Polyvinyl chloride exposure induces Liver injury: A biochemical and histological evaluation

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ABSTRACT

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Objective: Microplastics are ubiquitous in our environment, with evidence of its presence in various body tissues, however the extent of its toxicity at low dose from chronic administration and bioaccumaulation in humans remains unknown. This study aims at evaluating the toxicological impact of polyvinyl chloride on the liver.
Methods: 50 Male wistar rats were administered 10 ml/kg of deionised water (control), 0.1,0.2 and 0.3mg/kg daily of PVC orally administered, for 42 days using an oro-gastric tube. We examined the liver enzymes, oxidative biomarkers and the histoarchitecture for distortion
Results: showed there was an increase in distortion in liver enzymes, range suggesting hepatic dysfunction, and histoarchitectural distortion with loss of radial symmetry.
Conclusion: this study suggested that PVC has hepatotoxic, with evident histoarchitectural distortion..

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Keywords: PVC, Bilirubin, Bioxidative markers, liver

1. INTRODUCTION

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The global use of synthetic products such as plastics increased dramatically after World War II, particularly during the Second Industrial Revolution (Pilapitiya et al., 2024). Between 1950 and 2019, an estimated 9.2 billion tons of plastic were produced globally, significantly contributing to the growth of the global economy (Bashir et al., 2021; Williams & Rangel-Buitrago, 2022; Li et al., 2023). The demand for this versatile substrate, which is used to manufacture a wide range of products, remains high, with a projected global growth of over 245 million tons (Kumar et al., 2021; Chawla et al., 2022).

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Plastics possess several desirable properties, including light weight, resilience, durability, bio-inertness, resistance to corrosive agents like air and moisture, and cost-effectiveness. They serve as effective substitutes for traditional packaging materials such as glass and paper. The life cycle of plastics encompasses production, usage, and disposal, and at every stage of this cycle, minute particles are released. These particles, known as microplastics and nanoplastics,

are typically less than 5 mm in size, with nanoplastics being smaller than 1 µm (Zhao et al., 2017; Zimmermann et al., 2021).

Microplastics exist in two forms: primary and secondary. Primary microplastics are intentionally manufactured for industrial use, such as resin pellets used in textile fibers, toothpaste, plastic products, and cosmetic microbeads (Begum et al., 2020; Bashir et al., 2021; Lee et al., 2022). Secondary microplastics are generated as byproducts from environmental degradation processes such as hydrolysis, photodegradation, thermo-oxidative degradation, and biodegradation (Sharma & Chatterjee, 2017; Zarus et al., 2021; Ziani et al., 2023; Mathew et al., 2024). These degradative processes, often induced by sunlight and oceanic activity, cause plastic debris to fragment into microparticles that are frequently carried by residential and commercial drainage systems, eventually contaminating wastewater streams (Zimmermann et al., 2021).

Although modern sewage treatment plants can filter out up to 99.9% of these particles, a significant proportion can still bypass these systems and enter freshwater bodies (Imhof et al., 2016; Horton et al., 2017; Li et al., 2020).

According to Andrade (2011), microplastics can also be categorized based on their monomer composition, which includes polyethylene (PE), polypropylene (PP), polystyrene (PS), polyethylene terephthalate (PET), and polyvinyl chloride (PVC). Among these, PVC is the most widely used globally (Amobonye et al., 2023) due to its industrial utility, cost efficiency, thermoplastic properties, and resistance to chemicals such as salts, alkalis, and polar solvents (Lewandowski & Skórczewska, 2022; Zhang et al., 2020; Xiu et al., 2024). PVC is employed in numerous sectors, including the production of fibers, plumbing materials, water pipes, electric cable insulation, car interiors, and laminates (Chen et al., 2024). Its chlorine content also makes it suitable for producing fire-retardant materials (Makris et al., 2020).

Plastic degradation products contaminate air, water, and soil, especially due to widespread usage in food packaging like for dairy products, meat, fish, and bottled beverages allowing transfer of microparticles into the food (Chen et al., 2022). These particles leach into soil, contaminate crops, and enter the food chain, posing health risks by altering nutritional quality and causing toxicity (Zarus et al., 2021; Ziani et al., 2023).

Microplastic by-products have been detected in various environments including soil, surface water, coastal sediments, beach sands, and even deep-sea ecosystems. This is largely due to the mismatch between the volume of plastic waste generated and the efficiency of waste management systems (Rajvanshi et al., 2024). The chemical structure of PVC, especially during its lifecycle (production, usage, degradation), is believed to pose neurological risks, including

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memory impairment and liver dysfunction (Tickner et al., 2001; Isobe et al., 2017; Banerjee et al., 2021). Furthermore, biomagnification through the food chain may contribute to human health hazards (Tran-Lam et al., 2023; Saidon et al., 2024).

One key organ at risk is the liver, the body's main metabolic hub and a crucial part of the reticuloendothelial (monocyte-phagocytic) system. It contains Kupffer cells (sinusoidal endothelial cells) which help remove foreign particles from the bloodstream (Zhao et al., 2023). However, via enterohepatic circulation, reabsorbed toxins from the intestines are transported to the liver through the portal vein, leading to potential hepatocellular accumulation (Wang et al., 2023; Wang et al., 2024). Repeated microplastic exposure through this cycle can lead to oxidative stress, inflammation, and metabolic disruption, causing damage to liver cells and potentially leading to insulin resistance and non-alcoholic fatty liver disease (NAFLD) (Muncke et al., 2020; Chiang et al., 2024).

Liver failure to contain microplastics may allow their translocation into systemic circulation, reaching organs such as the brain and compromising neurological health (Li et al., 2022; Wang et al., 2022; Zhou et al., 2023). The study investigates the effects of sub-chronic exposure to microplastic polyvinyl chloride (PVC) on the liver and brain of male Wistar rats.

2.0 MATERIALS AND METHODOLOGY

2.1 Experimental site

This study was conducted at the Animal House of the Department of Pharmacology, Faculty of Basic Medical Sciences, Delta State University, Abraka.

2.1.1 Experimental Animals

Forty-two (50) adults male Wistar rats weighing between 90–140 g were procured from the Animal House Unit, Faculty of Basic Medical Sciences, Delta State University, Abraka. The animals were acclimatized for two weeks under standard laboratory conditions: a 12-hour light/dark cycle, temperature range of 20–31°C, with unrestricted access to standard rat feed and water. Ethical approval was obtained from the Delta State University Animal Care and Use Research Ethics Committee, in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1985).

2.1.2 Apparatus/Equipment

The following equipment was used: plastic cages (42 × 30 × 27 cm), needles, syringes, oral cannula, wash bottles, hand gloves, Y-maze, open-field apparatus, tissue homogenizer, refrigerated centrifuge, digital weighing balance (JA 2003), VIS spectrophotometer (722N), thermostatic water bath (DK 420), incubator (Techmel and Techmel USA), refrigerator (Haier Thermocool), micropipettes (REMI) 100–1000 µl, mortar and pestle, cotton filters, plastic

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containers, test tubes, racks, floating bath, microtome, tissue processor, cassettes, microscope slides, measuring cylinders, staining racks, cover slips, dissecting kit, and laboratory coats.

2.1.3 Chemicals/Reagents

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Analytical-grade reagents were used, including: Polyvinyl chloride (PVC), 5,5′-dithiobis (2-nitrobenzoic acid) (DTNB), trichloroacetic acid (TCA), thiobarbituric acid (TBA), Tris (hydroxymethyl)aminomethane (Tris buffer), acetic acid, sodium bicarbonate, sodium carbonate, disodium hydrogen phosphate monohydrate, sodium dihydrogen phosphate monohydrate, potassium dichromate, potassium chloride, and sodium hydroxide—all sourced from reputable suppliers such as Aldrich, BDH, and Sigma-Aldrich.

2.2.0 Experimental Design

2.2.1 PVC and Cyclohexanone Stock Preparation

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PVC stock was prepared by dissolving 0.01 g of PVC in 1 ml of cyclohexanone (modified from Finlayson & Cooke, 1951), followed by the addition of 9 ml of absolute ethanol and 190 ml of distilled water to make a final volume of 200 ml (adapted from Herrera et al., 2018).

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2.2.2 In vivo exposure

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The Fifty Adult Male Wistar rats, will be grouped into 4 main groups: A-E containing 10 animals each. Group A will serve as negative B (Positive control), C, D and E will serve as treatment groups respectively. Group A (negative control) will receive food and deionized water only, while B (positive control will receive 0.1mg/kg of cyclohexanone), while group C, D and E will receive 0.1mg/kg, 0.2mg/kg and 0.3mg/kg of PVC and cyclohexane, food and water. Treatment of animals will be administered daily and terminated on Day 42 following which animals will be euthanized after behavioral evaluation.

2.2.3 Dosage selection

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The doses of PVC that will be utilized for this study are 0.1mg/kg, 0.2mg/kg and 0.3mg/kg; and these doses will be selected from a range based on previous conducted studies on microplastics (Deng et al., 2017) and duration of 45days for sub-chronic toxicity will be modelled based on the study by Said, *et al*., (2023).

2.2.4 Protein estimation

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Total protein concentration was estimated using the biuret method. Briefly, 0.1 mL of sample was diluted with 0.9 mL distilled water and 3 mL of biuret reagent was added. The mixture was incubated at room temperature for 30 minutes and absorbance was measured at 540 nm. A bovine serum albumin standard (0.01–0.1 mg/mL) was used for calibration (Mahesha, 2012).

2.2.5 Assessment of total bilirubin

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Total bilirubin level will be determined by colorimetric method using assay kit (Randox, United Kingdom) according to the manufacturer's protocol fol-lowing the method earlier described by Jendrassik and Grof, 1983. About 0.2 mL of sample was added to 3.0 mL of working solution (dilute hydrochloric acid; 0.7 mmol/L, pH 0.7: containing, 2.5 mmol of sodium nitrite, 10 mmol of sulfanilic acid, 1.0 mol of citric acid, 0.5 mol of caffeine, 3.0 mol of urea, and 0.5 g of surfactant) for the test and the sample blank, respectively. Thereafter, the mixture will be incubated at room temperature (25 ^{o}C) for 5 min and read at 578 nm vs the sample blank.

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2.2.6 Assessment of alanine aminotransferase

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Alanine aminotransferase (ALT) activity in serum will be determined spectrophotometrically. Blood will be collected from each mouse through ocular puncture with the aid of heparinized capillary tube into a lithium heparinized sample bottle and centrifuged at 10000 rpm for 15 min using cold centrifuge. The serum will be collected separately for each animal and 0.1 mL of each sample and mixed with 0.5mL solution consisting of sodium phosphate buffer (100 mmol/L, pH 7.4), L-alanine (200 mmol/L), and α-oxoglutarate (2 mmol/L). Thereafter, the mixture will be incubated for exactly 30 min at 37˚C. Then, 0.5 ml of 2, 4 dinitrophenylhydrazine (2 mmol/L) was added to the reaction mixture and allowed to stand for exactly 20 min at 25˚C. Thereafter, 5.0 ml of sodium hydroxide (0.4 mol/L) was added, and the absorbance will be read against the reagent blank after 5 min at 546 nm. The units of ALT were expressed as U/L. (George et al., 2011).

2.2.7 Assessment of aspartate aminotransferase

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Aspartate aminotransferase (AST) activity in serum will be determined spectrophotometrically. Blood was collected from each mouse through ocular puncture with the aid of heparinized capillary tube into a lithium heparinized sample bottle and will be centrifuged at 10000 rpm for 15 min using cold centrifuge. The serum will be collected separately for each animal and 0.1 mL of each sample was mixed with 0.5mL solution consisting of sodium phosphate buffer (100 mmol/L, pH 7.4), L-aspartate (100 mmol/L), and α-oxoglutarate (2 mmol/L). Thereafter, the mixture will be incubated for exactly 30 min at 37˚C. Then, 0.5 ml of 2, 4 dinitrophenylhydrazine (2 mmol/L) will be added to the reaction mixture and allowed to stand for exactly 20 min at 25˚C. Thereafter, 5.0 ml of sodium hydroxide (0.4 mol/L) will be added, and the absorbance will be read against the reagent blank after 5 min at 546 nm. The units of AST will be expressed as U/L (George et al., 2011).

2.2.8 Assessment of alkaline phosphatase

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Alkaline phosphatase (ALP) activity in serum will be determined spectrophotometrically. Blood will be collected from each mouse through ocular puncture with the aid of heparinized capillary

tube into a lithium heparinized sample bottle and centrifuged at 10000 rpm for 15 min using cold centrifuge. The serum will be collected separately for each animal and 0.05 mL of each sample will be mixed with a 0.5mL solution consisting of diethanolamine buffer (1 mol/L, pH 9.8) and Magnesium Chloride (0.5 mmol/L) in a test tube. Then, 3 ml of p-nitrophenyl phosphate (10 mmol/L) will be added to the reaction mixture and allowed to at 25˚C. Thereafter, absorbance will be read at time 0, 1, 2 and 3 min, respectively at 405 nm (Augustine 2019). The units of ALP were expressed as U/L (George et al., 2011).

2.3.0 Determination of glutathione (GSH) concentration

Aliquots of brain supernatant of individual mice in the respective treatment groups will be taken and GSH concentration was determined using the method of Moron *et al.* (1979). Equal volume (0.4 ml) of brain homogenate and 20% TCA (0.4 ml) will be mixed and then centrifuged using a cold centrifuge at 10,000 rpm at 4°C for 20 min. The supernatant (0.25ml) will be added to 2 ml of 0.6mM DTNB and the final volume was made up to 3 ml with phosphate buffer (0.2M, pH 8.0). The absorbance was then read at 412 nm against blank reagent using a spectrophotometer. The concentrations of GSH in the brain tissues were expressed as micromoles per gram tissue (µmol/g tissue). (Igben et al., 2023).

2.3.1 Estimation of malondialdehyde level

The liver level of MDA, a biomarker of lipid peroxidation, was estimated according to the method of Adam-Vizi and Seregi (1982). An aliquot of 0.4 ml of the supernatant was mixed with 1.6 ml of Tris–KCl buffer to which 0.5 ml of 30% TCA was added. Then, 0.5 ml of 0.75% TBA was added and placed in a water bath for 45 min at 80°C. This was then cooled in ice and centrifuged at 3000 rpm for 15 min. The clear supernatant was collected and absorbance measured against a reference blank of distilled water at 532 nm using a spectrophotometer. The MDA concentration was calculated using a molar extinction coefficient of 1.56×10^{5} M^{-1} cm^{-1} and values were expressed as µmoles of MDA per gram tissue (Yilgor & Demir, 2024).

2.3.2 Determination of superoxide dismutase (SOD) activity

The level of SOD activity was determined by the method of Misra and Fridovich, (1972). Briefly, 0.1 ml of brain supernatant was added to 2.6 ml of 0.05 M carbonate buffer (pH 10.2) to equilibrate in the spectrophotometer and the reaction started by the addition of 0.3 ml of freshly prepared 0.3 mM adrenaline to the mixture, which quickly mixed by inversion. The reference cuvette contained 2.6 ml buffer, 0.3 ml of adrenaline and 0.1 ml of distilled water. Then, the increase in absorbance at 480 nm was monitored at 60 s intervals for 3 min. Superoxide dismutase (SOD) activity was expressed as units of adrenaline consumed per minute per mg protein (igben et al., 2025).

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2.3.3 Estimation of catalase activity

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Catalase activity determined according to the method previously described (Sinha, 1971). Aliquots of mouse brain supernatant (0.1 ml) will be added to 2 ml of sodium phosphate buffer (0.05 M; pH 7.4) and 0.9 ml of H_2O_2 (800 µmoles). The reaction mixture was mixed by a gentle swirling motion at room temperature and 1 ml of this mixture was added to 2 ml dichromate/acetic acid reagent. The absorbance was read using a spectrophotometer at a wavelength of 570 nm and change in absorbance at 60 s intervals. The catalase activity was expressed as µmol of H_2O_2 decomposed per minute per mg protein (Eduviere, *et al*., 2015).

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2.4.0 Animal sacrifice

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At the end of the 45-day exposure period, rats were weighed and sacrificed by cervical dislocation to avoid interference from anaesthetics.

2.4.1 Sample collection

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Liver, hippocampus and prefrontal cortex was carefully dissected, weighed, and fixed in 10% formal-saline for histological analysis.

2.4.2 Tissue processing

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Histology tissues were processed manually through standard histological stages: fixation, dehydration, clearing, embedding, sectioning, mounting, staining, and photomicrography.

2.4.3 Photomicrograph

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Prepared slides were viewed under a digital microscope (SCOPETEK DCM 500, 5.0 MP) connected to a computer. Photomicrographs were used to evaluate the histological and cytological effects on the liver, hippocampus and prefrontal cortex.

2.4.4 Statistical analysis

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Statistical analysis was performed using GraphPad Prism® version 7.01 (GraphPad Software, Inc., La Jolla, CA, USA). Data were presented as mean ± standard error of mean (SEM). One- or two-way ANOVA followed by Bonferroni post hoc test was used to determine statistical significance. A p-value of = .05 was considered statistically significant.

3. RESULTS AND DISCUSSION

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3.0 RESULTS

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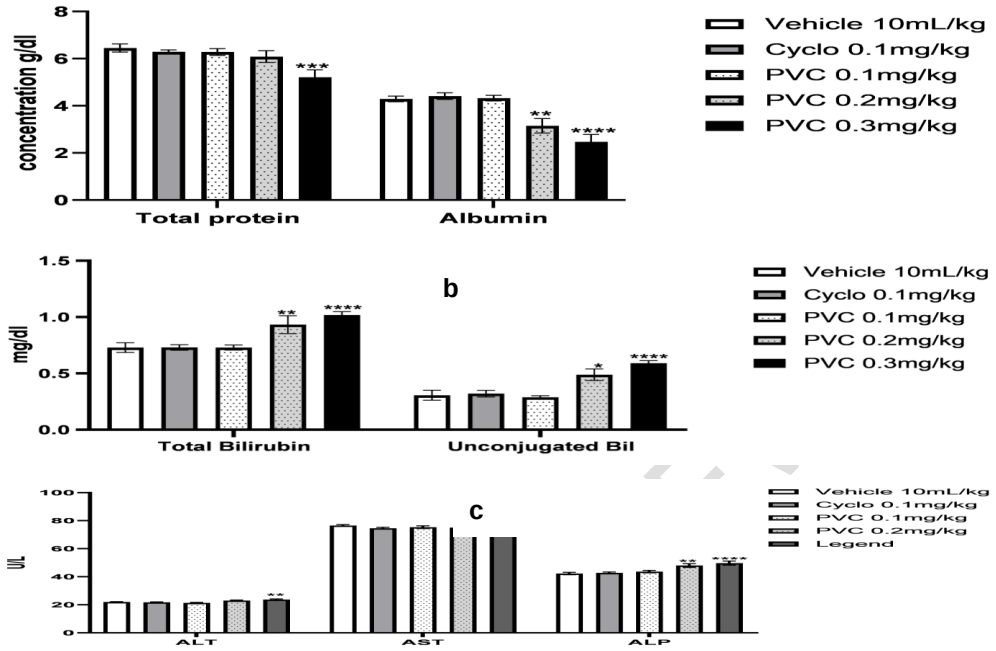
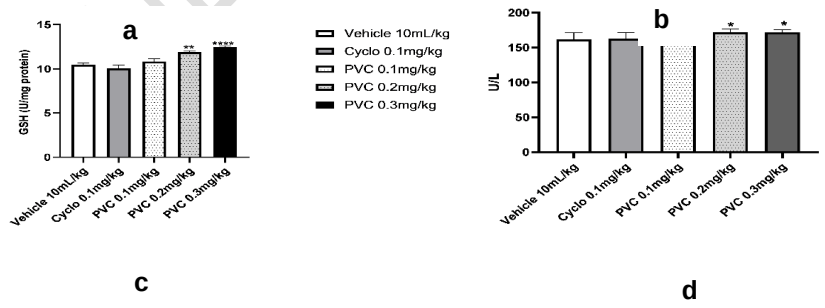


Fig 1- Effect of PVC on serum total protein, albumin levels, total bilirubin, unconjugated bilirubin levels and liver function enzyme levels (ALT, AST, and ALP) in Wister rats

4.5 Effect of PVC on Liver function test and Liver protein level in wistar rats (a) Bilirubin level (b) Liver protein level (c) Liver enzymes of male wistar rats

Bars represent the Mean ± SEM (n=5). *P < 0.05, **P < 0.01, ***P < 0.001 vs control using one-way ANOVA followed by Bonferroni's post hoc test.



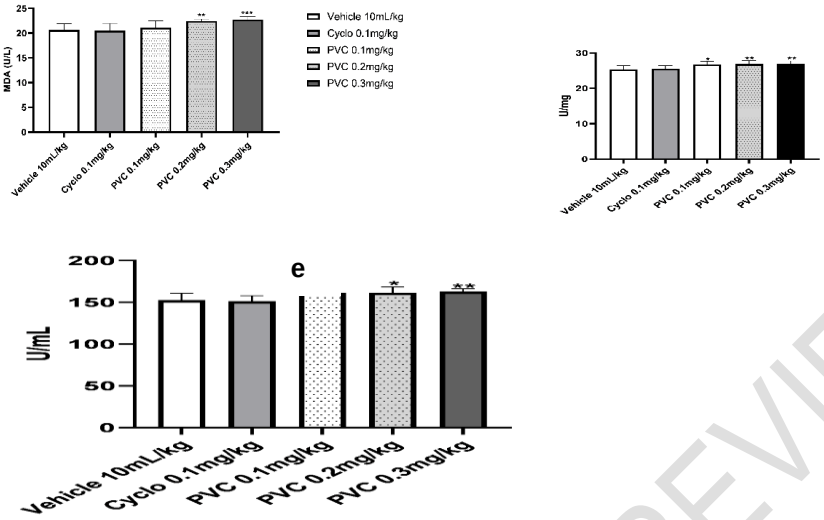
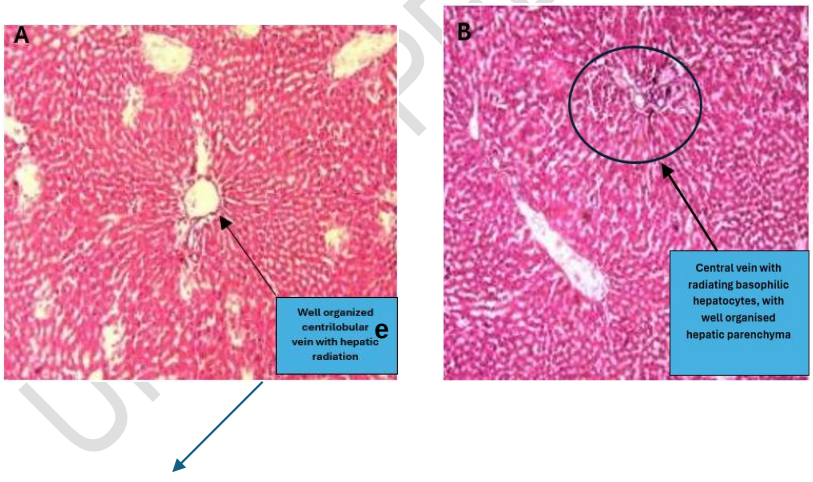


Fig. 2. Effect of PVC on liver oxidative biomarkers a. GSH (b) GPx (c) MDA (d) CAT (e) SOD Liver enzymes of male wistar rats. Bars represent the Mean ± SEM (n=5). *P < .05, **P < 0.05, ***P < .001 vs control using one-way ANOVA followed by Bonferroni's post hoc test. **GSH-Glutathione, GPx-Glutathione Peroxidase, MDA-Malondialdehyde, CAT-Catalase, SOD-Super oxide Dismutase**



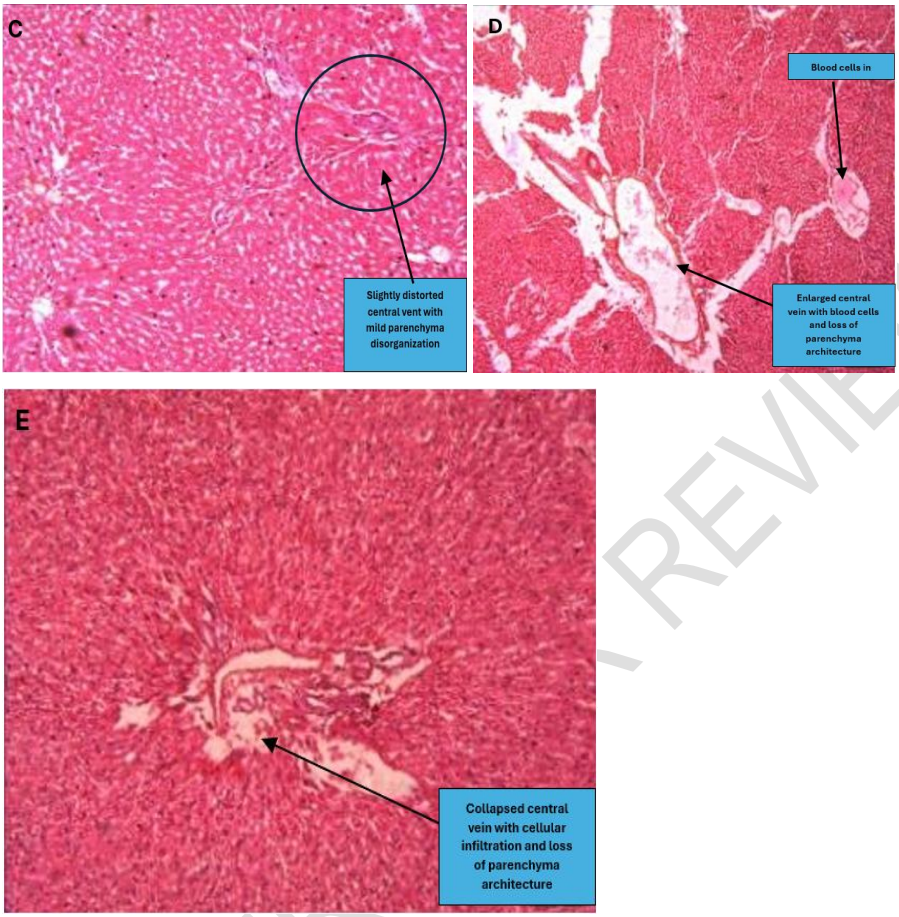


Fig 3- Photomicrographs of hematoxylin and eosin (H&E) stained liver sections, **(A)** there is preservation of the hepatic lobular architecture with clear central veins and radiating hepatic cords, sinusoidal spaces are intact, and hepatocytes display uniform morphology with no necrotic or signs of inflammation **(organized hepatic radial symmetry, with conserved central venule) (B)** the liver histoarchitecture appears normal, with well-organized hepatic cords radiating from the central vein. There is visible central nucleus in the hepatocytes with uniform well and distributed sinusoidal spaces. no visible signs of necrotic changes **(reactive hepatocytes, with increase basophilic nucleus, possible cell regeneration from repeated insults)** ((**C**) there is mild disorganization of hepatic cords, and slight dilation of sinusoids, hepatocellular vacuolation and cytoplasmic granularity, as well as early ballooning degeneration in scattered hepatocytes, with minimal portal inflammation **(circle encircling disruption in radial symmetry of the hepatocytes) (D)** there is disorganization of lobular histoarchitecture with disruption of the radiating hepatic cords, there is observed inflammatory cell infiltration in periportal areas, along with early signs of vascular congestion. displays more pronounced changes, including increased cytoplasmic

vacuolation and hepatocyte swelling, sinusoidal dilation, and mild inflammatory cell infiltration. Notably, focal necrosis is observed in some lobules **(blue arrow pointing at disorganization of the parenchyma architecture) (E)** there is significant hepatocellular degeneration, necrosis, and loss of lobular architecture. prominent vascular congestion, central vein dilation, and haemorrhagic foci are evident. Moderate portal inflammation accompanied by marked disruption of normal lobular architecture, widespread ballooning and necrotic hepatocytes, dense inflammatory cell infiltration, and sinusoidal congestion **(black circle shows loss of radial symmetry, and coalescent of the central venules)**. Furthermore, there is evidence of beginning fibrosis, areas with cell dropout, and possible regeneration nodules.
(A: Control, B: Cyclohexanone 2ml/kg, C: 0.1 PVC mg/kg, D: 0.2 PVC mg/kg, E. 0.3 PVC mg/kg)

4.0 DISCUSSION

Microplastics and nanoplastics (MPs/NPs) induce the production of reactive oxygen species (ROS) both extracellularly and intracellularly following internalization (Wahlang, et al., 2020). Within cells, they disrupt mitochondrial membrane integrity and potential, leading to redox imbalance (Das, A., 2023; Lee, et al., 2024). This oxidative stress triggers DNA damage, protein oxidation/misfolding, and lipid peroxidation, ultimately destabilizing cellular membranes (Zou, et al., 2025), these processes critically affect liver function (Chen, et al., 2022). MPs/NPs have been implicated in metabolic dysfunction-associated steatotic liver disease (Lolescu, et al., 2024; Romeo, et al., 2025). Although MASLD pathogenesis typically involves factors such as diet, obesity, and insulin resistance, emerging evidence identifies MPs/NPs as environmental toxins that exacerbate disease progression via ROS-mediated mechanisms (Chen, et al., 2024)

Hepatocellular injury is specifically marked by elevated alanine aminotransferase (ALP) levels reliable biomarker of liver damage. In contrast, aspartate aminotransferase (AST) and alkaline phosphatase (ALT), though commonly used, are less specific due to their expression in other organs, including the kidneys, pancreas, bones, and intestines. To improve specificity in our study, liver homogenate was used for enzyme analysis. Although ALP elevation may indicate hepatobiliary involvement, it is not a definitive marker of hepatocellular damage.

Histological sections of liver tissue revealed parenchymal distortion characterized by vascular stasis, nuclear enlargement, and disruption of hepatocyte radial symmetry.

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Hepatocytes appeared irregular in shape, and the central vein was congested, dilated, and infiltrated with inflammatory cells and erythrocytes. These changes occurred in a dose-dependent manner in groups treated with 0.2 mg/kg and 0.3 mg/kg PVC, as compared to controls findings consistent with previous studies.

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This architectural distortion was accompanied by impairment of physiological, synthetic, biochemical, metabolic, and enzymatic functions. Liver enzyme levels (AST, ALT, ALP) were significantly elevated in the 0.2 mg/kg group and even more so in the 0.3 mg/kg group, reaffirming findings from previous studies that indicated similar enzymatic alterations.

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Alanine transaminase (ALT) is a liver-specific biomarker that more accurately indicates hepatocellular damage compared to aspartate transaminase (AST) or alkaline phosphatase (ALP) (Kalas et al., 2021). Liver synthetic function can also be assessed through parameters such as protein synthesis (Jagdish et al., 2021; Sheinenzon et al., 2021). In this study, exposure to the toxin resulted in decreased total protein and albumin levels in the 0.2 mg/kg group, with more pronounced reductions in the 0.3 mg/kg group. These findings support the role of serum albumin as a predictor of long-term mortality in patients with acute pulmonary embolism and chronic liver disease, likely due to liver cell death and impaired albumin synthesis (Carvalho & Machado, 2018). The decrease in protein and albumin levels may disrupt homeostasis, affecting various essential functions, including hormone and mineral transport, blood clotting, and vascular oncotic pressure (Chen, et al., 2021; Cunningham, and Porat-Shliom, 2021).

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Bilirubin, a product of hemoglobin catabolism, is normally conjugated in the liver to facilitate excretion (Vitek et al., 2023). Elevated bilirubin levels can indicate liver damage (Guerra Ruiz et al., 2021; Vítek & Tiribelli, 2021). In our study, treated rats showed increased total and indirect (unconjugated) bilirubin levels, suggesting impaired liver function in conjugating bilirubin. Elevated unconjugated bilirubin can lead to increased free bilirubin (Bf) levels, which plays a key role in neurotoxicity and conditions such as kernicterus, where bilirubin deposits in the brain (Brites and Silva, 2021), this may be a synergistic contribution to the observed impaired memory function in the neurobehavioral paradigm.

Comment [E184]: Indent

According to Hy's law, concurrent elevations in AST/ALT and bilirubin suggest drug-induced hepatotoxicity (Re et al., 2015; Barritt, et al., 2022), which supports our postulation, that PVC induces liver injury direct toxicity, oxidative stress, and hypoxia from vascular stasis or thrombosis.

Comment [E185]: Italic

Comment [E186]: and

Comment [E187]: Correct

Comment [E188]: Delete

Malondialdehyde (MDA) is a compound that is derived from the peroxidation of polyunsaturated fatty acids. It is a has been used as a biomarker to measure oxidative stress in various biological samples in patients who are affected by a wide range of diseases (Cordiano, et al., 2023). This study reported an increase in MDA levels in treated groups, supporting our hypothesis that PVC induces hepatotoxicity through ROS generation.

Comment [E189]: Correct

Comment [E190]: OS

Oxidative stress occurs when there's an imbalance between oxidants and antioxidants, leading to increased levels of free radicals like reactive oxygen species (ROS) and reactive nitrogen species (RNS). Elevated oxidant levels can damage biomolecules, including lipids, proteins, and DNA. The immune system and antioxidant defense mechanisms work to mitigate this damage. These mechanisms include enzymatic antioxidants like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants like glutathione (GSH) (Carmo et al., 2022; Tekin & Seven, 2022; Zarezadeh et al., 2022). Initially, these enzymes are upregulated, but chronic exposure leads to their depletion. In our study, levels of GSH, GPx, SOD, and CAT were significantly decreased, especially in the 0.3 mg/kg group, suggesting compromised antioxidant defences and increased vulnerability to oxidative damage.

Comment [E191]: Delete

Comment [E192]: Italic

Comment [E193]: Also

4. CONCLUSION

Comment [E194]: ????

This study investigated the histopathological effects of PVC exposure on the liver of Wistar rats. Results revealed a dose-dependent pattern of tissue injury at PVC doses of 0.1–0.3 mg/kg. The liver showed progressive damage ranging from ballooning degeneration to necrosis and inflammation corroborating oxidative stress as a central mechanism. PVC and its metabolites, particularly vinyl chloride monomer (VCM), appear to induce damage via oxidative stress, mitochondrial dysfunction, and inflammation. The systemic bioactivity of PVC, as reflected in liver, highlights its

potential health risks and reinforces the need for stricter regulatory control of plastic exposure, particularly in occupational and industrial environments

CONSENT (WHERE EVER APPLICABLE)
Not applicable

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