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N-acetyl cysteine and zinc sulphate ameliorated crude oil-induced hepatotoxicity in Wistar rats

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Abstract

Even while crude oil offers many advantages, its toxic chemical composition has been shown to negatively interfere with the body's ability to maintain homeostasis. This investigation examined the effects of crude oil on the liver function of Wistar rats as well as the protective effects of N-acetyl cysteine (NAC) and zinc sulphate ($ZnSO_4$). The experimental group and control group consisted of 42 Wistar rats, which were divided into groups of six each. The experimental group had six groups, while the control group only consumed food and water. In the experimental group, three groups received a diet contaminated with crude oil for two, three, and four weeks, respectively. In addition, another three groups received NAC (100 mg/kg), $ZnSO_4$ (0.5 mg/kg), and a combination of NAC and $ZnSo_4$ for three weeks each. Rats' body weights were recorded both before and after the administration of crude oil. Using commercial kits and histological examinations carried out using conventional histopathological methods, the liver's toxicity was assessed. As a result of eating food contaminated with crude oil, the results showed a significant drop ($p < 0.05$) in body weight. Additionally, there was liver cell injury. The levels of alkaline phosphatase and alanine transaminase considerably increased. Histological analysis revealed abnormal changes to the liver's typical structure. NAC and $ZnSO_4$ therapy reduced the elevated Alanine transaminase and alkaline phosphatase levels. The study's findings highlight the negative impacts of crude oil and the therapeutic effects of NAC and $ZnSO_4$..

Keywords: NAC; ZnSo4; Bonny light crude oil; Liver damage; Liver enzymes; Histology

1. Introduction

One of the most valuable mineral resources in the world for many nations is crude oil. Crude oil has been continually explored in Nigeria for the past thirty years and is the country's main source of income (Wegwu & Omeodu, 2010). Oil spills, whether they are caused by human activity or natural disasters, contaminate the environment, especially drinking water supplies like water bodies, putting locals at risk of ingesting crude oil (Naiho et al., 2014 and 2018).

According to Hawkey (1981), crude oil is a complex mixture of many different chemical substances, including thousands of straight and branched chain, cyclic and aromatic hydrocarbon, sulfur and nitrogenous compounds, and very few metals. Depending on where it is found, crude oil can be dark brown or blackish in color and is quite viscous (Ma et al., 2021). Eating marine organisms (seafoods) from water that has been contaminated with crude oil is one way that crude oil is indirectly ingested. The complex chemicals included in crude oil pose a serious threat to humans and aquatic life, harming tissues and organs and impairing growth and performance (George & Sese, 2012). According to Onyije et al. (2021), the pollution of food and water due to crude oil exploration is linked to a number of diseases that are fatal, and it may also be a factor in the increased incidence of cancer worldwide.

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Ogara et al. (2016) found that groups of animals given meals polluted with crude oil experienced a concentration-related significant loss in mass weight. Depending on the duration of exposure and the quantity of crude oil in the meal, the mass weights of the rats decreased during the three-week study period. In a prior study on crude oil and its consequences, Ikanone et al. (2017) found that sub-acute administration of crude oil resulted in liver function impairment, which may cause liver disease. Due to the frequent and frequent spills that have occurred in our coastal waterways, Nigeria is seeing an increase in the exposure of crude oil to aquatic ecosystems, and this contamination is transferred to creatures that feed from those water bodies (Ordinioha & Brisibe, 2013). The goal of this study is to confirm that crude oil has a hepatotoxic effect and to ascertain whether N-Acetyl Cysteine and zinc sulphate, which have antioxidant and cofactor activities, can reduce the hepatotoxic effects of crude oil exposure.

2. Material and methods

2.1. Experimental Animals

Forty-two albino rats of Wistar strains weighing 160-220 g were purchased from the animal house of the faculty of basic medical sciences, Ambrose Ali University, Ekpoma. The rats were housed in the animal house of the faculty of basic Medical science, at Delta State University, Abraka. Rats were fed with commercial growers' mash for two weeks for effective acclimatization before the commencement of the experiment. They were separated into three major groups, the inducing group, the treatment group, and the control group. The inducing group and the curative group were then divided into three subgroups each. Crude oil was obtained from the Nigeria National Petroleum Corporation (NNPC), Warri, Nigeria. N acetyl cysteine and Zinc sulphate were obtained from safari pharmacy in Warri.

2.2. Experimental design

- Control Group (n=6): The Control Group was restricted to normal rat feed and water.
- Experimental Group (n=36): this group was divided into two (Crude oil exposed only (COE) and treatment groups (CO+).

Crude oil exposed Group (COE) (n=18): This group was served Crude oil treated rat feeds to induce the effects of crude oil exposure. However, to understand the relationship between degree of effect and duration of effects, this group was divided into three (3) sub-groups:

- CO 4 weeks (n=6): was given Crude oil contaminated rat feeds (0.1 ml/g of feed) for four (4) weeks
- CO 3 weeks (n=6): they received Crude oil contaminated rat feeds (0.1 ml/g of feed) for three (3) weeks
- CO 2 weeks (n=6): this set was given Crude oil contaminated rat feeds (0.1ml/g of feed) for two (2) weeks. All rats received an average of 10g of feed per day.

Treatment Group (CO+) (n=18): This group was given in addition to Crude Oil, NAC, and Zinc sulphate. This group was divided into three (3) sub-groups:

- CO+NAC (n=6) was served NAC at 100 mg/Kg for Three (3) weeks during feeding with crude oil-contaminated feed.
- CO+$ZnSO_4$ (n=6) was served $ZnSO_4$ at 0.5 mg/Kg for three (3) weeks during feeding with crude oil-contaminated feed
- CO+NAC/$ZnSO_4$ (n=6) was served a combination of NAC (100 mg/Kg) and $ZnSO_4$ (0.5 mg/Kg) during three weeks of feeding with Crude Oil contaminated feed.

The treatments of experimental rats were in accordance with the National Institute of Health (NIH) guidelines for the care and use of laboratory animals. Experimental rats received an average daily ration of 10 g of crude oil contaminated feed

2.3. Experimental Procedure

On the first day that crude oil administration was to start and at the end of the six-week period, the animals' body weights were recorded. Samples were obtained from the occula median Cantus vein of the rats using capillary tubes and put into sterile sample containers that were properly labeled. An enzyme assay was conducted using a blood sample. Animals were slaughtered, and the experimental animals' livers were taken. The tissues were promptly stored in 10% formalin in individual, universal bottles with the appropriate labels. For histological investigation, the tissues were removed.

2.4. Biochemical Studies

The end point colorimetric diagnostic kit (Randox Laboratories Limited, England) was used to estimate the activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) using the Reitman and Frankel (1957) method. Using Sigma diagnostic kits (Sigma Diagnostic, USA), alkaline phosphatase (ALP) activity was assessed using Englehardt's method from 1970.

2.5. Histological Study

Liver tissues were kept in 10% buffered formalin for microscopic examination, dried in ethanol alcohols of increasing strength, washed in xylene, cast, embedded, microtomed at 5 m thickness, and stained with hematoxylin-eosin (Oyovwi et al., 2023).

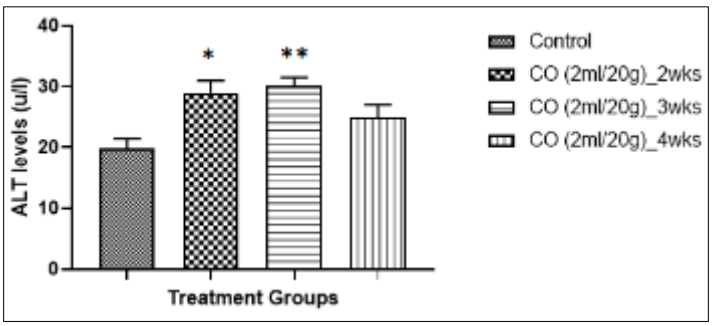
2.6. Statistical Analysis

The GraphPad PRISM 8 program was used to analyze differences between groups using a one-way ANOVA and a post hoc Bonferronis t-test. Statistics were presented as mean ± SEM and statistical significance was set at ≤ P 0.05.

3. Results

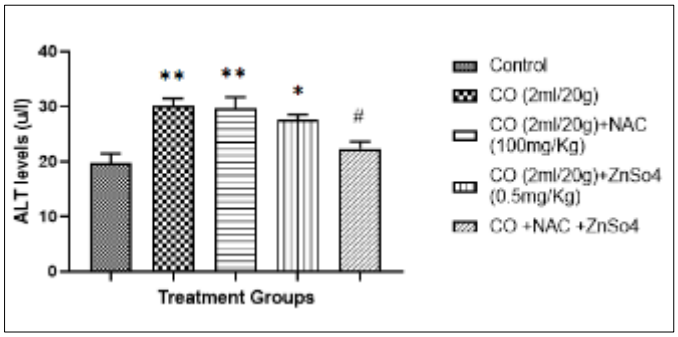
3.1. Effects of Crude Oil Administration on ALT, AST, and ALP Levels

Crude oil administration for two and three weeks was found to significantly increase ALT levels when compared to the control ($p \leq 0.05$; $p \leq 0.01$) (Figure 1). However, the co-administration group treated with crude oil+NAC+ $ZnSO_4$ was found to significantly decrease ALT levels when compared to the crude oil-treated group ($p<0.05$) (Figure 2). There were no significant changes in AST levels in both the inducing groups and treatment groups when compared to the control (Figure 3; Fig 4). Crude oil administration for two and three weeks significantly increased ALP levels when compared to the control ($p \leq 0.001$; $p \leq 0.001$) (Figure 5). However, selective co-treatment with NAC and $ZnSO_4$ respectively was shown to significantly reduce ALP levels when compared to the crude oil-treated group ($p \leq 0.05$; $p \leq 0.001$). (Figure 6).



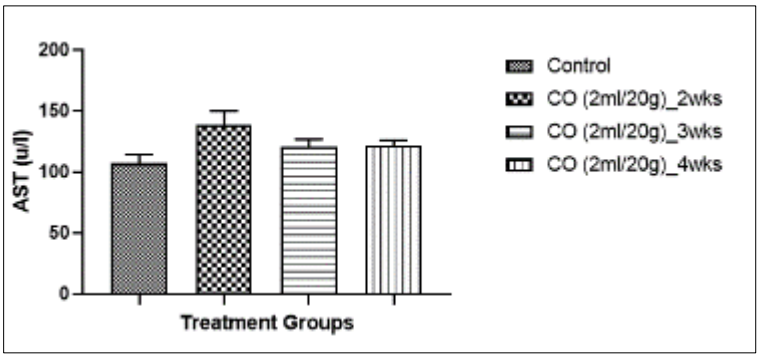
Data are expressed as Mean ± S.E.M (n = 5) (One-way ANOVA followed by Bonferroni *post hoc* test). *p<0.05, **p<0.01 when compared with control.

Figure 1 Duration dependent effects of Crude Oil administration on ALT



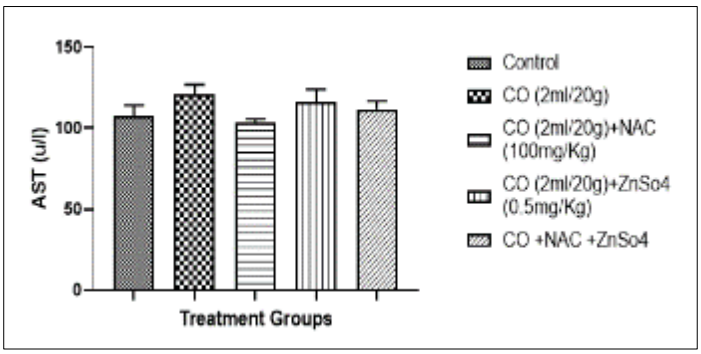
Result is presented as Mean ± S.E.M. *p<0.05, **p<0.01 when compared with control; #p<0.05 when compared with crude oil

Figure 2 Effects of Crude Oil, NAC, and $ZnSO_4$ on ALT



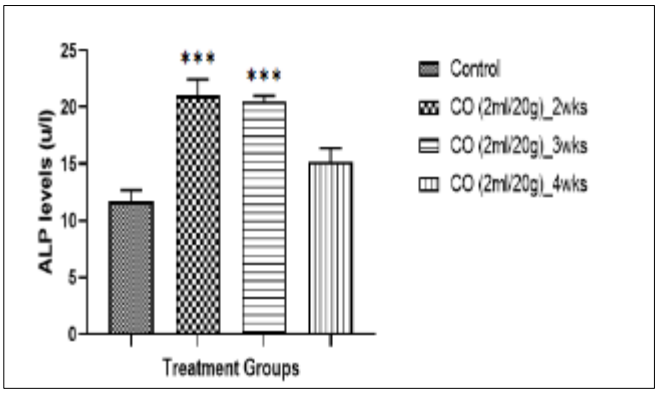
The result is presented as Mean ± S.E.M.

Figure 3 Duration-dependent effects of Crude Oil administration on AST



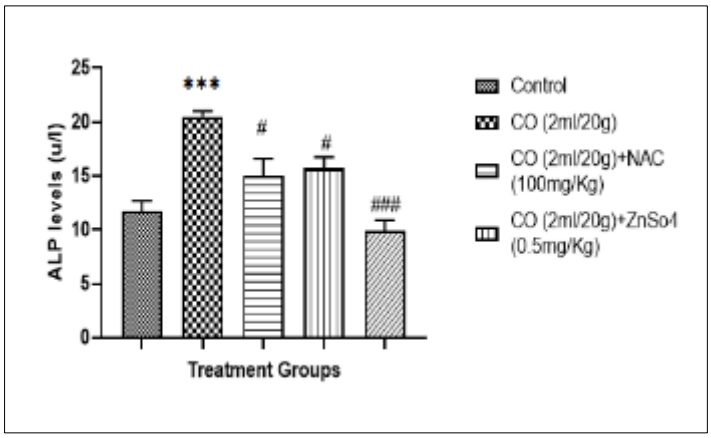
Result is presented as Mean ± S.E.M.

Figure 4 Effects of Crude Oil, NAC, and $ZnSO_4$ on AST



Data are expressed as Mean ± S.E.M (n = 5) (One-way ANOVA followed by Bonferroni *post hoc* test). ***p<0.01 when compared with control

Figure 5 Duration-dependent effects of Crude Oil administration on ALP



Data are expressed as Mean ± S.E.M (n = 5) (One-way ANOVA followed by Bonferroni *post hoc* test). ***p<0.01 when compared with control; #p<0.05, ###p<0.001 when compared with crude oil

Figure 6 Effects of Crude Oil, NAC, and $ZnSO_4$ on ALP

3.2. Duration Dependent effect of Crude Oil on the histology of the Liver

Photomicrograph of the control (a) liver sections show a normal portal vein (Figure 7). Bile ducts and hepatocytes. However, intake of crude oil contaminated food (b-d) at different duration of exposure results to pyknotic and necrotic hepatocytes, sinusoidal congestion, enlargement and proliferation of bile ducts, rupturing of the central vein and clogging of the portal veins (Figure 7; Figure 8). The degree of damage is directly proportional to the duration of exposure.

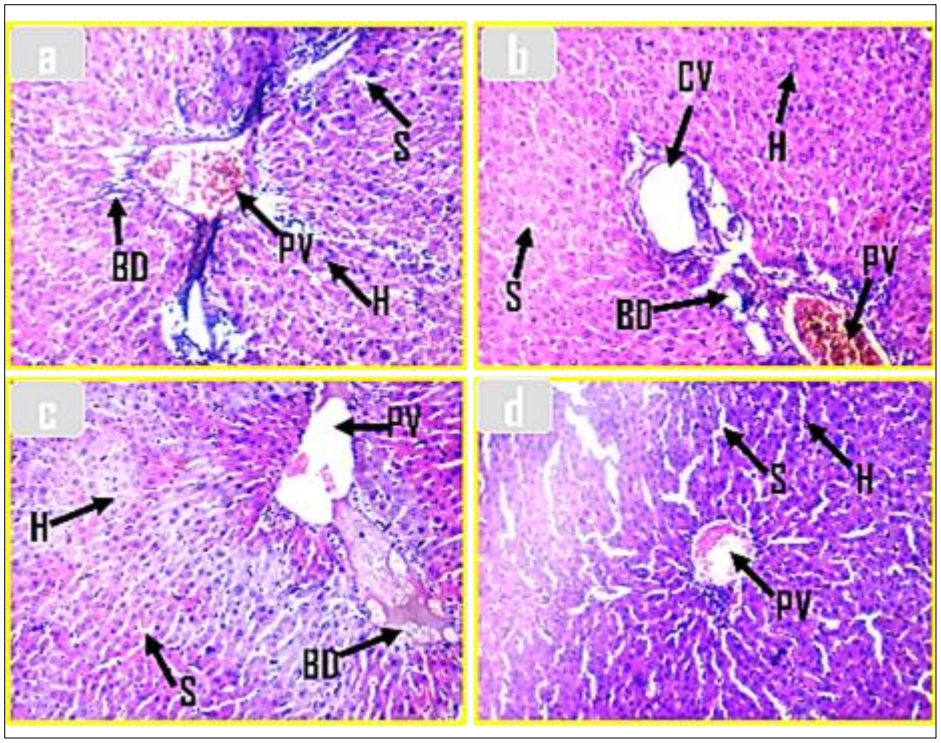


Figure 7 Histology of the liver across experimental groups at x100 resolution investigated with haematoxylin and eosin stain. The cellular assortment reveals the hepatocytes (H), portal vein (PV), central vein (CV), sinusoids (S) and the bile ducts (BD). Group a = Control, Group b = Crude oil (2 ml/20 g) for 4wks, Group c = Crude oil (2 ml/20 g) for 3wks, Group d = Crude oil (2 ml/20 g) for 2wks

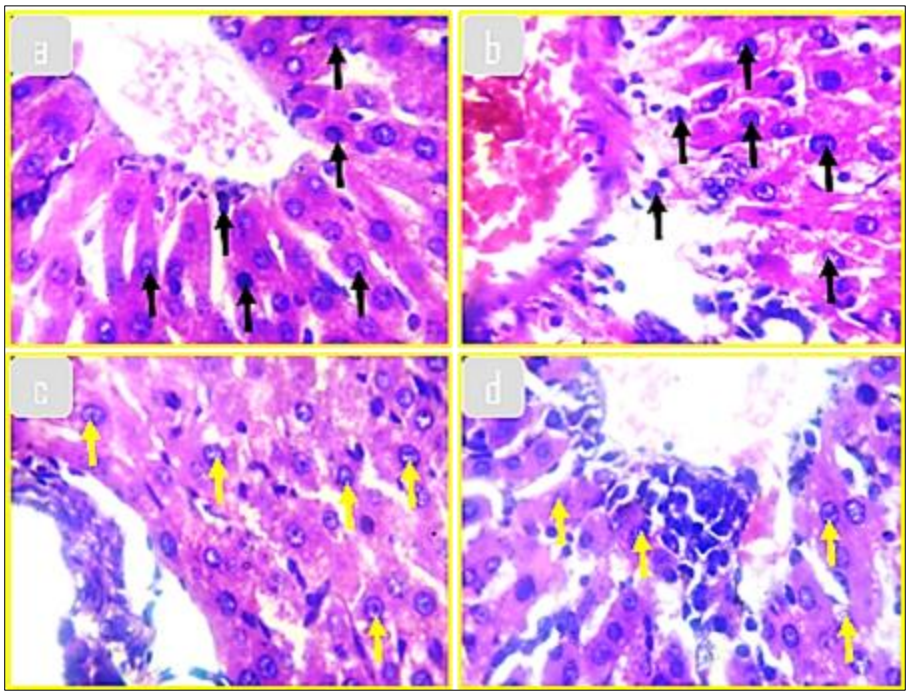


Figure 8 Histology of the liver across experimental groups at x400 resolution investigated with haematoxylin and eosin stain. The cellular assortment reveals the hepatocytes (H), portal vein (PV), central vein (CV), sinusoids (S) and the bile ducts (BD). Group a = Control, Group b = Crude oil (2ml/20g) for 4wks, Group c = Crude oil (2ml/20g) for 3wks, Group d = Crude oil (2ml/20g) for 2wks

3.3. Effects of N-Acetyl Cysteine (Nac) and Zinc Sulphate ($ZnSO_4$) Treatment in Crude Oil-Induced Hepatotoxicity

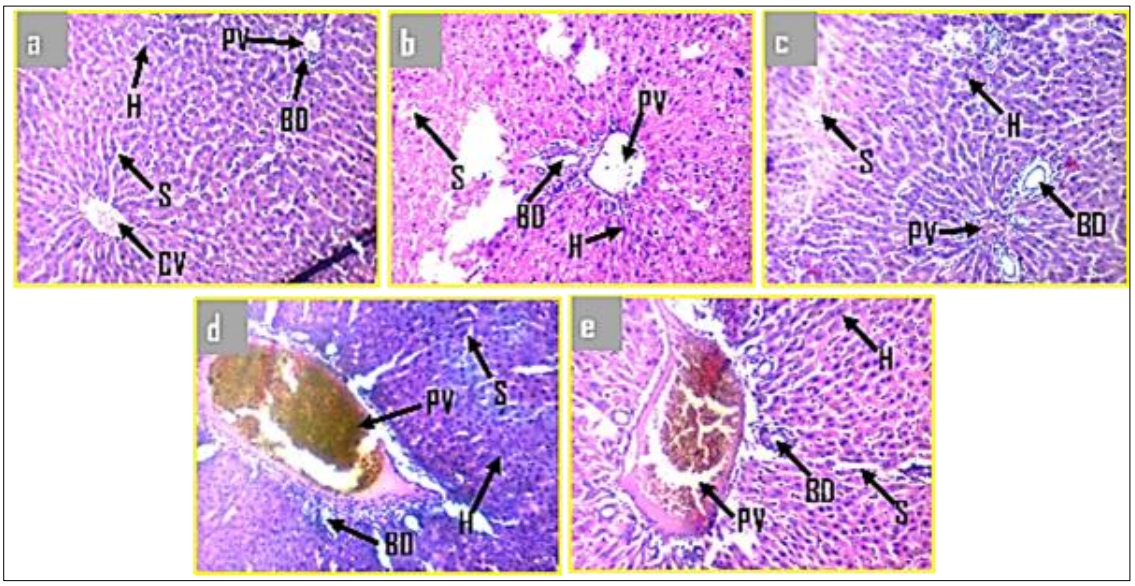


Figure 9 Histology of the liver across experimental groups at x100 resolution investigated with haematoxylin and eosin stain. The cellular assortment reveals the hepatocytes (H), portal vein (PV), central vein (CV), sinusoids (S) and the bile ducts (BD). Group a = Control, Group b = Crude oil (2 ml/20 g) for 3wks, Group c = Crude oil (2 ml/20 g) for 3wks and NAC, Group d = Crude oil (2 ml/20 g) for 3wks and $ZnSO_4$. Group e = Crude oil (2 ml/20 g) for 3wks and NAC and $ZnSO_4$

The liver sections in the control groups (a) shows a normal cytoarchitecture with normal portal vein (Figure 9). Bile ducts and hepatocytes. Exposure to crude oil contaminated diet resulted in fragmented cytoarchitecture, pyknotic and necrotic hepatocytes, sinusoidal disruption and congestion, enlargement and proliferation of bile ducts, rupturing of the central vein and clogging of the portal veins (Group b). Treatment with N-Acetyl Cysteine (NAC) (c) following exposure

of crude oil contaminated diets protected the liver and improved significantly the cytoarchitecture and cellular integrity that is similar to that of the control group. Treatment with $ZnSO_4$ and the combine treatments of both NAC and $ZnSO_4$ improved slightly the histoarchitecture of the liver in these groups (Figure 10). The hepatocytes presented few necrotic cells, sinusoidal integrity was intact, and the bile ducts shows no enlargement nor proliferation, however there was a slight clogging in the portal veins in these groups.

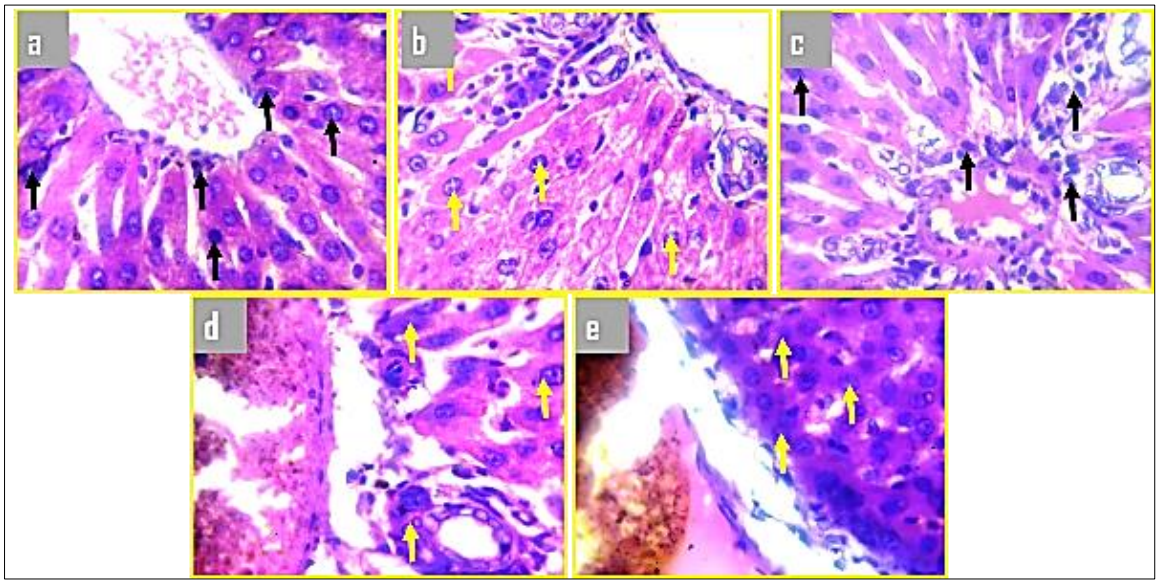


Figure 10 Histology of the liver across experimental groups at x400 resolution investigated with haematoxylin and eosin stain. The cellular assortment reveals the hepatocytes (H), portal vein (PV), central vein (CV), sinusoids (S) and the bile ducts (BD). Group a = Control, Group b = Crude oil (2 ml/20 g) for 3wks, Group c = Crude oil (2 ml/20 g) for 3wks and NAC, Group d = Crude oil (2 ml/20 g) for 3wks and $ZnSO_4$. Group e = Crude oil (2 ml/20 g) for 3wks and NAC and $ZnSO_4$

4. Discussion

One of the primary organs that bonny light crude oil (BLCO) poisoning affects is the liver (Adedara & Farombi, 2012). Additionally, exposure to bonny light crude oil at duration-dependent levels results in elevated serum levels of liver enzyme markers and significant changes to the cytoarchitecture of the liver. However, for healthy liver function, zinc and NAC are essential due to their anti-inflammatory, anti-oxidant, and anti-apoptotic properties (Emojevwe et al., 2022a, 2022b).

In this study, the weight of the Wistar rats exposed to bonny light crude oil reduced considerably when compared to the control group. This might be caused by the way crude oil affects Wistar rats' digestive systems, the loss of body proteins, and the interference of free radicals produced by BLCO in protein synthesis (Ita et al., 2014). According to earlier investigations (Raji and Hart, 2012; Ikanone et al., 2017), this observation is accurate. As the amount of time the crude oil was administered for decreased, so did the fall in body weight. However, due to its strong antioxidant properties, N-acetyl cysteine (NAC) and zinc sulphate ($ZnSO_4$) were found to work well together to restore body weight.

It is advised to evaluate liver enzymes in preclinical investigations since they are thought to be a more accurate and sensitive sign of liver damage when they are present in serum and are typically linked to hepatocellular damage.

This study shown that when compared to the control, administering crude oil for two or three weeks dramatically elevated ALP and ALT. According to Shah et al. (2011), a rise in ALT and ALP activity is a symptom of liver damage. More precisely, increased ALT activity in serum is a sign of liver cell membrane leakage and a loss of functional integrity (Bomprezzi et al., 2015).According to Jaruslaw et al. (2009), the enzyme alkaline phosphatase (ALP) is frequently utilized as a sign of hepatobiliary illness.

This study's findings concur with those of Ikanone et al. (2017), who found that crude oil significantly altered the liver's pathology. When compared to the group treated with crude oil, selective co-treatment with NAC and $ZnSO_4$ was found to dramatically lower ALP levels. Histological analyses showed that eating food contaminated with crude oil causes

pyknotic and necrotic hepatocytes, sinusoidal congestion, expansion and proliferation of bile ducts, rupturing of the central vein, and clogging of the portal veins depending on the time of exposure. The extent of the damage was inversely correlated with the exposure time.

5. Conclusion

Conclusively, treatment with N-Acetyl Cysteine or Zinc Sulphate alone resulted in significant reductions in liver enzymes (ALT and AST) which reflected the reduction in liver dysfunction/damage induced by the crude oil. The combination of N-Acetyl Cysteine and Zinc Sulphate had an even greater protective effect, significantly reducing both ALT and AST levels compared to levels observed with either treatment alone. The findings indicate that treatment with N-acetyl cysteine and Zinc Sulphate is an effective and safe approach to ameliorating the hepatotoxic effects of crude oil in Wistar rats. Therefore, N-Acetyl Cysteine and Zinc Sulphate could be beneficial for the management and treatment of hepatic toxicity induced by crude oil exposure in Wistar rats.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Before proceeding with the study, Ethical Approval was obtained from the Research, Ethics and Grants Committee of the Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria. Ethical approval number: RBC/FBMC/DELSU/23/178

Author Contributions

NAO, and OO designed the study; they also measured biochemical parameters, performed statistical analysis, and created and assessed the report. The animal grouping was created with assistance from OMO, NAO, and OO. The study's design, statistical analysis, and manuscript review were all assisted by OMO, and NAO. Following examination of the manuscript, all authors concurred on the final version.

Data Availability

The authors confirm that the data supporting the study's conclusions are included in the article.

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