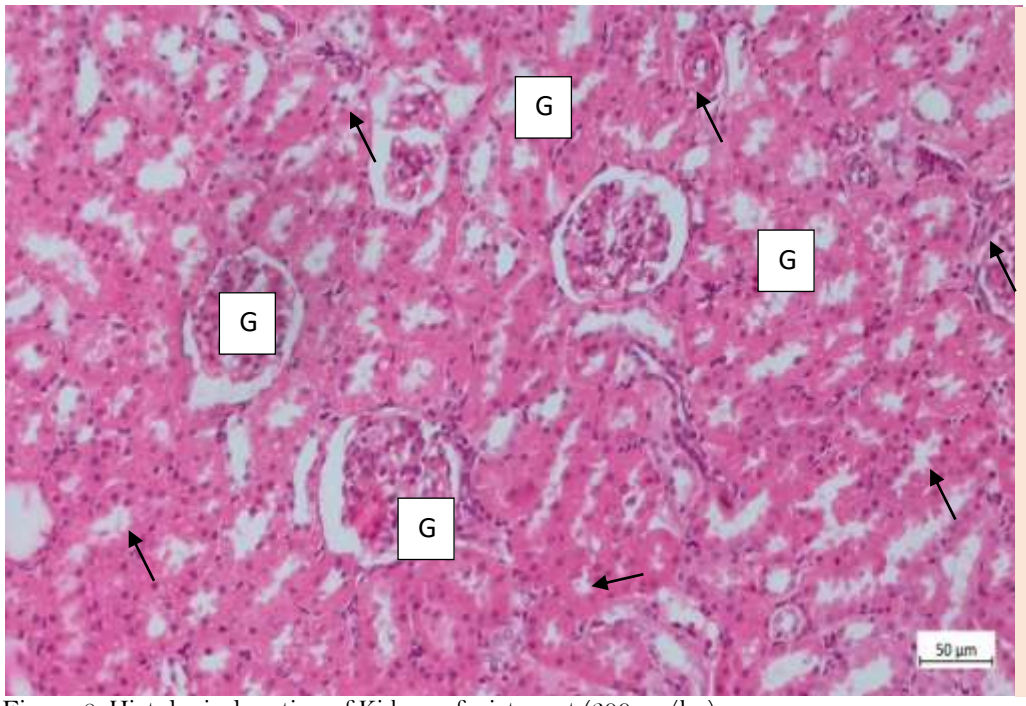
Sections of the liver presented in this group showed the normal hepatic histomorphology.

Central vein (V)

Portal triad (P)

HE x200.

Figure 7: Histological section of Liver of wistar rat (200mg/kg)



Sections of the kidney presented on this slide showed the normal renal histomorphology.

Glomeruli (G)

Renal tubules (arrow)

HE x200.

Figure 8: Histological section of Kidney of wistar rat (200mg/kg)

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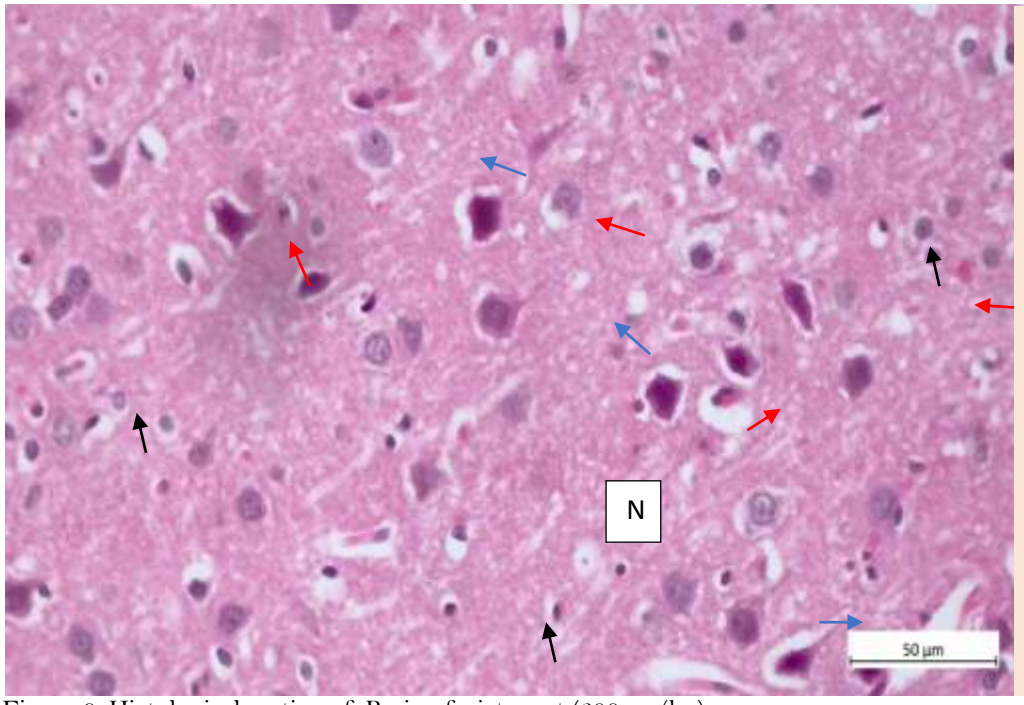


Sections of the brain presented on this slide showed neuronal necrosis. Affected neurons appear deeply basophilic and shrunken (red arrow)

Normal neurons (blue arrow)

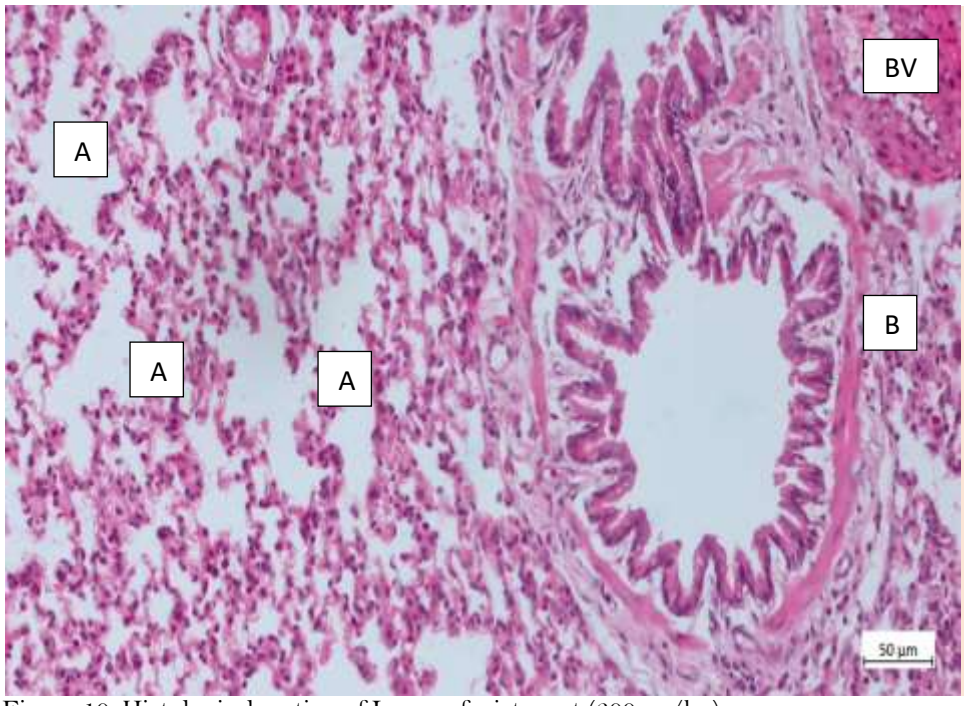
Glial cells (black arrow)

Blood capillaries (green arrow).

Neuropil (N).

HE x200.

Figure 9: Histological section of Brain of wistar rat (200mg/kg)



Sections of the lungs presented on this side showed the normal pulmonary histomorphology.

Alveoli (A)

Bronchiole (B)

A branch of the pulmonary artery (BV)

HE x200.

Figure 10: Histological section of Lungs of wistar rat (200mg/kg)

DISCUSSIONS

Lethal dose toxicity (LD_{50}): The Lethal dose toxicity of Bisphenol A carried out showed dullness in the rats. they became stable after sometime. No animal died during the fourteen days test for toxicity for doses ranging from 100mg/kg, 1000mg/kg, 2000mg/kg, 300mg/kg and 5000mg/kg.

Histological Results: Microscopic examination revealed varying degrees of tissue damage among the treatment groups when compared to the control group, providing insight into the potential toxicological effects of BPA on organ structure and function.

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PRINT ISSN: 2992-6041

Liver Histomorphology: Both the control group and the 200 mg/kg BPA group displayed normal liver architecture, with hepatocytes organized in radial plates surrounding central veins and intact portal triads. In contrast, the 50 mg/kg and 100 mg/kg groups exhibited mild to moderate hepatocellular swelling, particularly in the periportal and mid-zonal regions. The presence of cloudy cytoplasm in affected cells is suggestive of cellular injury potentially caused by BPA-induced oxidative stress or membrane dysfunction. These patterns are in agreement with studies that have shown BPA to promote oxidative damage and lipid peroxidation in liver tissues, contributing to hepatocyte swelling and possible impairment [9], [10]. The observed dose-dependent liver alterations support the theory that BPA's hepatotoxic effects are linked to its ability to accumulate and interfere with cellular redox systems [11].

Kidney Histomorphology: Kidney tissues from all experimental groups, including those exposed to BPA, appeared histologically normal with well-preserved glomeruli and renal tubules. This finding suggests that the exposure levels and duration may have been insufficient to produce overt nephrotoxic effects, or that renal compensatory mechanisms were able to mitigate damage under the experimental conditions. Although other studies have documented renal abnormalities such as tubular degeneration and glomerular hypertrophy following higher BPA doses or extended exposure periods [12], the absence of significant renal pathology in this study may indicate a threshold effect.

Brain Histomorphology: Evidence of neuronal degeneration was found in the brains of rats exposed to 200 mg/kg BPA, characterized by shrunken and deeply stained (basophilic) neurons—features indicative of necrosis. This outcome aligns with earlier research highlighting BPA's capacity to disrupt neuronal integrity, particularly in the hippocampus, potentially impairing synaptic function and plasticity [13], [14]. BPA's neurotoxicity may stem from mechanisms such as oxidative stress, excitotoxicity, and disturbances in neurotransmitter balance. Furthermore, BPA-induced neuroinflammation and oxidative insults can modify epigenetic regulation of neuroendocrine-related genes, with some of these changes potentially passed on to offspring [15].

CONCLUSION

The histological findings indicate that BPA exposure led to noticeable pathological changes primarily in the liver and brain, including mild hepatocellular degeneration and neuronal necrosis, respectively. In contrast, the kidneys and lungs did not exhibit overt structural alterations under the current experimental parameters. This study demonstrates that sub-chronic BPA exposure induces significant histopathological alterations in the brain, liver, and kidney of Wistar rats. Regulatory efforts should be intensified to limit BPA use and encourage safer alternatives in consumer products.

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CITE AS: Oti-Wilberforce R.O., Edeogu C.O. and Oti W.J.O.(2025). Histopathological Impact of Bisphenol A on the Brain, Liver, and Kidney of Wistar Rats (Rattus norvegicus). NEWPORT INTERNATIONAL JOURNAL OF RESEARCH IN MEDICAL SCIENCES,6(3):9-17
https://doi.org/10.59298/NIJRMS/2025/6.3.917