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A Mixture of Bisphenol-B, Bisphenol-F and Bisphenol-S Induces Dose-Dependent Renal Dysfunction and Cardiopulmonary Damage in Female Rats

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ABSTRACT

Exposure to mixtures of Bisphenols-B (BPB), -F (BPF), and -S (BPS) is increasingly common; as these chemicals are widely used to enhance rigidity of industrial and domestic products. In this study, we assessed the impact of low doses of these environmental contaminants on the kidney, heart, and lung of female rats. Female rats were divided into seven groups of 6 animals each. The first group serving as control was administered just olive oil, while groups 2 – 7 were intoxicated with graded doses (12 – 384 µg/kg body weight) of Bisphenols -B, -F and -S for 49 days. The analogues induced oxidative stress by inducing lipid peroxidation and dysregulating reduced glutathione, glutathione transferase, superoxide dismutase, and lactate dehydrogenase. Significant increase ($p < 0.05$) in serum uric acid (32%-103%) and albumin (56%-305%); and significant ($p < 0.05$) decrease in serum creatinine (37%-65%) and urea (17%-81%) were also observed compared with control; indicating a dose-dependent kidney damage. These results were corroborated by histological assessment which revealed degenerative changes, signs of glomerulosclerosis and glomerulonephritis, pyknotic renal parenchymal cells, signs of hemorrhage, and concentrated mesangial cells. Histological evaluation of the heart and lung also revealed severe morphological damage in the exposed animals. Our findings suggest that chronic exposure to low doses of Bisphenol-A analogues may increase the risk of damage to multiple organs, particularly the liver and kidneys.

Keywords: Bisphenol-B, Bisphenol-F, Bisphenol-S, renal toxicity, oxidative stress, cardiopulmonary damage, environmental toxicants

INTRODUCTION

Kidney failure, alongside heart and lung dysfunction, is increasing globally, and poses a major public health threat. This ugly public health trend is consequent of continuous exposure to diverse environmental contaminants, which is characteristic of modern lifestyle (Akintunde *et al.*, 2020). And correlation/link between diverse environmental contaminants and multiple organ failure including kidney and heart has been reported (Akintunde *et al.*, 2020, 2021; Oseni and Okoh, 2020;)

Bisphenols, a class of industrial chemicals widely used in the production of plastics, resins, and other consumer products, have come under increasing scrutiny due to their potential adverse effects on human health and the environment. Among these, Bisphenol-A (BPA) has been the most extensively studied and is known to exert various detrimental effects on different organ systems, including the kidney, heart, and lung. However, emerging research indicates that other bisphenol analogues such as Bisphenol-B (BPB), Bisphenol-F (BPF), and Bisphenol-S (BPS) may also present considerable health concerns. Experimental studies have reported neurodevelopmental and systemic toxic effects associated with these compounds, suggesting that their safety may not be significantly different from that of BPA (Okoh *et al.*, 2025).

BPA, which is regarded as the prototypical bisphenol, has been widely linked to several adverse health outcomes including renal dysfunction, cardiovascular diseases, and respiratory disorders. Evidence from both epidemiological and experimental studies has shown a relationship between BPA exposure and impaired kidney function. These effects are often reflected in changes in renal structure, disturbances in normal renal function, and the eventual development of renal conditions such as chronic kidney disease (CKD) and nephropathy (Shankar, 2011; Rochester, 2013). At the cellular level, BPA has been reported to interfere with normal renal processes by promoting oxidative stress, triggering inflammatory responses, and inducing apoptosis in kidney cells (Lee *et al.*, 2008; Ferguson *et al.*, 2011; Hyun *et al.*, 2021).

In addition to its effects on the kidney, BPA exposure has also been associated with an increased risk of hypertension, which is a major contributing factor in the development of cardiovascular diseases (Sun *et al.*, 2019). This relationship highlights the broader impact that BPA may have on cardiovascular health. Furthermore, BPA exposure has been associated with the development and worsening of respiratory disorders. Studies have reported links between BPA and conditions such as asthma and chronic obstructive pulmonary disease (COPD). These effects are believed to occur through inflammatory and fibrotic processes that affect lung tissues (Shabir *et al.*, 2020; Hatziri *et al.*, 2021).

Although BPA has received the most scientific attention, increasing concern is now being directed toward other bisphenol analogues, particularly BPB, BPF, and BPS, which are increasingly used as substitutes for BPA in many consumer products. These compounds are also considered environmental contaminants. Epidemiological and animal studies have reported associations between exposure to environmental contaminants and an increased risk of damage to several organs including the kidney, heart, and lungs (Akintunde and Oboh, 2016; Akintunde, 2021). Despite their structural similarity to BPA, these bisphenol analogues differ in certain chemical characteristics

and biological activities. Such differences may influence how they interact with biological systems and could result in varying toxicological effects.

Recent studies have suggested that BPB, BPF, and BPS possess endocrine disrupting properties and are capable of interfering with hormonal signaling pathways that regulate renal, cardiovascular, and pulmonary functions (Rochester and Bolden, 2015; Guo *et al*., 2019). In addition, these bisphenols have been detected in various environmental and biological samples, which indicates that exposure among human populations is widespread (Geens *et al*., 2012; Liao and Kannan, 2013).

Given the structural similarities between BPA and its analogs, it is plausible to hypothesize that BPB, BPF, and BPS may elicit similar adverse effects on renal, cardiovascular, and pulmonary health. However, limited research has been conducted to evaluate the toxicological effects of these bisphenols, especially in combination, which may better reflect real-life exposure scenarios. Therefore, the present study aimed to investigate the renal, cardiovascular, and pulmonary effects of a mixture of BPB, BPF, and BPS in female rats and compare them with the effects of BPA. We hypothesized that chronic exposure to a mixture of BPB, BPF, and BPS would induce dose-dependent renal, cardiac, and pulmonary toxicity in female rats. Understanding the toxicological effects of these bisphenols is crucial for informing regulatory decisions and public health policies aimed at minimizing human exposure and mitigating associated health risks.

MATERIALS AND METHODS

Bisphenols -B, -F, and -S, were sourced from Sigma. Other chemicals and reagents were of analytical grade, and purchased from reputable suppliers.

Experimental Design

Ethical clearance, was obtained from the University of Ibadan Animal Care Use and Research Ethics Committee. For this study, forty-two newly weaned female rats were procured from Lagos University Teaching Hospital, Lagos, and accommodated in adequately ventilated plastic cages within the animal facility at Anchor University, Lagos. The rats were provided *ad libitum* access to commercial feed and subjected to a 12-hour light/dark cycle. The experiment commenced when the rats reached 7 weeks of age, weighing approximately 150 g each. Subsequently, the rats were grouped into seven; each group comprising six animals. A mixture of BPB, BPF, and BPS (MBPAA) was prepared in an equimolar ratio (1:1:1). Animals were administered with the mixture at total doses of 12, 24, 48, 96, 192, and 384 µg/kg body weight. At each dose level the total mixture dose was equally distributed among the three components (i.e. each bisphenol contributed one-third of the total dose; for example, 12 µg/kg corresponded to 4 µg/kg each of BPB, BPF, and BPS).

Group 1 (Control) received olive oil, as olive oil served as the vehicle.

Group 2 (MBPAA_12) was administered with total mixture dose of 12 µg/kg body weight.

Group 3 (MBPAA_24) was given total mixture dose of 24 µg/kg body weight.

Group 4 (MBPAA_48) was exposed to 48 µg/kg body weight total mixture dose.

Group 5 (MBPAA_96) received 96 µg/kg body weight total mixture dose.

Group 6 (MBPAA_192) was administered 192 µg/kg body weight total mixture dose.

Group 7 (MBPAA_384) was subjected to 384 µg/kg body weight total mixture dose.

The toxicants were orally administered via gavage every day around 10 am for a duration of forty-nine days. Following the final administration, rats underwent an overnight fasting period, after which blood samples were collected from the retro-orbital sinus into plain containers. Subsequently, the rats were anesthetized with diethyl ether, and their kidneys, hearts and lungs were excised. The organs were promptly rinsed in Tris-HCl buffer with 1.15% KCl kept on ice, and then weighed.

Kidney Homogenate Preparation

A 10% kidney homogenate was prepared by combining 1 g of kidney tissue with 10 ml of chilled 0.1 M phosphate buffer (pH 7.4), and gently homogenizing the mixture on ice. The kidney homogenate was then subjected to centrifugation at 10,000 g for 20 minutes at 4°C. The supernatant was carefully transferred into a pre-chilled Eppendorf tube for subsequent biochemical analyses. Renal protein content was quantified using the Biuret method, as described by Gornall *et al* (1949).

Bioassays

Lipid Peroxidation Assay

The assessment of lipid peroxidation was conducted by measuring malondialdehyde (MDA) concentration, following the protocol outlined by Varshney and Kale (1990).

Estimation of Reduced Glutathione (GSH)

Reduced glutathione (GSH) concentration was assessed using a previously established method as described by Jollow *et al.* (1974).

Antioxidant Enzyme activities- SOD, GST and CAT

The activities of catalase (CAT), and superoxide dismutase (SOD), and glutathione S-transferase (GST) were assessed using methods outlined in publications by Sinha (1972), Misra and Fridovich (1972), and Habig *et al.* (1974) respectively.

Lactate Dehydrogenase (LDH) Activity

LDH activity was determined using a commercial kit from Fortress Chemicals Ltd, England.

Estimation of Kidney Damage Biomarkers – Serum Uric Acid, Urea, Creatinine and Albumin

The concentrations of serum uric acid, urea, creatinine, and albumin were measured using commercial kits (Fortress Diagnostics, England).

Kidney, Heart and Lung Histology

Representative samples of kidney, heart, and lung tissues were fixed in 10% buffered formalin. These tissues were then sectioned thinly using a microtome after embedding in paraffin. Hematoxylin and eosin stains were applied to the sections, and histological

examination was carried out using light microscopy with both low and high magnification lenses. The histological features were captured using a camera.

Statistical Analysis

Data were analyzed and visualized using ggplot2 (Wickham, 2016) in R version 4.1 (R Core Team, 2021) and GraphPad prism version 4. One way ANOVA followed post hoc – Tukey HSD was used in determining and estimating the level/significant difference at 95% confidence interval. Results are expressed as mean ± SEM.

RESULTS AND DISCUSSION

Effect of Bisphenol Analogues Mixture on Organ Weights

Chronic exposure to the mixture, MBPAA for 49 days did not induce significant alterations in the absolute or relative weights of the kidney, heart, or lung when compared with the control group (Figure 1A–C). No dose-dependent trend was observed across the treatment groups.

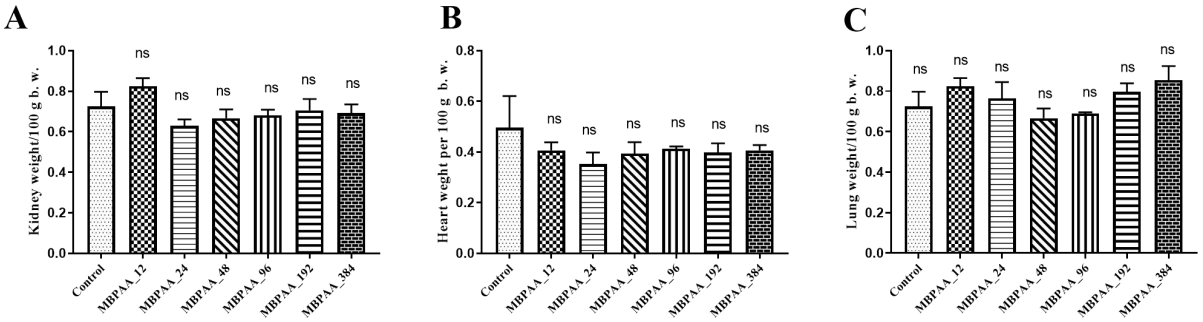

Figure 1: Effect of BPB, BPF and BPS mixture on relative weight of **A:** kidney; **B:** heart; **C:** lung per 100 g body weight. ns depicts non-significant difference at $p < 0.05$

Effect of Bisphenol Mixtures on Lipid peroxidation in Renal and Cardiopulmonary Tisues

Exposure to the bisphenol analogue mixture significantly ($p < 0.05$) elevated renal lipid peroxidation levels, as reflected by malondialdehyde (MDA) concentrations compared to the control (Figure 2A). The Bisphenol-A analogues mixture also elicited significant ($p < 0.05$) MDA concentration increase in the hearts and lungs of the rats in a dose-dependent manner compared to the control rats as shown in Figure 2B and C respectively.

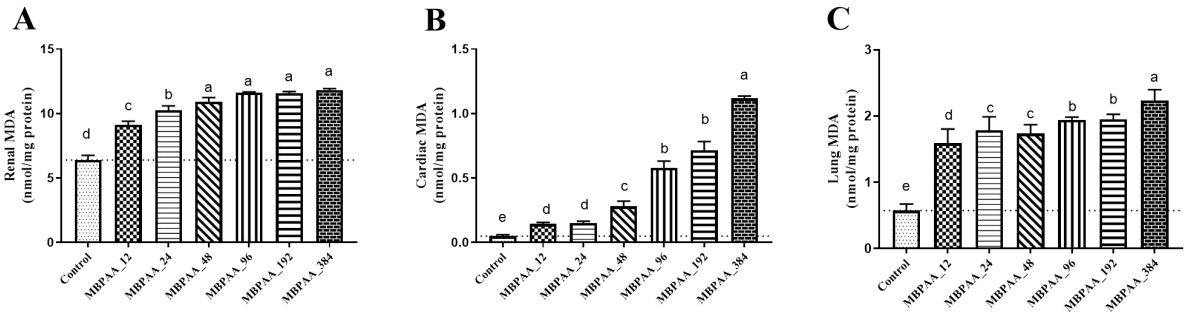

Figure 2: Effect of MBPAA on **A:** renal; **B**: cardiac; and **C:** pulmonary lipid peroxidation assessed as malondialdehyde level the respective organs. Results expressed as mean ± SEM. Difference in alphabets on bar indicates significant difference between groups.

Oxidative Stress and Antioxidant Status in Kidney Tissues

Reduced glutathione (GSH) levels decreased significantly ($p < 0.05$) in all exposed groups (Figure 3A) while glutathione-S-transferase (GST) activity (Figure 3B) were significantly increased ($p < 0.05$) in all dosed groups. The Bisphenol-A analogues mixture also elicited marked alterations in superoxide dismutase (SOD) activities in form of dose-dependent increased inhibition (Figure 3C). The Bisphenol-A analogues mixture significantly decreased Lactate dehydrogenase (LDH) activity (Figure 3D) relative to the control ($p < 0.05$).

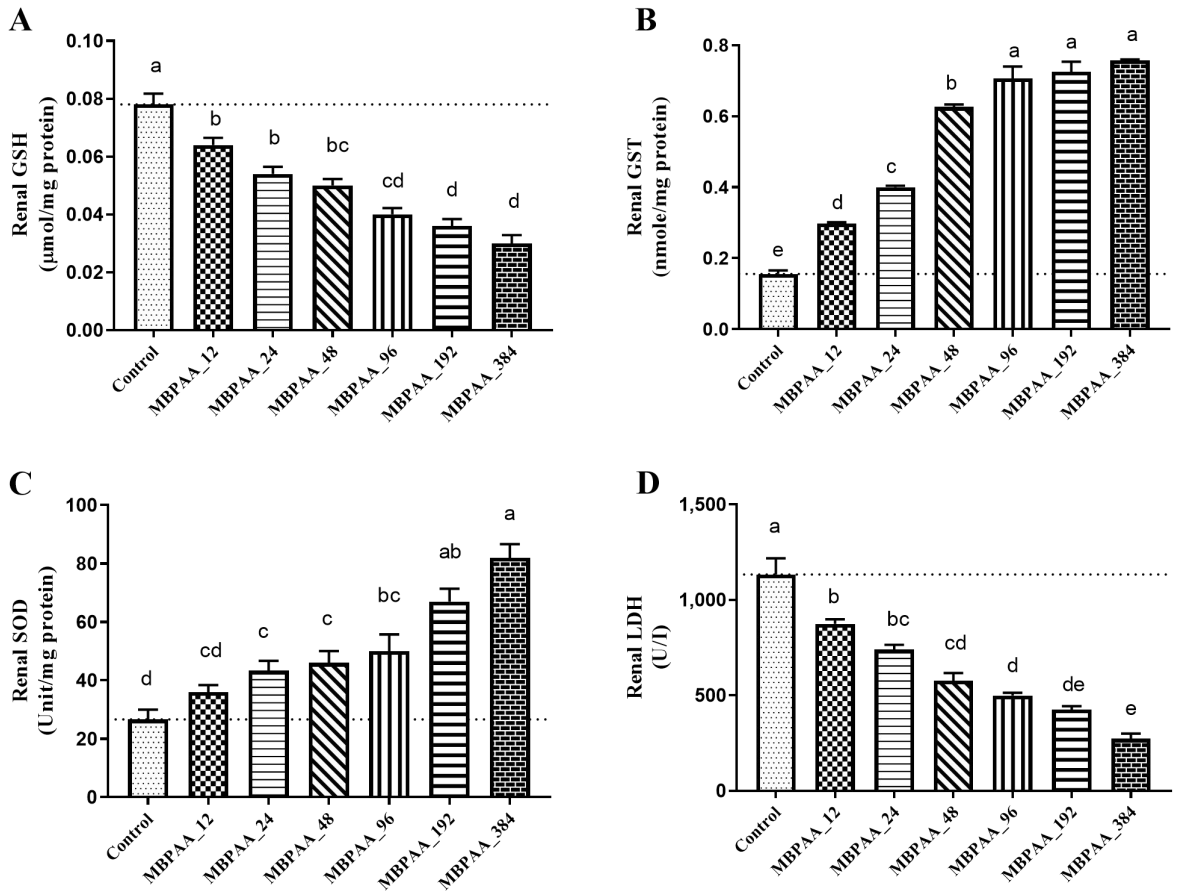

Figure 3: Effect of Bisphenol-A analogues mixture (MBPAA) on antioxidative status in the kidney; **A**: reduced glutathione (GSH)**; B**: GST**; C**: SOD inhibition; and **D:** Lactate dehydrogenase. Results expressed as mean ± SEM. Difference in alphabets on bars indicates significant difference between groups.

Renal Biochemical Markers

Serum renal function parameters exhibited dose-dependent changes following exposure to the bisphenol analogue mixture (Figure 4). Serum uric acid (Figure 4A)

concentrations remained comparable to the control at 12 µg/kg body weight, but were significantly elevated ($p < 0.05$) at higher doses (≥ 24 µg/kg). Conversely, serum creatinine (Figure 4B) and serum urea (Figure 4C) concentrations showed significant decreases ($p < 0.05$) in animals exposed to ≥ 24 µg/kg and ≥ 12 µg/kg, respectively. Serum albumin increased significantly ($p < 0.05$) at all tested doses (Figure 4D).

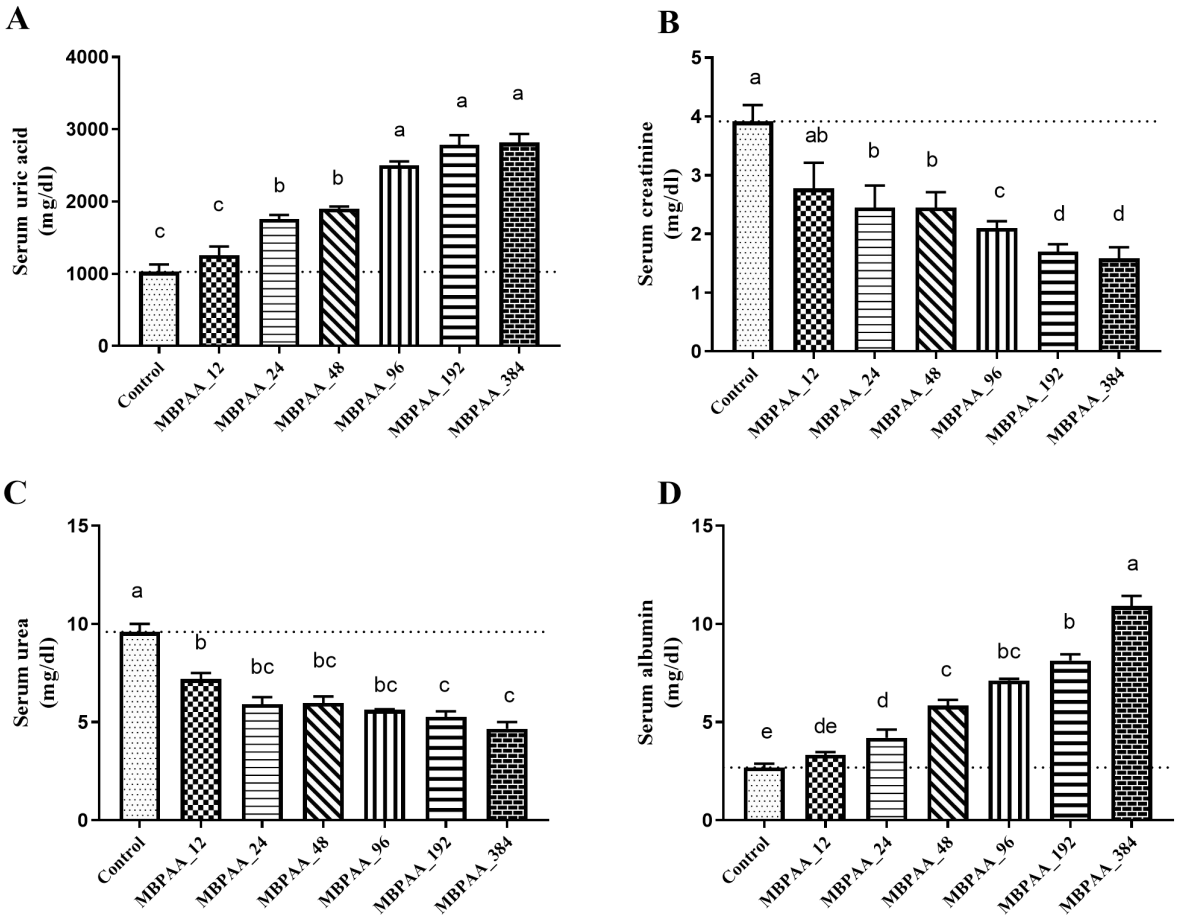

Figure 4: Effects of BPA analogues mixture on some kidney damage biomarkers **A**: serum Uric acid, **B**: serum creatinine, **C**: serum urea, and **D**: serum albumin. Results expressed as mean ± SEM. Difference in alphabets on bars indicates significant difference between groups.

Histopathological Findings

Kidney

Renal architecture appeared normal in control and low-dose groups (12 and 24 µg/kg), with preserved glomeruli, intact mesangial cells, and unobstructed renal tubules (Plate 1). However, mid- and high-dose groups exhibited dose-dependent degenerative changes (Plate 2). These included tubular dilation, interstitial haemorrhage, infiltration by inflammatory cells, widened Bowman's spaces, pyknotic nuclei in renal parenchymal cells, and evidence of glomerulosclerosis and glomerulonephritis.

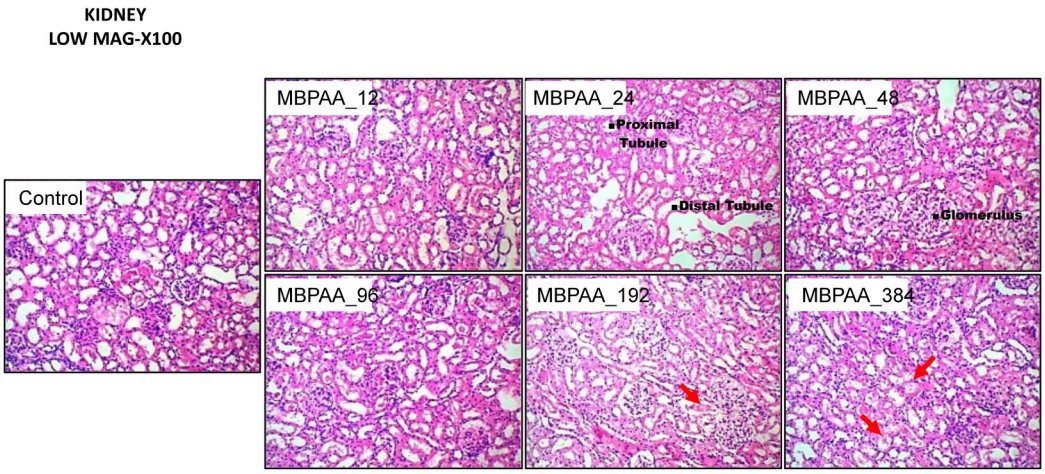

Plate 1: Photomicrographs of kidney sections stained with H&E at low magnification (x 100) showing preserved renal architecture across all groups, with clearly delineated renal cortex, glomeruli, renal tubules, and intact renal parenchyma.

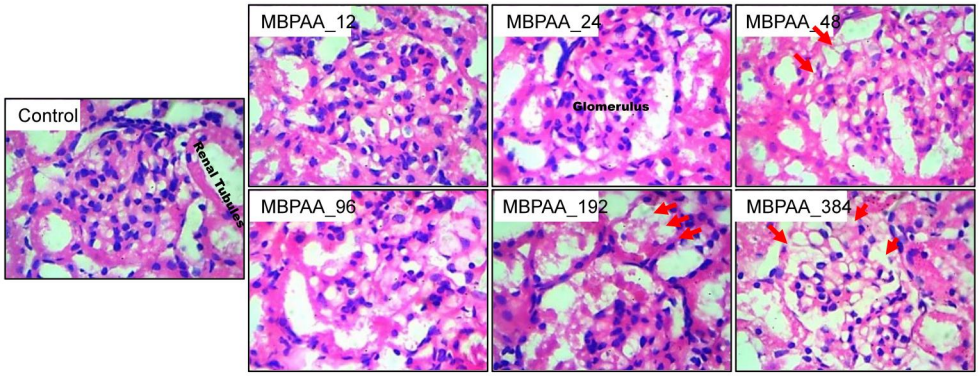

Plate 2: High magnification (x400) H&E photomicrographs of kidney sections revealing cellular details of the renal cortex, including well-defined glomerular tufts, mesangial cells, Bowman's capsule, and intact proximal and distal convoluted tubules across the experimental groups.

Heart

Cardiac tissues from the control group and the low dose group showed normal structural features. The cardiomyocytes were well aligned, intercalated discs were clearly visible, and the myocardial striations appeared normal (Plate 3). In contrast, noticeable degenerative changes were observed in rats exposed to doses equal to or greater than 96 µg/kg. These changes included distortion of myocytes, fenestration, fibrosis, and the presence of clotted blood aggregates (Plate 4). The severity of these lesions became more pronounced in the 192 and 384 µg/kg groups.

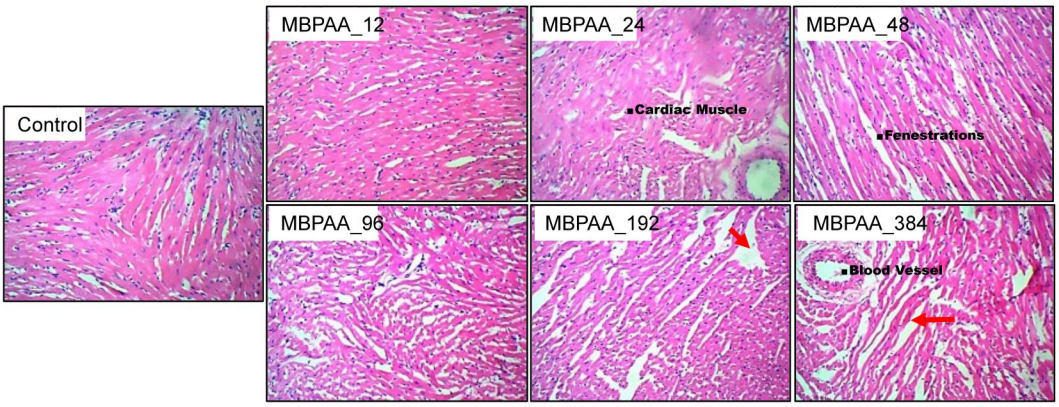

Plate 3: Low-magnification H&Ee photomicrographs of heart sections showing the general myocardial architecture across experimental groups. The epicardium, myocardium, and endocardium are well delineated. Disruption of myocardial organization with areas of degeneration, focal clotted blood, and mild fibrosis is evident in treatment groups 5 – 7, with more pronounced changes in groups 6 and 7 (red arrows). Other groups show preserved myocardial structure.

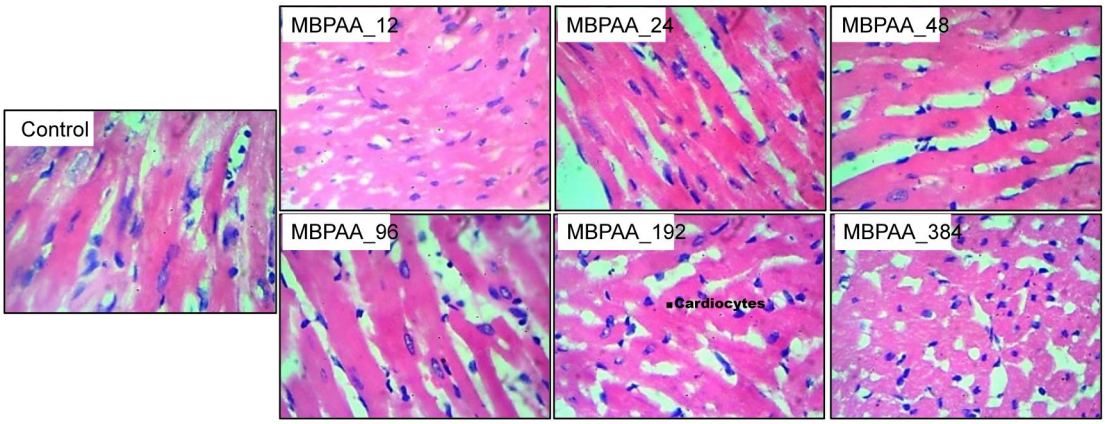

Plate 4: High-magnification (x400) H&E photomicrographs of heart sections highlighting cellular and subcellular alterations. Degenerated and distorted cardiomyocytes, loss of normal striations (fenestration), disrupted intercalated discs, and focal fibrosis are prominent in groups 6 and 7; while groups 1 – 4 exhibit intact cardiomyocyte morphology and preserved striations.

Lung

Pulmonary tissues from the control group showed normal histological features, with well-defined alveoli and intact bronchial structures (Plate 5). However, the treated groups displayed noticeable structural changes that became more pronounced with increasing dose. These changes included loss of normal alveolar parenchyma, cellular disorganization, interstitial haemorrhage, and infiltration of inflammatory cells (Plate 6).

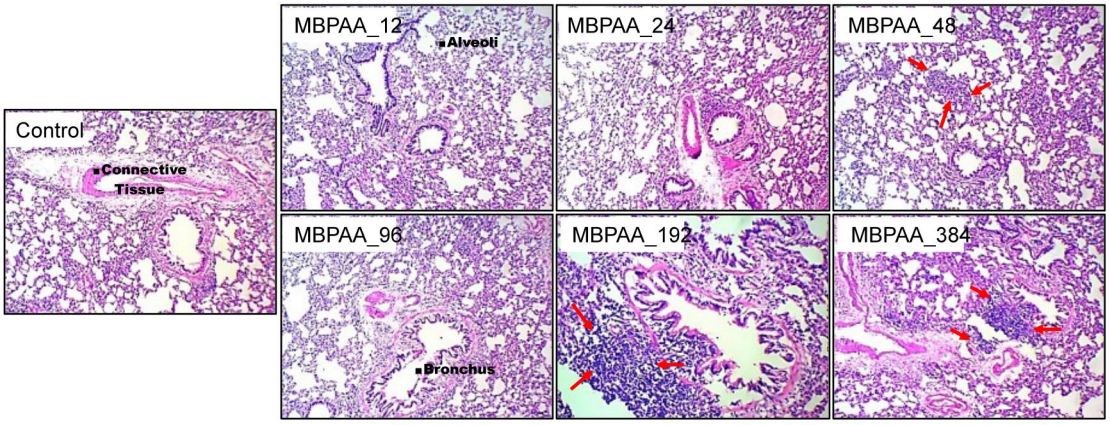

Plate 5: Low-magnification (x40) H&E photomicrographs of lung sections showing the general pulmonary architecture across experimental groups. The alveoli, alveolar ducts, alveolar sacs, bronchi, bronchioles, smooth muscle layer, and connective tissue framework are well delineated. Focal areas of structural alteration are observed in groups 4, 6, and 7 (red arrows).

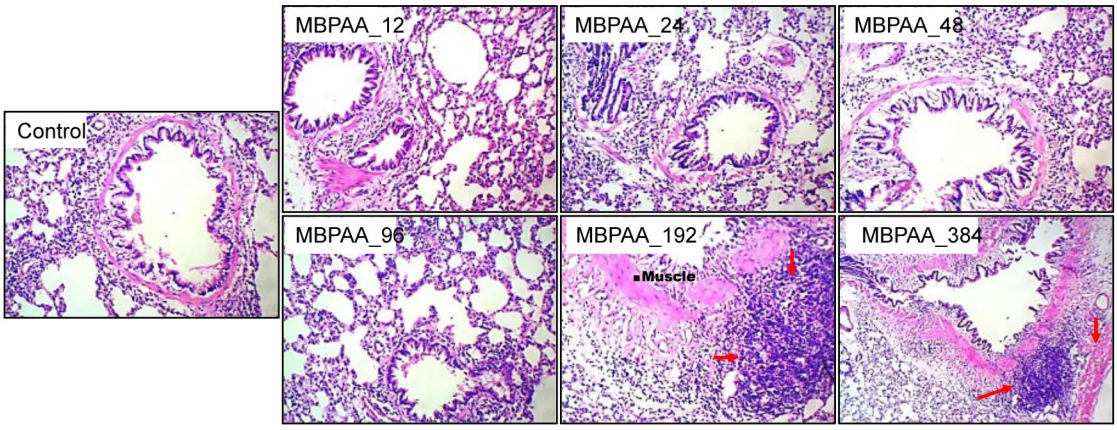

Plate 6: High-magnification (x1000) H&E photomicrographs of lung sections highlighting cellular-level alterations. Groups 6 and 7 shows focal distortion of alveolar architecture with thickened alveolar septa and increased cellular density (red arrows), while lower-dose and control groups exhibit preserved alveolar morphology.

Discussion

This study examined the effects of chronic low dose exposure to a mixture of Bisphenol B (BPB), Bisphenol F (BPF), and Bisphenol S (BPS), referred to as MBPAA, on renal, cardiac, and pulmonary tissues in female rats. The findings show that prolonged exposure to MBPAA promotes oxidative stress, alters renal biochemical parameters, and produces dose dependent histopathological changes in the kidney, heart, and lung. These changes were observed even though there were no significant differences in organ weights among the treatment groups.

The absence of significant differences in both absolute and relative organ weights across the experimental groups suggests that MBPAA toxicity occurred without obvious organ enlargement or reduction. Similar patterns have been reported in toxicological studies where biochemical disturbances and cellular injury appear before detectable changes in organ mass. This finding suggests that organ weight alone may not be a sensitive indicator of early or sub chronic toxicity caused by environmental contaminants.

One of the key findings of this study is the marked increase in lipid peroxidation in renal, cardiac, and pulmonary tissues following exposure to MBPAA. Increased malondialdehyde (MDA) levels indicate enhanced oxidative degradation of membrane lipids and reflect an imbalance between the production of reactive oxygen species and the capacity of antioxidant defense systems. Previous studies have shown that bisphenol analogues can induce oxidative stress through excessive production of reactive oxygen species (Chen *et al.*, 2019). Persistent oxidative stress has been widely associated with the development of multiple organ dysfunction, including renal, cardiac, and pulmonary injury (Akintunde *et al.*, 2021). Related studies have also reported harmful effects of bisphenol analogue mixtures on other organ systems. For example, neuroinflammatory and developmental abnormalities have been observed in rodent models exposed to similar compounds (Okoh *et al.*, 2025). These findings further emphasize the wide toxicological potential of these chemicals. The dose dependent increase in MDA levels that was particularly evident in cardiac and pulmonary tissues suggests that these organs may be especially vulnerable to oxidative injury following exposure to bisphenol mixtures.

The reduction in reduced glutathione (GSH) levels observed in renal tissues provides further evidence of oxidative stress induced by MBPAA. Glutathione plays an important role in maintaining cellular redox balance. A decrease in its concentration weakens the ability of renal cells to neutralize reactive oxygen species. In contrast, the increase in glutathione S transferase (GST) activity observed in this study may represent an adaptive response aimed at enhancing the detoxification of reactive metabolites generated during bisphenol exposure. Changes in superoxide dismutase (SOD) activity, reflected by increased inhibition, also indicate impairment of the enzymatic antioxidant defense system, which may further aggravate oxidative damage. These results agree with earlier reports that described oxidative stress mediated renal toxicity following exposure to BPA and related analogues (Yang *et al.*, 2018; Chen *et al.*, 2019). The significant reduction in lactate dehydrogenase (LDH) activity may suggest disruption of cellular metabolic processes or leakage of intracellular enzymes as a result of membrane damage.

Biochemical indicators of renal function also showed dose dependent alterations following exposure to MBPAA. The marked elevation in serum uric acid at higher doses suggests impaired renal regulation of uric acid and may indicate the presence of renal dysfunction. Elevated uric acid levels have been associated with kidney injury through mechanisms that involve oxidative stress, endothelial dysfunction, and inflammatory responses (Akintunde *et al.*, 2020). In contrast, the reduction in serum creatinine and urea concentrations appears somewhat unexpected. However, similar findings have been reported in experimental toxicology studies. These reductions may reflect changes in protein metabolism, increased tubular excretion, or endocrine related effects on nitrogen balance. Epidemiological studies have also reported associations between

urinary levels of BPA analogues and alterations in renal function indicators, including decreased estimated glomerular filtration rate (Li *et al*., 2020). These observations highlight the complexity involved in interpreting renal biochemical markers after exposure to environmental chemicals and emphasize the need to support biochemical findings with histopathological evidence.

Histological examination of renal tissues provided clear evidence of structural damage that became more pronounced with increasing dose. The lesions observed included tubular dilation, interstitial haemorrhage, inflammatory cell infiltration, widening of Bowman's spaces, pyknotic nuclei, glomerulosclerosis, and glomerulonephritis. These features are commonly associated with progressive nephrotoxicity. Interestingly, biochemical alterations were already present at lower doses before clear histological damage became evident. This suggests that oxidative stress and functional disturbances may occur before visible structural injury develops. Similar renal structural alterations have been reported in experimental studies involving exposure to BPF and BPS in animal models (Yang *et al*., 2018).

In addition to renal effects, MBPAA exposure produced notable damage in both cardiac and pulmonary tissues. Cardiac sections obtained from animals exposed to higher doses showed disruption of cardiomyocyte structure, loss of normal striations, evidence of fibrosis, and the presence of clotted blood aggregates. These features are consistent with myocardial injury that is associated with oxidative stress. Earlier studies have also linked bisphenol exposure to cardiovascular dysfunction through mechanisms that involve oxidative stress and inflammation (Akintunde *et al*., 2020). Examination of pulmonary tissues also revealed dose related changes. These included loss of normal alveolar structure, thickening of alveolar septa, haemorrhage, and infiltration of inflammatory cells. Such changes suggest significant impairment of lung tissue integrity. Previous studies have shown that bisphenol analogues can activate inflammatory pathways and interfere with hormonal signaling processes that are important for maintaining normal pulmonary function (Miao *et al*., 2019; Zhao *et al*., 2021). The pattern of renal and cardiac injury observed in this study, including oxidative damage and structural abnormalities, is also similar to organ toxicities reported with other xenobiotics such as doxorubicin in rodent models (Oseni and Okoh, 2020).

Collectively, the findings of this study demonstrate that chronic exposure to a mixture of BPA analogues induces multisystem toxicity mediated, at least in part, by oxidative stress and inflammatory processes. Importantly, the use of a bisphenol mixture better reflects real-world exposure scenarios, as humans are rarely exposed to single environmental chemicals in isolation. However, the absence of molecular inflammatory markers and functional cardiopulmonary assessments represents a limitation of the present study and warrants further investigation.

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Histological examination of renal tissues provided clear evidence of structural damage that became more pronounced with increasing dose. The lesions observed included tubular dilation, interstitial haemorrhage, inflammatory cell infiltration, widening of Bowman's spaces, pyknotic nuclei, glomerulosclerosis, and glomerulonephritis. These features are commonly associated with progressive nephrotoxicity. Interestingly, biochemical alterations were already present at lower doses before clear histological damage became evident. This suggests that oxidative stress and functional disturbances may occur before visible structural injury develops. Similar renal structural alterations have been reported in experimental studies involving exposure to BPF and BPS in animal models (Yang *et al*., 2018).

In addition to renal effects, MBPAA exposure produced notable damage in both cardiac and pulmonary tissues. Cardiac sections obtained from animals exposed to higher doses showed disruption of cardiomyocyte structure, loss of normal striations, evidence of fibrosis, and the presence of clotted blood aggregates. These features are consistent with myocardial injury that is associated with oxidative stress. Earlier studies have also linked bisphenol exposure to cardiovascular dysfunction through mechanisms that involve oxidative stress and inflammation (Akintunde *et al*., 2020). Examination of pulmonary tissues also revealed dose related changes. These included loss of normal alveolar structure, thickening of alveolar septa, haemorrhage, and infiltration of inflammatory cells. Such changes suggest significant impairment of lung tissue integrity. Previous studies have shown that bisphenol analogues can activate inflammatory pathways and interfere with hormonal signaling processes that are important for maintaining normal pulmonary function (Miao *et al*., 2019; Zhao *et al*., 2021). The pattern of renal and cardiac injury observed in this study, including oxidative damage and structural abnormalities, is also similar to organ toxicities reported with other xenobiotics such as doxorubicin in rodent models (Oseni and Okoh, 2020).

Collectively, the findings of this study demonstrate that chronic exposure to a mixture of BPA analogues induces multisystem toxicity mediated, at least in part, by oxidative stress and inflammatory processes. Importantly, the use of a bisphenol mixture better reflects real-world exposure scenarios, as humans are rarely exposed to single environmental chemicals in isolation. However, the absence of molecular inflammatory markers and functional cardiopulmonary assessments represents a limitation of the present study and warrants further investigation.

CONCLUSION

In conclusion, chronic low-dose exposure to a mixture of Bisphenol-B, Bisphenol-F, and Bisphenol-S induces oxidative stress, disrupts renal biochemical indices, and causes dose-dependent histopathological damage in the kidney, heart, and lung of female rats. These toxic effects occurred without significant changes in organ weights, indicating that biochemical and cellular alterations precede gross anatomical changes. These findings challenge the common assumption that BPA analogues are safer substitutes. Instead, they draw attention to the possible health risks that may arise from prolonged exposure to mixtures of these bisphenol compounds. The present study provides important evidence that BPA substitutes can produce toxic effects across multiple organ systems. It also emphasizes the need for stricter regulatory oversight and further research to better understand the long-term health consequences associated with their use

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest

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