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Full length Research Article

D-Ribose-L-Cysteine Protects Against Sodium Arsenite-induced Hepato-Nephrotoxicity in Rats

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Summary: D-Ribose-L-Cysteine (Riboceine)- an antioxidant supplement that may help to raise the glutathione levels by acting as a precursor for glutathione biosynthesis in biological systems. Effect of riboceine (Rb) on sodium arsenite (SA) induced hepatorenal toxicity was investigated in rats. Four groups (A-D) (six per group) were treated thus: Group A (water and normal diet only); while Group B (SA at 5 mg/kg body weight); Group C (riboceine at 10 mg/kg body weight) and Group D (riboceine and SA). The exposure to test substances lasted for a total of 14 days in each case in which pre-treatment was done with riboceine. Exposure to SA triggered a significant reduction in the entire weight and relative organ weight, increase in ALT (alanine aminotransferase), AST (aspartate aminotransferase), ALP (alkaline phosphatase) activities, decrease in liver total protein and increase in serum levels of urea and creatinine. Furthermore, SA caused a significant reduction in GSH (glutathione) level and CAT (Catalase) activity, while the LPO (lipid peroxidation) and NO (nitric oxide) levels were significantly increased. Pre-treatment with riboceine, restored the levels of the aforementioned parameters. Riboceine also promote restoration of hepatocytes and renal cells integrity. Findings from this study reaffirm the hepatorenal toxicities of sodium arsenite and show the protective role of riboceine against SA-induced toxicities. Protective effects of riboceine may be via the enhancement of the level of glutathione, a natural scavenger of free radicals.

Keywords*: D-Ribose-L-Cysteine, antioxidant, sodium arsenite, hepatotoxicity, nephrotoxicity, lipid peroxidation*

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INTRODUCTION

Arsenicals are considered potent human carcinogens, causing cancer of the skin, lung, bladder, liver and kidney (IARC, 1987; Tchounwou *et al*., 2004). A large population of humans is chronically exposed to arsenic throughout the world, via ingestion, inhalation, dermal contact and the parenteral route (Tchounwou *et al*., 2004). The carcinogenic effect of arsenicals has been linked to the of free radicals' generation and alteration of cellular redox states which cumulates into oxidative stress due to an imbalance between the cellular antioxidant defense and ROS (reactive oxygen species) generation (Xu *et al*., 2017). Exposure to arsenicals can also result to the following health defects: keratosis, hyperpigmentation, hypopigmentation, cardiovascular disease, diabetes mellitus, central nervous disorders etc. (Janga *et al*., 2016). It was earlier proposed that arsenic induction of oxidative stress is by cycling between its metallic oxidation states or by antioxidants imbalance and high inflammation rate, thereby causing cellular accumulation of free radicals (Halliwell *et al*., 2004).

Riboceine is a synthetic compound designed to replenish glutathione levels thereby complementing the anti-oxidant defense system of the body (Chandra *et al*., 2015; Falana *et al*., 2017). D-Ribose-L-Cysteine which is abbreviated as riboceine provides a means of delivering cysteine to the cell. Cysteine, which cannot be delivered directly to the cell due to its fragility, has been proposed as the key player amino acid in the antioxidant effect of riboceine (Falana *et al*., 2017; Adelakun *et al*., 2018). Whole glutathione consumption also cannot be effective because it would be destroyed in the digestion process before reaching the target cell (Falana *et al*., 2017). Riboceine avail the body cells of cysteine for the synthesis of glutathione, while ribose is channeled into producing cellular energy. The glutathione within a cell protects it against destruction from free-radical damage (Flora, 2011).

Variations in the systemic antioxidant have been reported in many pathological conditions involving oxidative stress induced by metals (Beyersmann and Hartwig, 2008). Enzymatic antioxidant response has been shown to play key roles in response to arsenic-induced oxidative stress (De Vizcaya-Ruiz *et al*., 2009). Furthermore, a time-dependent relationship in the enzymatic antioxidant response was observed in the levels of CAT and SOD (superoxide dismustase) as there was an initial increase but latter decrease on further exposure to arsenic (De Vizcaya-Ruiz *et al*., 2009; Nandi *et al*., 2005). Non-enzymatic antioxidants have been shown to be highly efficient in combating metal-induced oxidative stress and

preventing cellular oxidative injury. Non-enzymatic antioxidants are currently in use as therapeutic and preventive agents to combat damages induced by oxidative stress which occur during arsenic exposure (De Vizcaya-Ruiz *et al*., 2009). Such antioxidants include vitamin C, vitamin E, flavonoids, carotenoids, amino acids, for example taurine, methionine, cysteine, and other thiol-containing compounds which include: glutathione, alpha-lipoic acid, thioredoxin and N-acetyl Cysteine (De Vizcaya-Ruiz *et al*., 2009).

Riboceine, as a non-enzymatic antioxidant, helps in combating oxidative stress. There are limited reports in literature regarding the use of riboceine against metal-induced oxidative stress. We designed this study to assess the effect of riboceine on sodium arsenite-induced oxidative stress and toxicity in rats.

MATERIALS AND METHODS

Chemicals and reagents: Sodium arsenite was procured from Sigma Aldrich Co. St. Loius United States and riboceine was obtained from a pharmacy store in Ibadan, Nigeria. Serum alkaline phosphatase (ALP) activity, aspartate aminotransferase (AST), with alanine aminotransferase (ALT) activities were evaluated alongside the urea and creatinine levels using reagent kits obtained from RANDOX Laboratories Ltd., Ardmore, United Kingdom. The kits were used according to the respective manufacturers' protocol for the measurement of enzymes activities.

Experimental Animals: Twenty-four mature male Wistar rats each weighing 160 ± 20g, obtained from the preclinical facilities of Faculty of Basic Medical Sciences, were used for this study. Prior to the commencement of treatment, the rats were made to acclimatize for a period of one week and kept in well ventilated cages stationed in the animal house of our department. All animals had unrestricted access to fresh rat chows and water. Experimental rats were exposed to photoperiod of 12 hrs light/dark cycles in synchrony with natural light cycle, and cared for adequately and were handled in adherence to the guide for the care and use of experimental animals, as specified by the National Institute of Health (NIH publications number 85–93 revised in 1985).

Experimental design:
Group A: This is the control group that received distilled water only.
Group B: Administered sodium arsenite (SA) at 5 mg/kg for a total of 14 days at a day interval.
Group C: Administered riboceine (10 mg/kg) for 14 days
Group D: Pretreated with riboceine (10 mg/kg) daily for 14 days and then administered SA (5 mg/kg) for a total of 14 days at a day interval and this dose was chosen be with reference to previous studies (Falana *et al*., 2017; Adelakun *et al*., 2018) at 30mg/kg and since pre-treatment was utilized a lower dose of 10mg/kg was used for this study.

All treatments were done by oral gavage. Each group has 6 animals per group. Sodium arsenite was administered according to the published report (Gbadegesin *et al*., 2009).

Tissue preparation: Rats were sacrificed by cervical decapitation 24hrs after the last dose of the treatments. Blood samples were collected. Harvested liver and kidney organs were rinsed in ice cold 1.15% KCl solution, blotted with filter paper and weighed to determine their initial weights. Thereafter, the liver samples were sectioned for histological examination and submerged in 10% Formalin. The remaining portions of the harvested liver were homogenized with 0.1M Phosphate buffer (pH 7.4) using a Teflon homogenizer. The homogenates gotten were then centrifuged at 10,000 revolution per minute for 15 minutes in a cold centrifuge (4 degrees) to obtain the post mitochondrial fraction. After centrifugation, the supernatants were collected stored at -20 degrees prior to the biochemical analyses.

Preparation of Serum: Blood samples collected via the venous plexus into plain tubes and left to clot at room temperature. Preparation of serum was done by centrifugation of the clotted blood at 3,000 g for 10 min. The supernatant (serum) was removed and stored at -20 degrees prior to the analyses

Blood analysis: The blood samples were taken via the periorbital sinus into lithium heparinized bottles. The PCV (packed cell volume) was evaluated using the microhematocrit method and the Hb (hemoglobin) concentration was also assessed by the cyanmethemoglobin. The new improved Neubauer hemocytometer was used in the estimation of red blood cells (RBC) and white blood cell (WBC) counts. Differential leukocyte counts were evaluated using standard method Jain (Jain, 1986).

Biochemical assays:

Total protein level assay: Total Protein level was determined following the protocol outlined in Randox Laboratories Limited kits.

Kidney function assay: Serum urea and creatinine levels were estimated by the method of Fawett and Scott (Fawett and Scott, 1960).

Liver function assay: Activities of ALT and AST were evaluated by the method of Reitman & Frankel (Reitman and Frankel, 1957). Estimation of serum ALP activity was evaluated by the method described by (Rec, 1972).

Assays for antioxidant markers: The CAT activity was assessed by the method earlier described by Claiborne, 1985. SOD activity was assessed based on the method described by Misra and Fridovich, 1972. GST (glutathione-S-transferase) activity was estimated by following the method described by Habig,1974. The GPx (glutathione peroxidase) activity was estimated using the method of Rotruck *et al*., 1973. The GSH (glutathione) activity was determined following the method of Beutler *et al*., 1963. Also, LPO activity was evaluated by the method earlier described by Rice-Evans which involves the reaction between 2-thiobarbituric acid (TBA) and malonaldehyde (MDA). MDA level was calculated following the method of (Adam-Vizi and Seregi, 1982).

Assay for markers of inflammation: The MPO (myeloperoxidase) activity was assessed by slight modification of the method described by Trush *et al*., (1994) Nitric oxide (NO) activity was evaluated by the method of Green *et al*., (1982).

Histological evaluations: Sections of tissues were obtained from the liver and kidney and fixed in 10% neutral buffered formalin. The tissues were thereafter processed for histological examinations with the use of a routine paraffin-wax embedded method. The tissue section of 5 micrometer thickness was stained with hematoxylin and eosin and afterwards processed for light microscopy at a magnification of X400.

Statistical analysis: The data obtained were analyzed by the one-way analysis of variance (ANOVA). This was followed by a post hoc test (Bonferroni) to verify the level of significance between groups using GraphPad prism-6 software (version 6; GraphPad Software, La Jolla). Levels of significant difference between mean values were set at $p < 0.05$.

RESULTS

Sodium arsenite caused a reduction in the body and relative liver weight: A significant $p < 0.05$ decrease was noticed in the body weight of the animals in Group B, treated with sodium arsenite only in comparison to the control (Figure 1). Also, there was a significant decrease $p < 0.05$ in the relative liver weight of the Group B and of Group D pretreated with riboceine before sodium arsenite when juxtaposed with the control group. No significant difference in the relative kidney weights across the groups (Figure 1).

Riboceine offered protection against sodium arsenite-induced hepatotoxicity in the treated rats: There was an increase in the mean serum ALT, AST and ALP activities of the rats in the group administered only sodium arsenite (Group B) when compared with the control Group A (Figure 2). Pretreatment with riboceine before sodium arsenite (Group D) however, led to significant reduction in the serum ALT, AST and ALP activities relative to the group treated with sodium arsenite only (Group B).

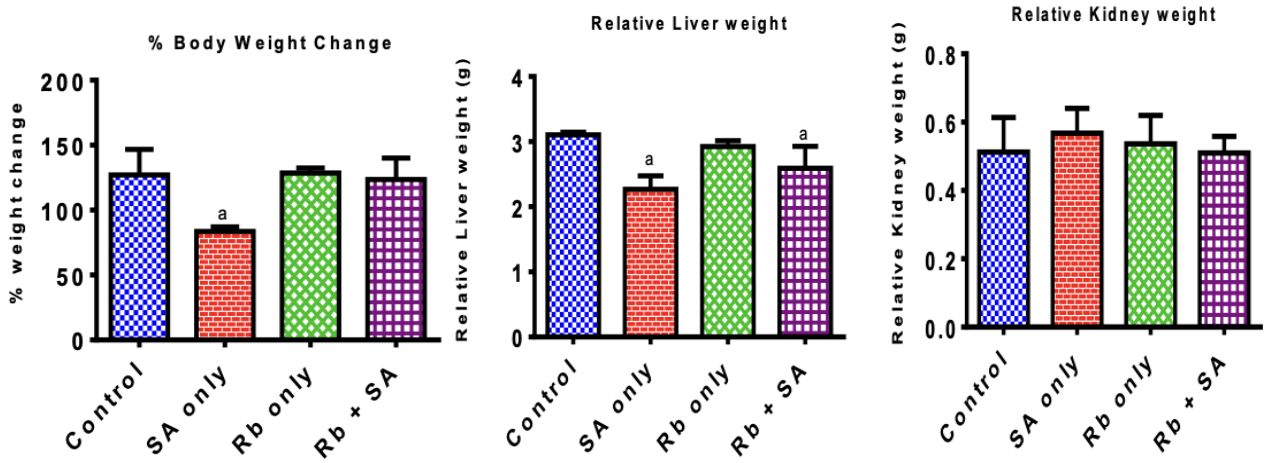

Figure 1:
Effect of Sodium arsenite and riboceine on percentage body weight, and relative liver and kidney weights respectively. Values are expressed as mean ± SD (n=6). a= significant difference ($p < 0.05$) when compared with the negative control.

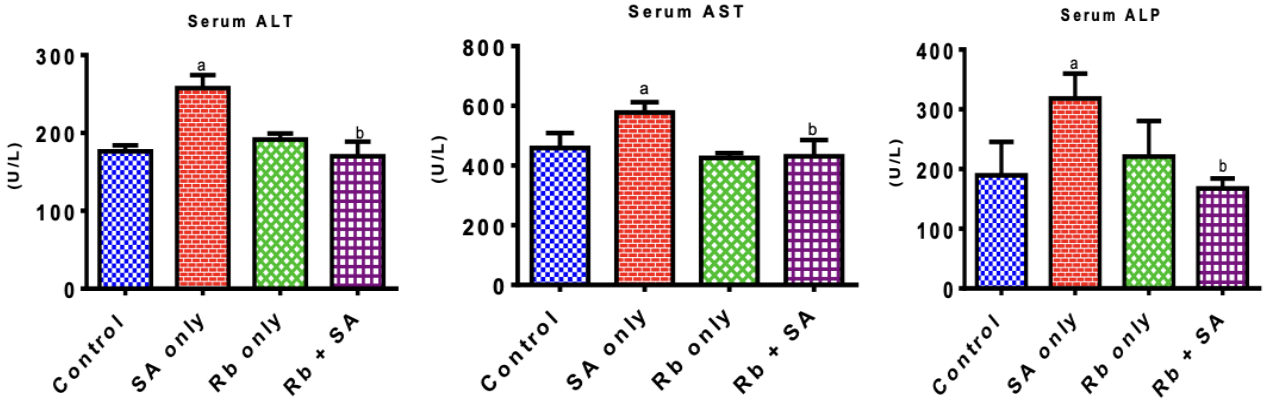

Figure 2:
Riboceine (Rb) protects against sodium arsenite-induced hepatotoxicity in the serum of treated rats. Values are presented as mean ± SD (n=6). a= significant difference ($p < 0.05$) relative to the negative control while b = significant difference ($p < 0.05$) in comparison to the group treated with sodium arsenite (SA) alone.

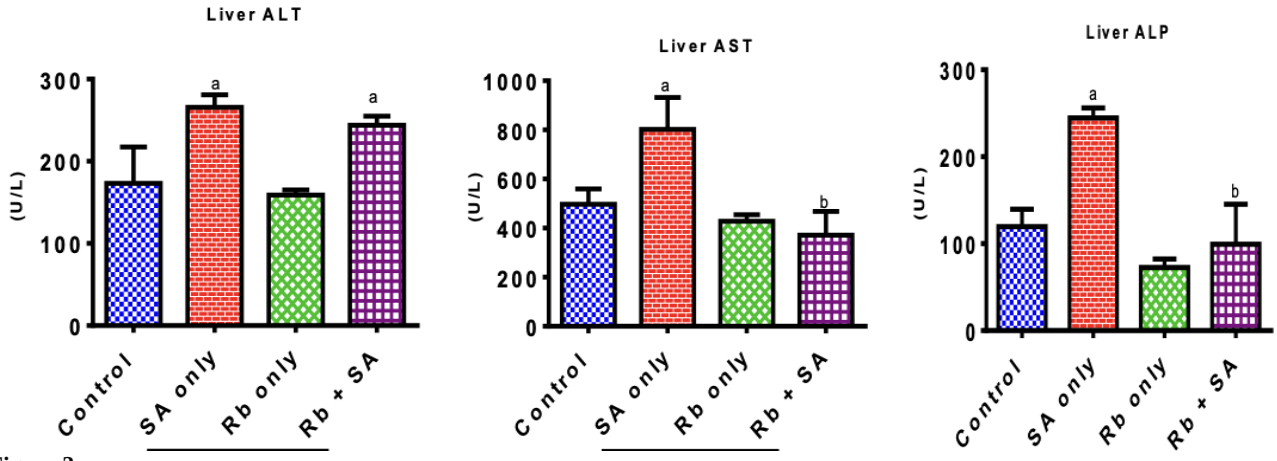

Figure 3:
Riboceine (Rb) protects against sodium arsenite-induced hepatotoxicity in the liver of treated rats. Values are presented as mean ± SD (n=6). a= significant difference ($p < 0.05$) relative to the negative control while b = significant difference ($p < 0.05$) in comparison to the group treated with sodium arsenite (SA) alone.

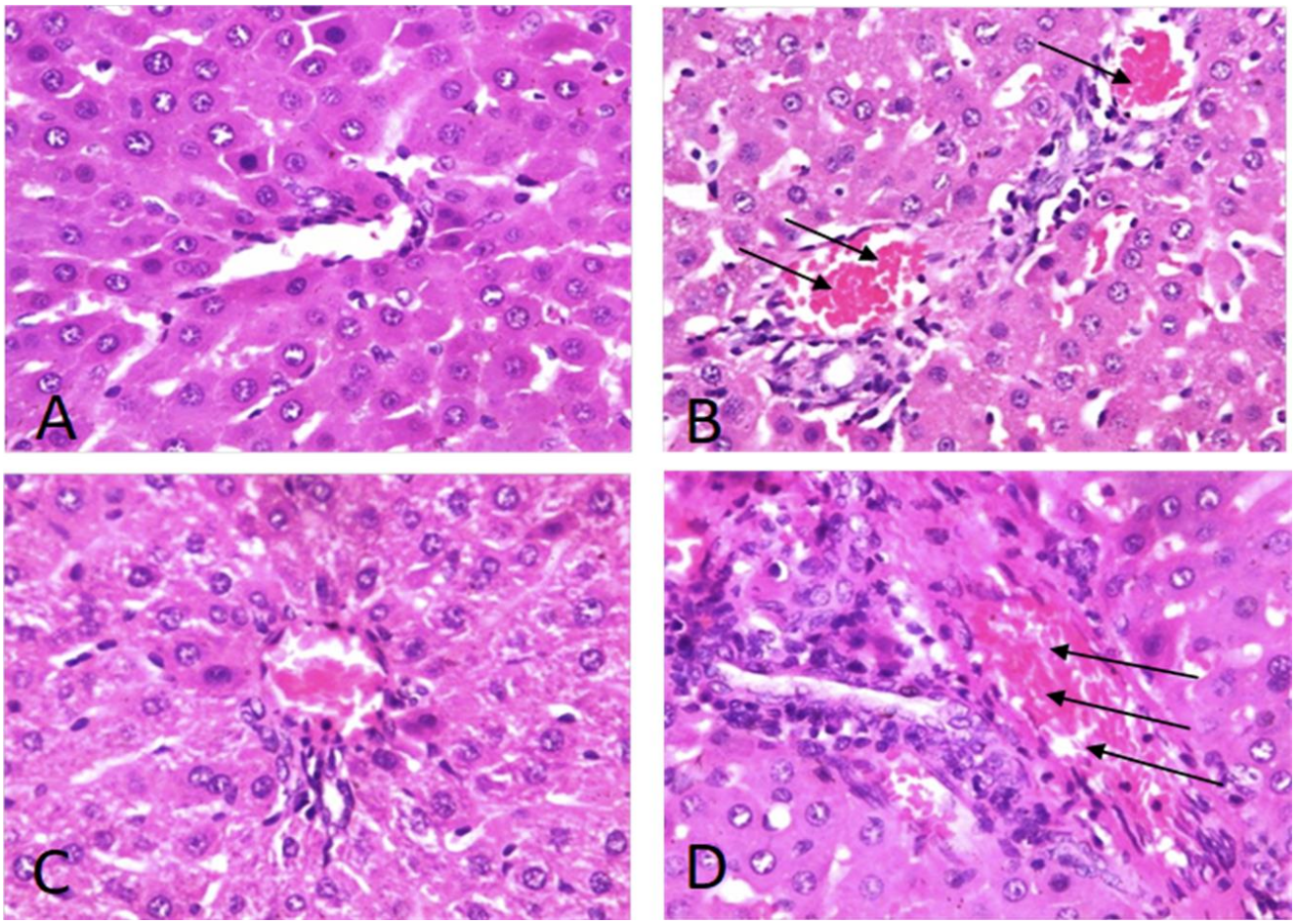

Plate 1:
Photomicrograph of liver sections of rats treated with riboceine and sodium arsenite for 14 days (Mag X400). (A) Control showing normal hepatocytes. (B) SA only (5 mg/kg body weight) showing mild vascular congestion and mild inflammation. (C) Riboceine (10 mg/kg body weight) showing no visible lesion. (D) Rb + SA (10 mg/kg and 5 mg/kg body weight) showing mild inflammation and hepatocytes regeneration

Similar observations were seen in the liver activities of ALT, AST, and ALP (Figure 3). There were increases in the activities of ALT, AST, and ALP in the rats treated with sodium arsenite only (Group B) when compared with the negative control, and pretreatment with ribociene (Group D) resulted in a significant reduction of AST and ALP activities, with a slight decrease in ALT activities (Figure 3)

Histology: Histology results also confirmed the toxicity of sodium arsenite on the liver and prevention of such effects in the liver cells of rats pretreated with riboceine in Group D (Plate 1).

Protective effects of riboceine on sodium arsenite-induced renal toxicity: Administration of sodium arsenite (Group B) caused a significant increase ($p < 0.05$) in serum urea levels when examined along with the negative control (Group A) given distilled water only (Figure 4). Pretreatment of rats with riboceine before the administration of sodium arsenite (Group D), led to significant decrease ($p < 0.05$) in the serum urea in comparison to Group B treated with sodium arsenite only. In addition, treatment with sodium arsenite resulted in significant ($p < 0.05$) increase in creatinine levels in the serum in Group B which received sodium arsenite when examined with the negative control group (Figure 4). Pre-treatment with riboceine before administration of sodium arsenite resulted in significant ($p < 0.05$) reduction in serum creatinine levels in comparison to Group B. Histological analysis showed mild lesions observed in renal tissue in the group exposed to sodium arsenite (Group B). However, pre-treatment with riboceine (Group D) prevented such degeneration in the renal cells (Figure 5).

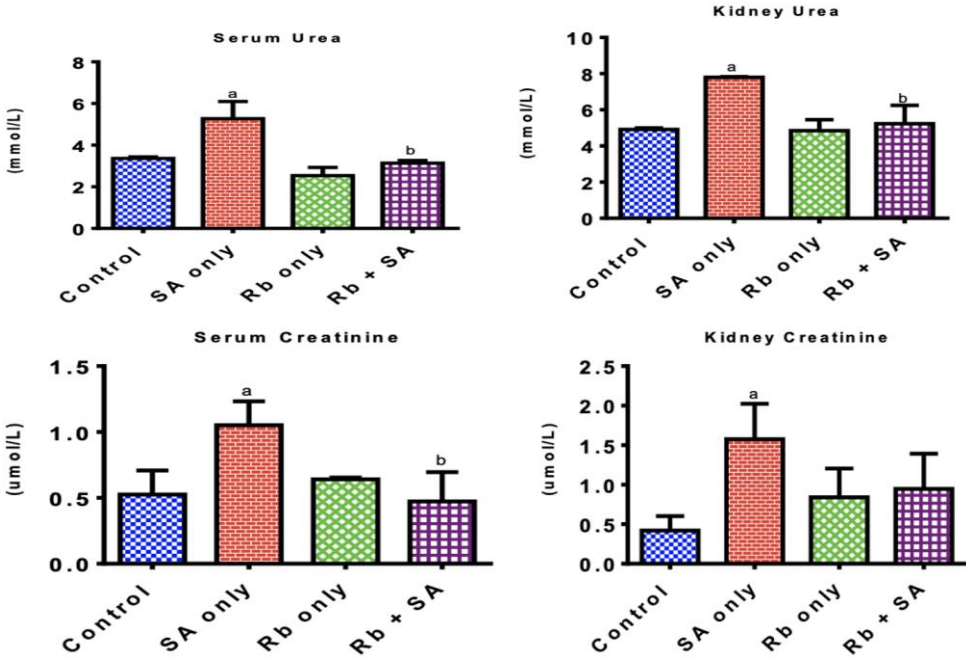

Figure 4:
Protective effects of riboceine (Rb) on sodium arsenite-induced renal toxicity. Each bar represents mean ± SD (n=6). *a* = significant difference ($p < 0.05$) in comparison to the negative control; b = significant difference ($p < 0.05$) relative to the group treated with sodium arsenite (SA) alone.

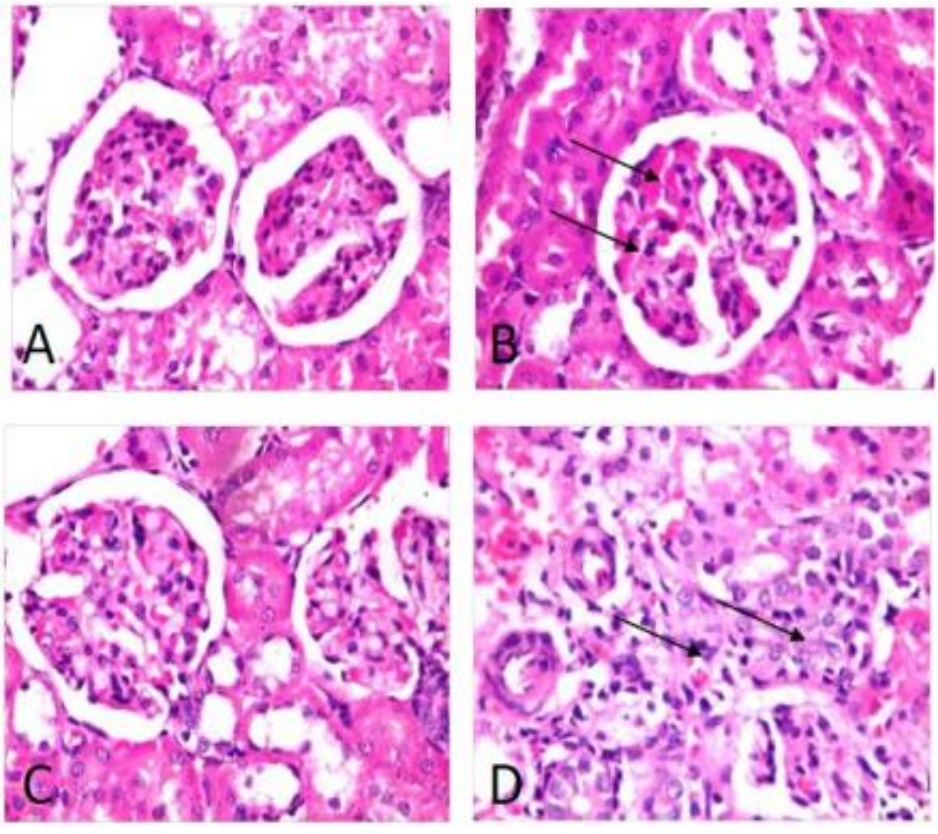

Plate 2:
Photomicrograph of kidney sections of rats treated with riboceine and sodium arsenite for 14 days (Mag X400). (A) Control showing normal renal cells. (B) SA only (5 mg/kg body weight) showing mild vascular congestion and mild peritubular inflammation. (C) Riboceine (10 mg/kg body weight) showing no visible lesion. (D) Rb + SA (10 mg/kg and 5 mg/kg body weight) showing mild peritubular inflammation and renal cell regeneration

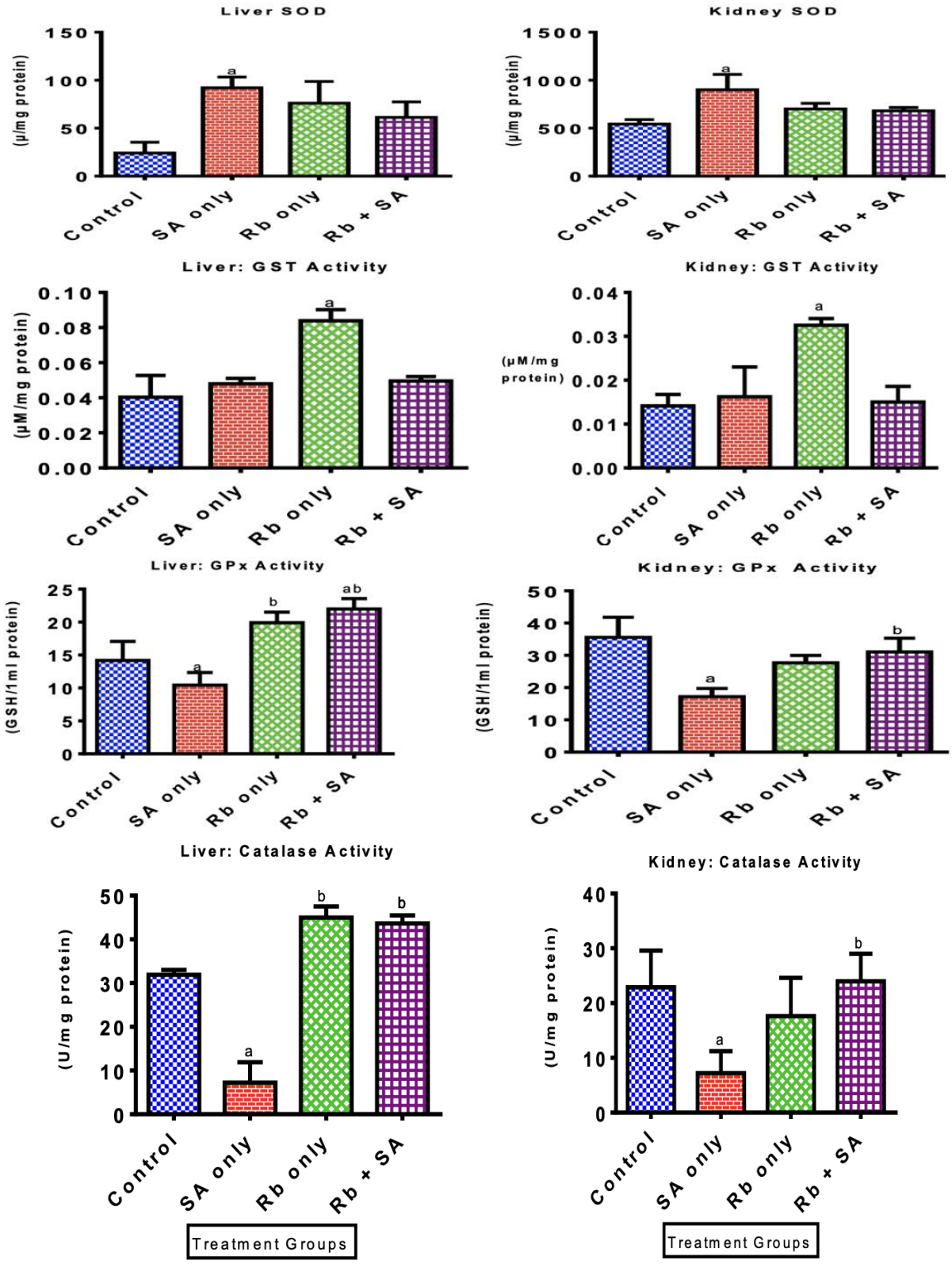

Figure 5:
Riboceine (Rb) ameliorated sodium arsenite induction of distortion of enzymatic antioxidant in liver and kidney of treated rats. Each bar represents mean ± SD (n=6). *a* = significant difference ($p < 0.05$) relative to the negative control; b = significant difference ($p < 0.05$) in comparison to the group treated with sodium arsenite (SA) alone.

Riboceine ameliorated sodium arsenite-induced distortion of antioxidant biomarkers in the treated rats: The activity of SOD in the liver significantly increased $p < 0.05$ in the group treated with only sodium arsenite (SA) in comparison to the control (Figure 5). Pretreatment with riboceine before sodium arsenite (Group D) however led to decrease in the mean SOD activity compared with Group B.

Observations made in the kidney regarding SOD were similar to the findings with the liver described above (Figure 6). In addition, hepatic GSH level decreased significantly in the group given SA only (Group B) when compared with the control (Group A). However, riboceine brought about a significant increase in GSH level ($p<0.05$) in Group D given SA and riboceine compared with Group B. Renal GSH level also decreased significantly in the group given SA only (Group B) when compared with the control (Group A). However, there was no significant change in the group given both SA and riboceine (Group D) when compared with Group B, given SA only. On the other hand, hepatorenal Glutathione-S-Transferase activity was found to increase but not significantly in the group given SA only. Group C (treated with riboceine only) however, showed a significant increase ($p < 0.05$) in the mean GST activity of the liver and kidney when compared with the control and the SA treated groups.

Hepatic GPx activity was found to be higher significantly ($p < 0.05$) in Group B (administered SA only) than the control (Group A). Pretreatment with riboceine before SA (Group D), effectively reversed the effect of SA on the GPx activity seen in Group B (Figure 5). On the other hand, treatment with SA had a contrary effect in the kidney cells with respect to GPx activity (Figure 5). Both hepatic and renal CAT activities decreased significantly ($p < 0.05$) in the group given SA when compared with the control. Pre-treatment with riboceine before SA (Group D) restored with the above parameters to values close to control. Similarly, both liver and kidney malonaldehyde levels were found to increase significantly ($p < 0.05$) in the group treated with SA only (Group B) when compared with the control (Group A), but values were reduced significantly ($p < 0.05$) in the rats pretreated with riboceine before SA exposure (Group D) as compared with Group A (Fig. 6).

Riboceine ameliorates the effects of sodium arsenite on inflammatory biomarkers in rats:

The NO level in both liver and kidney increased significantly $p < 0.05$ in the group given sodium arsenite alone compared with the negative control group (Figure 7). On the other hand, the effect of SA on the NO concentration was effectively reversed in Group D pretreated with riboceine prior to SA exposure when Group B was compared with Group D. Patterns similar to the observation made with NO concentrations were observed with effect of riboceine on SA treatment on liver MPO (Figure 7).

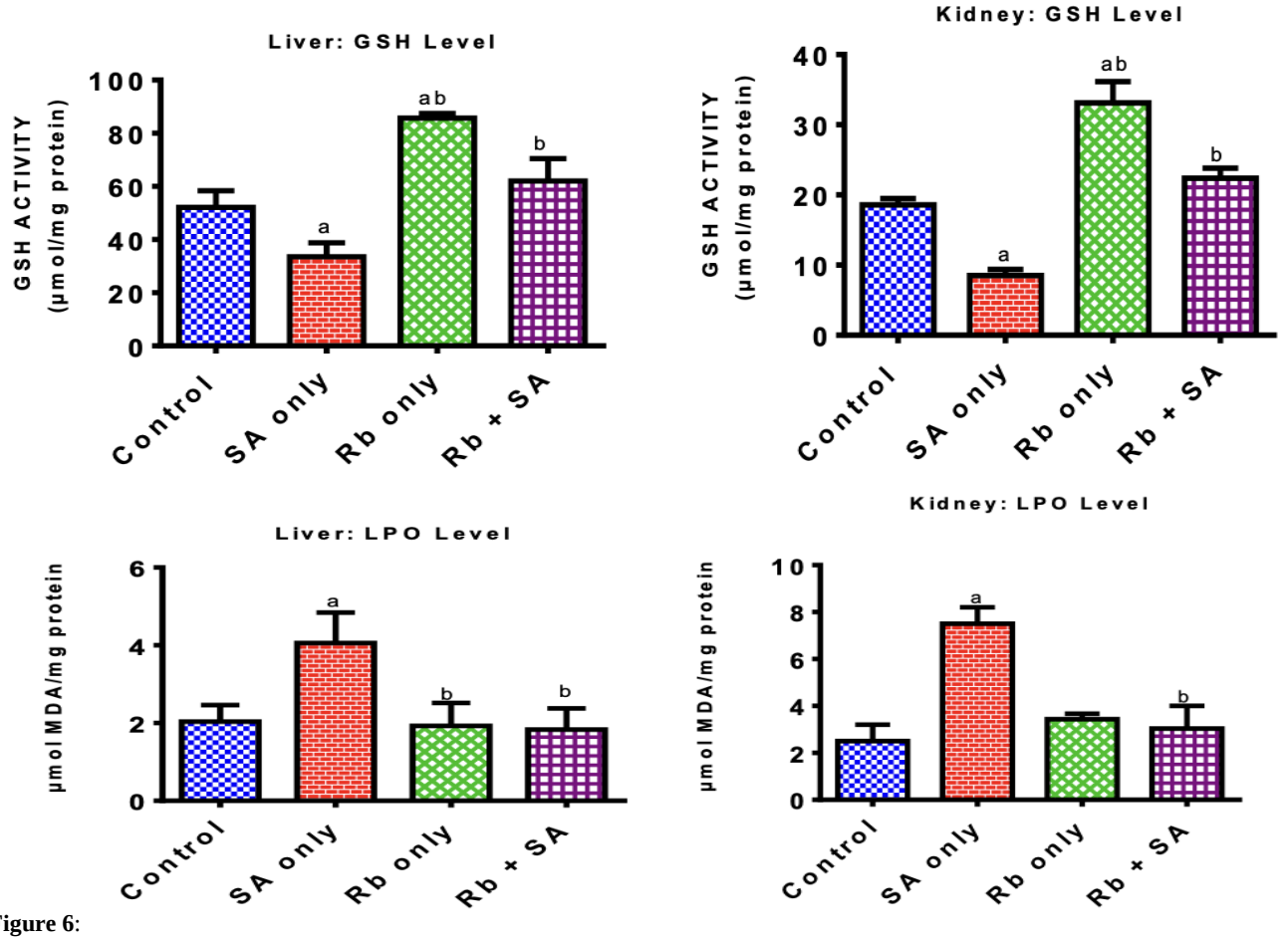

Figure 6:
Riboceine (Rb) ameliorated sodium arsenite induction of distortion of non-enzymatic antioxidant in liver and kidney of treated rats. Each bar represents mean ± SD (n=6). *a* = significant difference ($p < 0.05$) relative to the negative control; b = significant difference ($p < 0.05$) in comparison with group treated with sodium arsenite (SA) alone

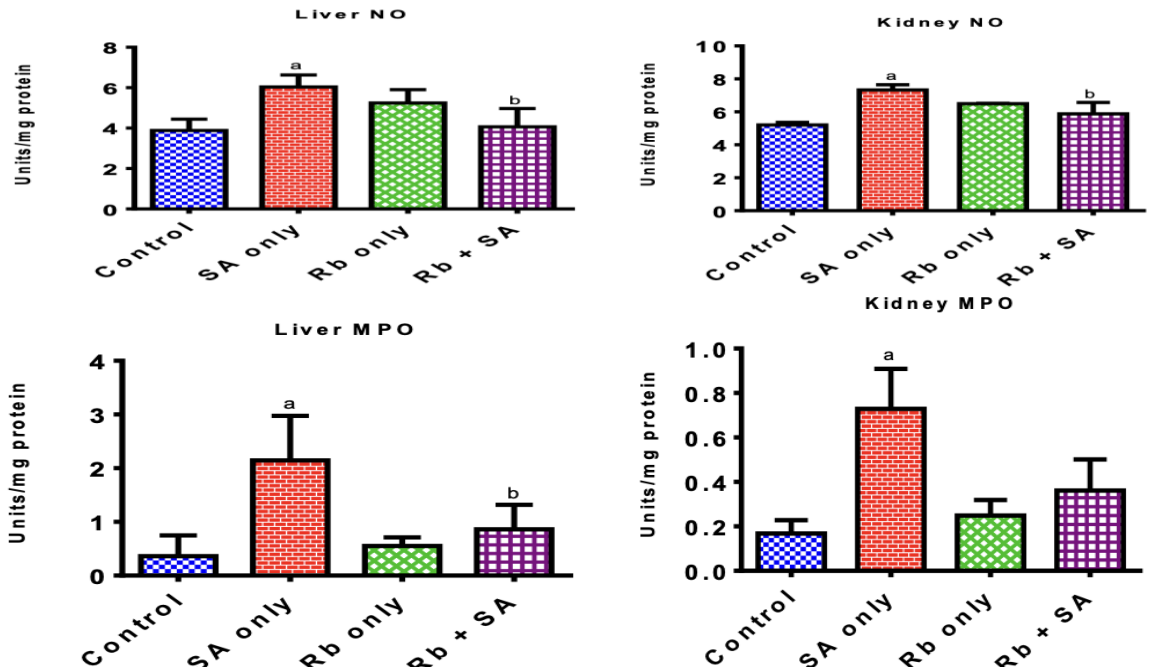

Figure 7:
Effects of sodium arsenite (SA) and/or riboceine (Rb) on biomarkers of inflammation in the liver and kidney of rats. Each bar represents mean ± SD (n=6). *a* = significant difference ($p < 0.05$) relative to the negative control; b = significant difference ($p < 0.05$) in comparison to the group treated with sodium arsenite (SA) alone.

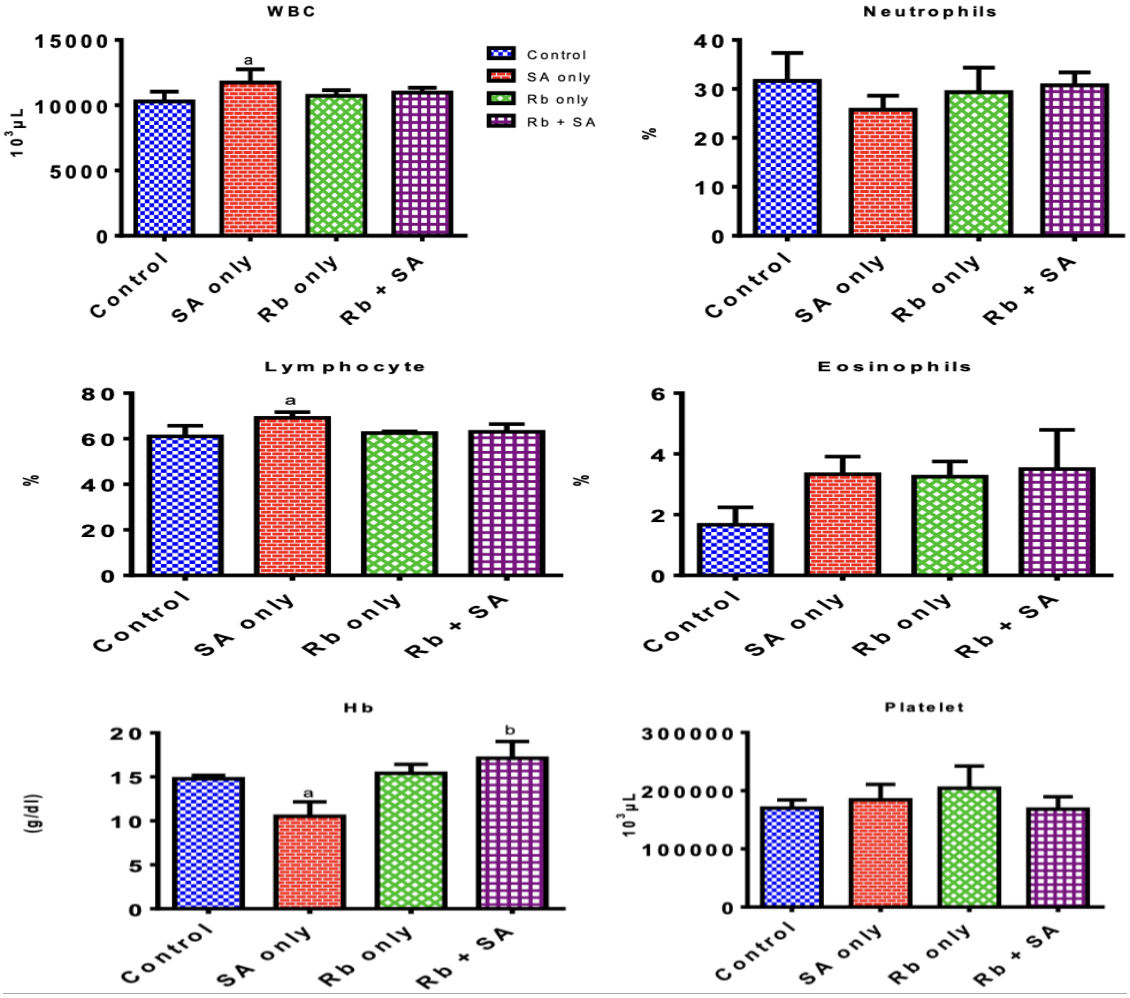

Figure 8:
Effects of sodium arsenite (SA) and/or riboceine (Rb) on hematological parameters in the treated rats. Each bar represents mean ± SD (n=6). *a* = significant difference ($p < 0.05$) relative to the negative control; b = significant difference ($p < 0.05$) in comparison to the group treated with SA alone.

Riboceine restores the normal levels of PCV, Hb and RBCs in the treated rats: The number of neutrophils, eosinophils and platelets were not significantly different across the groups (Figure 8). There was a significant increase $p < 0.05$ in the number of WBC and lymphocytes in the group treated with SA only. In addition, the PCV and RBCs diminished significantly in the SA group when compared with the control. However, both PCV and RBCs increased significantly ($p< 0.05$) in Group D pretreated with riboceine before SA when compared with the group given SA alone.

DISCUSSION

The carcinogenic effect of arsenic has been linked with ROS generation which cumulates into an alteration in cellular redox states and oxidative stress, an imbalance between the cellular antioxidant defense and ROS generation (Xu *et al*., 2017). This decline in the antioxidant capability of the body system affected, has led to the proposition of the use of antioxidants as therapeutic and preventive agents in circumstances of metal-induced oxidative damage and it has been effective in the protection of cells from these detrimental effects (Flora 2011; Nandi *et al*., 2005). The present study examined the effect of D-Ribose-L-Cysteine, a potent antioxidant, on sodium arsenite-induced hepatorenal toxicities in rats. An exposure of rats to sodium arsenite (SA) at 5 mg/kg body weight via oral gavage resulted in notable decrease in the percentage body weight gain of rats in the group treated with SA only when compared with the control. The inhibitory effect of SA on weight gain is consistent with reports of previous studies (Adil *et al*., 2015; Jana *et al*., 2006). More so, SA toxicity has been reported to destroy liver integrity in mouse, rat and goat (Sharma *et al*., 2009; Roy *et al*., 2009). Furthermore, the increased activities of AST, ALP and ALT seen in the serum of rats treated with SA alone when compared with the control, along with the significant decrease in the relative liver weight in the former group point in the direction of SA effect on systemic metabolism related to liver. Moreover, histological analysis of the liver samples confirms the toxic effects of SA which was prevented by pretreatment with riboceine.

The glutathione-stimulating effect of riboceine was also observed in groups treated with riboceine suggesting its cellular restorative capability. This is in consonance with the findings that the glutathione-stimulating effect of riboceine is key in combating oxidative stress in the body as it helps raise the level of this vital anti-oxidant in the cells (Falana *et al*., 2017).

Arsenite toxicity induces several metabolic disorders including urea and creatinine elevation following proximal tubule damage and glomerular injury (Anwar *et al*.,1999; Nandi *et al*., 2005). In the present study, sodium arsenite treatment had deleterious effects on kidney functions as seen by elevation of urea and creatinine levels in the serum in the rats treated with SA alone. Urea, a major waste product of protein catabolism, can rise especially when the kidney is defective (Higgins, 2016). Pretreatment with riboceine was observed to have a significant reversal effect on these parameters. Glutathione (GSH) is a tri-peptide non-enzymatic anti-oxidant that has a beneficiary role in the protection of the cell against metal-induced oxidative stress (Masella *et al*., 2005). It functions by binding metals at sulfhydryl groups, thereby preventing them from creating ROS (Andrews, 2000; Pinto *et al*., 2003). The present study revealed a significant decrease in hepatorenal GSH level on exposure to sodium arsenite. Riboceine treatment on the other hand, produced an increase in GSH levels supporting its capacity in restoring depleted GSH levels and therefore ability as a potent antioxidant agent.

A decrease in CAT activities in the liver and kidney in the group of rats treated with SA alone in this study signifies a decrease in free radical scavenging activities. These findings were in agreement with previous studies, which showed that intracellular ROS levels were increased and GSH contents were decreased and accompanied by reduction of SOD activity in cells after exposure to SA (Shi *et al*., 2003). On the other hand, we observed increased activities of hepatorenal GPx and SOD in the group exposed to SA. The observed difference in the behavior of SOD may relate to the dosage and length of time of exposure adopted in the study as explained in another study (Flora, 2011).
One major effect of ROS is lipid peroxidation that generate many relatively stable decomposition end-products, primarily unsaturated reactive aldehydes, like MDA, HNE and 2-propenal (acrolein) and isoprostanes. As indirect indicators of oxidative stress, these can be measured in plasma and urine (Dalle-Donne *et al*., 2008). In the present study, the lipid peroxidation product levels increased in both liver and kidney of rats treated with SA. This elevated level of MDA was brought to about normal by pretreatment with riboceine thereby showcasing its protective ability against SA-induced peroxidation of lipid and fatty lining membrane of functional organs such as the liver and kidney.

Related to the toxicity of SA is cellular inflammation. During inflammation, NO (nitric oxide) production, by the vasculature is considerably increased and, along with other ROS, add to oxidative stress (Lubos *et al*., 2008). In the present study, NO levels increased significantly in SA treated rats. However, this effect was reduced significantly in the group of rats pretreated with riboceine thereby showcasing the protective effects of riboceine, this is consistent with earlier report (Adil *et al*., 2014). Trends similar to the observation with NO were seen in the MPO levels. There was a significant reduction in MPO levels in the group of rats pretreated with riboceine before SA compare with the group administered SA only.

Considering the hematological parameters in the treated animals, PCV and RBCs were observed to diminish significantly in group treated with SA alone when compared with the control. This reduction in PCV, Hb, and RBC counts might be a result of inhibition of porphyrin or heme synthesis. Arsenic is reported to cause inhibition of aminolevulinic acid dehydratase activity, thereby modifying the heme synthesis pathway (Gupta *et al*., 2005). However, both PCV and RBCs increased significantly when rats were pretreated with riboceine before SA exposure. This is in line with the report by (Ola-Davies and Akinrinde, 2016). The hematinic property of riboceine was observed in reversing anemia induced by sodium arsenite. No significant change in WBC and platelets levels across the treatment groups,

except for Group B animals, treated with SA alone, where a significant increase in the WBC level was observed which could be indicating that sodium arsenite can induce immune response indicated by increase in lymphocytes counts.

In conclusion, this study demonstrated a protective role of riboceine against toxicities induced with sodium arsenite in male Wistar rats. D-Ribose-L-Cysteine was found to be effective in preventing oxidative stress and damage to liver and kidney cells in the animals exposed to sodium arsenite. D-Ribose-L-Cysteine therefore showed strong antioxidant, cytoprotective and anti-inflammatory effects against oxidative stress and hepatorenal toxicity induced with sodium arsenite in rats (Figure 10). This is the first report showing the protective effect of D-Ribose-L-Cysteine on hepato-nephrotoxicity induced by sodium arsenite in rat model.

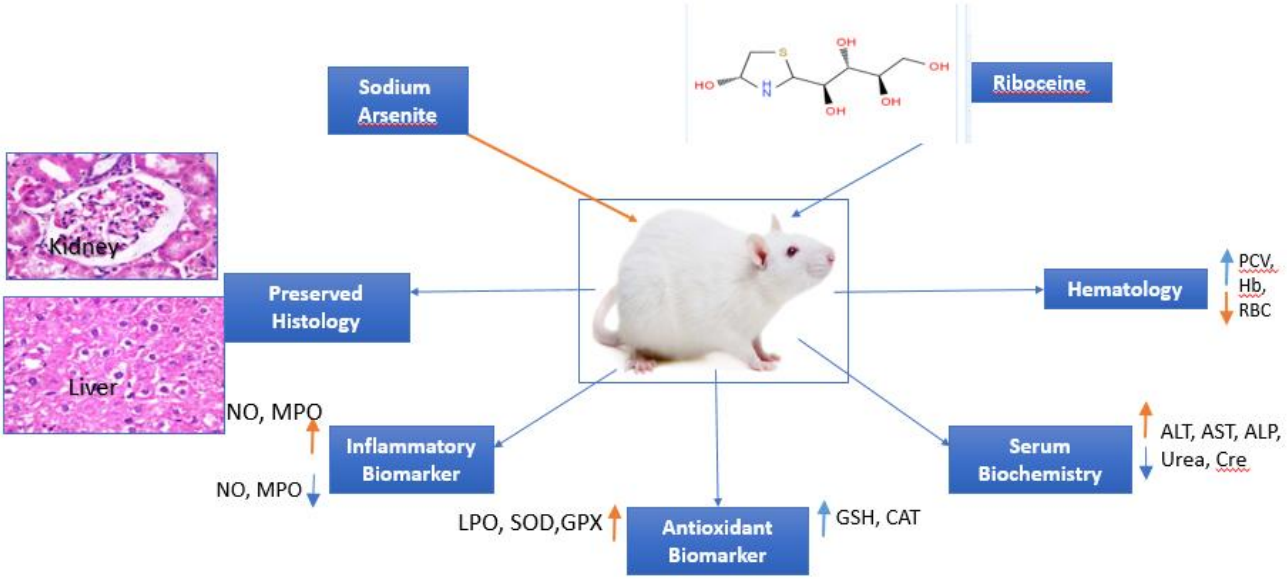

Figure 9:
Graphical summary of the protective role of riboceine against sodium arsenite-induced hepatotoxicity and nephrotoxicity in rats

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