



EFFECT OF *Irvingia gabonensis* STEM BARK ON LIVER FUNCTION IN SODIUM ARSENITE-EXPOSED WISTAR RATS



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ABSTRACT

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Arsenic is a known environmental pollutant that is detrimental to health. In this study, the effect of ethanol stem bark extract of *Irvingia gabonensis* (ESEIG) against sodium arsenite-induced hepatotoxicity in Wistar rats was investigated. Wistar albino rats of weights between 100 and 179g were assigned to eleven (11) groups of five (5) animals each. Group 1 (control) was given feed and water *ad libitum*. Group 2 was exposed to sodium arsenite (SA) at a dose of 4.1 mg/kg body weight (kgbw) for two weeks. Groups 3-11 were treated with ESEIG with or without SA. Treatment was done orally and lasted 28 days. Serum activities of AST, ALT, ALP, GGT as well as total bilirubin, (TBIL) and direct bilirubin, (DBIL) concentrations were assayed in serum in addition to histological assessment of liver tissues. Exposure to SA caused significant ($p < 0.05$) increases in all assayed parameters as well as histological anomalies such as vascular congestion and ulceration, infiltration of inflammatory cells and Kupffer cell activation when compared with control. However, treatment with ESEIG both simultaneously and 2 weeks after SA exposure, reversed the deleterious effects of SA. Paradoxically, administration of the ESEIG alone at different doses produced significant ($p < 0.05$) increases in all assayed parameters when compared with control except TBIL. The results obtained in this study suggest that ESEIG may be protective against SA-induced hepatotoxicity in Wistar rats and slightly toxic when administered alone, necessitating further studies.

Contribution/ Originality: This study is one of the very few studies that have investigated the effect ethanol stem bark extract of *Irvingia gabonensis* against sodium arsenite-induced hepatotoxicity in Wistar rats.

1. INTRODUCTION

Arsenic is a well-known environmental pollutant and a human carcinogen that contaminates groundwater in many parts of the World, including Nigeria [1-7]. Several epidemiological studies have shown that, exposure to trivalent and pentavalent forms of arsenic, which occurs Worldwide majorly through occupational and environmental exposure, causes characteristic skin alterations (ulceration), including hyperkeratosis and skin cancer [8]. Epidemiological studies conducted in some countries [9-13] indicated a connection between arsenic exposures from contaminated drinking water to carcinogenesis among the inhabitants. Cutaneous and hepatic manifestation of

arsenic-contaminated ground water is reported among a large number of inhabitants of various districts of West Bengal [14]. There are growing evidence that sodium arsenite intoxication can compromise liver integrity in mouse, rat, fish, and goat [15-18].

Attention has shifted to the use of medicinal plants especially those of high antioxidant properties in combating diseases, since most locals are unable to purchase orthodox drugs and therefore resort to readily available medicinal plants within their reach. *Irvingia gabonensis* O'Rorke Baill, also called bush mango or wild mango, is a non-timber forest product (NTFP) that is indigenous to most tropical forests in West and Central Africa [19, 20]. It is utilized in traditional and modern medicine for treatment of several illnesses [20, 21]. The stem bark has been reported to have antibacterial and antifungal activities [22]. Similarly, its stem bark is used to treat hunch back and infections in Cameroon [23]. There are also reports that the decoction of the stem bark is used for the treatment of gonorrhoea, hepatic and gastrointestinal disorders and the root bark is used in poultice form for treatment of wounds [24]. In French Equatorial Africa, the shavings of the stem bark are utilized for the treatment of hernias, yellow fever and dysentery, and to reduce the effects of poisons when consumed orally [25]. The stem bark is also mixed with palm oil for treatment of diarrhoea and for reducing breast-feeding period [25]. The hematological, hepatoprotective, anti-diabetic and prophylactic effects of its stem bark and leaf extracts have also been reported in animal models [26-29].

There is however a dearth of scientific information on the protective effects of its stem bark in conditions of toxicity, especially by a carcinogen. This study was therefore carried out to evaluate the effect of the ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill against sodium arsenite-induced hepatotoxicity in Wistar albino rats.

2. MATERIALS AND METHODS

2.1. Chemicals and Reagents

Sodium arsenite was obtained from BDH chemicals, Poole, England. Absolute ethanol was purchased from JHD, China. Teco diagnostic assay kits were used for liver function analyses. All other chemicals/reagents used in this study were of analytical grade and standard.

2.2. Collection, Authentication and Preparation of Plant Extract

Fresh and mature stem bark of *Irvingia gabonensis* O'Rorke Baill were harvested from Itak Ikot Akap village in Ikono local government area of Akwa Ibom State, Nigeria. The samples were identified and authenticated by a taxonomist of the Department of Pharmacognosy and Herbal Medicine, University of Uyo, Akwa Ibom State, Nigeria. They were washed using clean water to eliminate dust and other contaminants, prior to air-drying for 7 days on a clean table at room temperature in Biochemistry laboratory, University of Uyo, Uyo, Akwa Ibom State. They were then pulverized using a clean manual grinder and mortar and pestle and stored in an air-tight container prior to extraction.

Approximately 2800g of pulverized stem bark was macerated in absolute ethanol (JHD, China) and allowed to stay for 72 h with intermittent stirring to ensure proper extraction. The sample was filtered through a clean muslin cloth thrice and the filtrate was concentrated in stainless steel bowl using a water bath at 45°C. The paste-like gel extract obtained after continuous concentration was then transferred into pre-weighed transparent containers, weighed and stored in the refrigerator prior to use.

2.3. Experimental Animals

Fifty-five (55) healthy and non-pregnant female Wistar albino rats of weights between 100 and 179g were acquired at the animal house facility of Faculty of Basic Medical Sciences, University of Uyo, Uyo, Nigeria. They

were allowed access to feed and water *ad libitum*, and were acclimatized for seven (7) days in the same facility in a well-ventilated room under standard conditions.

2.4. Ethics

This study was carried out according to internationally accepted principles of laboratory animal use and care (NIH 85-23) and experiments were in accordance with CPCSEA ethical guidelines.

2.5. Experimental Design

After seven days acclimatization and just before the commencement of treatment, the experimental animals were assigned to eleven (11) groups of five animals each in standard animal cages. They were weighed using a digital weighing balance (Camry electronic scale EK5350, China) after overnight fast to obtain their initial body weights. Treatment was administered as shown in Table 1.

Table-1. Experimental design.

Groups	Treatment
1 (Normal control)	Feed and water <i>ad libitum</i>
2 (Positive control)	4.1mg/kgbw SA for 14 days
3 (Post-treatment)	4.1mg/kg bw SA for 14 days, followed by 100mg/kgbw extract for another 14 days
4 (Post-treatment)	4.1mg/kg bw SA for 14 days, followed by 200mg/kgbw extract for another 14 days
5 (Post-treatment)	4.1mg/kg bw SA for 14 days, followed by 400mg/kgbw extract for another 14 days
6 (Simultaneous treatment)	4.1mg/kgbw SA + 100mg/kgbw extract simultaneously for 14 days
7 (Simultaneous treatment)	4.1mg/kgbw SA + 200mg/kgbw extract simultaneously for 14 days
8 (Simultaneous treatment)	4.1mg/kgbw SA + 400mg/kgbw extract simultaneously for 14 days
9 (Extract only)	100 mg/kgbw extract only for 14 days
10 (Extract only)	200 mg/kgbw extract only for 14 days
11 (Extract only)	400 mg/kgbw extract only for 14 days

SA= Sodium arsenite; mg/kgbw = milligram per kilogram body weight.

2.6. Termination of Treatment, Collection of Blood Samples and Extraction of Liver Tissues

After the last treatment, all experimental animals were fasted overnight with access to water only, and their final body weights were obtained. The experimental animals were sacrificed under chloroform anesthesia by lower abdominal incision about 24 h after the last treatment. Blood samples were obtained by cardiac puncture using sterile syringes and needles and collected in sterile plain sample bottles for analyses. Sera were obtained from clotted blood samples in the plain bottles by centrifugation using a table top centrifuge (Model 800-1, Zeny Inc. Salt Lake, USA) at 3000 rpm for 15min. Separated sera were stored in the refrigerator at 4°C prior to analyses. Liver tissues were excised from the sacrificed experimental animals and rinsed with 1.15% ice cold potassium chloride (KCl, BDH, Poole, England) solution to remove traces of blood before weighing. A small portion of the excised liver was fixed in 10% neutral buffered formalin for histological assessment.

2.7. Liver Function Assays

Teco diagnostics assay kits (Anahaema, USA) were used for the determination of serum activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyltransferase (GGT) as well as the concentrations of total and direct bilirubin. Aspartate aminotransferase (AST) activity was determined according to the method of Young [30] while serum alanine aminotransferase (ALT) activity was determined according to the method of Young, et al. [31]. Serum alkaline phosphatase (ALP) activity was determined according to the method of Kochmar and Moss [32] serum gamma glutamyltransferase

(GGT) activity was determined according to the method of Young, et al. [31]. Serum total bilirubin (TBIL) and direct bilirubin (DBIL) were determined according to the method of Tietz [33].

2.8. Histological Assessment of Liver Tissues

Haematoxylin and eosin staining method (H&E) as described by Drury and Wallington [34] was used to prepare the liver tissues for histological assessment. After staining of tissues for histological studies, sections were viewed and examined under a Leica DM500 microscope and results were reported by a Consultant Histopathologist. Photomicrographs were taken using an attached Leica ICC50 digital camera.

2.9. Data Analysis

Results obtained are presented as mean \pm standard deviation (SD) and were analysed with one – way analysis of variance (ANOVA) for differences between groups with the aid of SPSS software (IBM, version 20). Values of $p < 0.05$ were considered statistically significant.

3. RESULTS

3.1. Effect of Ethanol Stem Bark Extract of *Irvingia gabonensis* O'Rorke Baill on Liver Function of Experimental Rats in Presence or Absence of Sodium Arsenite Toxicity

Results obtained showed that administration of sodium arsenite (group 2) led to significant ($p < 0.05$) increases in serum AST, ALT, ALP and GGT activities as well as significant ($p < 0.05$) increases in TBIL and DBIL concentrations when compared with the normal control. Post-treatment with the ethanol stem bark extract at the various doses produced significant ($p < 0.05$) decreases in serum activities of ALT, ALP and GGT in dose-dependent manner and significant ($p < 0.05$) decreases in serum AST activity in dose-independent manner when compared with group 2. Post-treatment with the extract also led to significant ($p < 0.05$) decreases in serum TBIL concentrations and non-significant ($p > 0.05$) differences in serum DBIL concentrations when compared with group 2. Similarly, simultaneous treatment with the extract at various doses produced significant ($p < 0.05$) decreases in all assayed parameters in dose-independent manner when compared with group 2.

Paradoxically, administration of the ethanol stem bark extract alone at various doses caused significant ($p < 0.05$) increases in serum activities of AST, ALT ALP and GGT as well as significant ($p < 0.05$) increases in serum DBIL concentrations at doses of 100mg/kgbw and 400mg/kgbw when compared with the normal control. However, administration of ethanol stem bark alone at various doses led to no significant ($p > 0.05$) differences in serum TBIL concentrations when compared with the normal control. The results are shown in Table 2.

3.2. Effect of Ethanol Stem Bark Extract of *Irvingia gabonensis* O'Rorke Baill on Liver Histology of Experimental Rats in Presence or Absence of Sodium Arsenite Toxicity

Intoxication of the experimental animals with sodium arsenite (SA) for a period of 14 days induced severe vascular ulceration, congestion perivascular infiltrates of inflammatory cells and Kupffer cell activation which are features of portal hepatitis in the liver. On administration of graded doses (100, 200, and 400mg/kgbw) of ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill both simultaneously and after 14 days of SA exposure (post-treatment), there was mild amelioration of the hepatitis with the post-treatment and a better amelioration with the simultaneous administration. The results are shown in the photomicrographs.

Table-2. Effect of ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill on liver function of experimental rats in presence or absence of sodium arsenite toxicity.

Groups	AST (U/L)	ALT (U/L)	ALP (U/L)	GGT (U/L)	TBIL (mg/dL)	DBIL (mg/dL)
Control	68.60±3.51 bcdefghijk	22.20±2.39 bcdefghijk	51.40±10.01 bcdefghijk	0.52±0.06 ^{bcdefghijk}	0.07±0.03 ^{bc}	0.03±0.01 ^{bcdeik}
Arsenite only	236.00±11.22 ^{acdefgh}	69.75±3.59 ^{acdefgh}	199.75±14.10 ^{acdefgh}	1.65±0.26 ^{acdefgh}	2.43±0.57 ^{acdefgh}	0.09±0.05 ^{afgh}
Post-treatment at 100 mg/kg	206.20±5.97 ^{ab}	57.80±4.32 ^{abe}	162.80±7.29 ^{abdef}	1.09±0.11 ^{abf}	1.50±0.35 ^{abdef}	0.09±0.01 ^a
Post-treatment at 200 mg/kg	207.20±5.40 ^{ab}	53.40±4.16 ^{ab}	150.20±4.87 ^{abc}	0.98±0.13 ^{ab}	0.18±0.02 ^{bc}	0.08±0.02 ^a
Post-treatment at 400 mg/kg	202.75±6.24 ^{abh}	49.75±4.50 ^{abc}	147.25±4.79 ^{abc}	0.88±0.10 ^{ab}	0.18±0.01 ^{bc}	0.07±0.01 ^a
Simultaneous at 100 mg/kg	202.00±9.59 ^{ab}	54.25±5.38 ^{abg}	143.50±7.59 ^{abc}	0.83±0.13 ^{abc}	0.18±0.02 ^{bc}	0.06±0.02 ^b
Simultaneous at 200 mg/kg	198.75±5.44 ^{ab}	48.00±4.24 ^{abf}	145.75±6.08 ^{ab}	0.85±0.13 ^{ab}	0.15±0.03 ^b	0.05±0.02 ^b
Simultaneous at 400 mg/kg	192.33±6.03 ^{abe}	48.67±2.52 ^{ab}	141.33±8.50 ^{ab}	0.77±0.15 ^b	0.17±0.04 ^b	0.05±0.02 ^b
Extract only at 100 mg/kg	191.67±1.53 ^a	51.67±4.51 ^a	143.67±7.51 ^a	0.47±0.35 ^{jk}	0.15±0.02	0.07±0.02 ^a
Extract only at 200 mg/kg	191.67±6.51 ^a	49.67±3.51 ^a	147.00±4.00 ^a	0.83±0.21 ^{ai}	0.15±0.01	0.05±0.02
Extract only at 400 mg/kg	190.00±5.29 ^a	52.67±3.51 ^a	142.33±9.02 ^a	0.80±0.20 ^{ai}	0.11±0.02	0.09±0.03 ^a

Data are expressed as mean ±SD, n=5; a= mean difference is significant at p≤0.05 when compared with group 1; b= mean difference is significant at p≤0.05 when compared with group 2 c= mean difference is significant at p≤0.05 when compared with group 3; d= mean difference is significant at p≤0.05 when compared with group 4 e= mean difference is significant at p≤0.05 when compared with group 5; f= mean difference is significant at p≤0.05 when compared with group 6; g= mean difference is significant at p≤0.05 when compared with group 7; h= mean difference is significant at p≤0.05 when compared with group 8 i= mean difference is significant at p≤0.05 when compared with group 9; j= mean difference is significant at p≤0.05 when compared with group 10 k= mean difference is significant at p≤0.05 when compared with group 11.

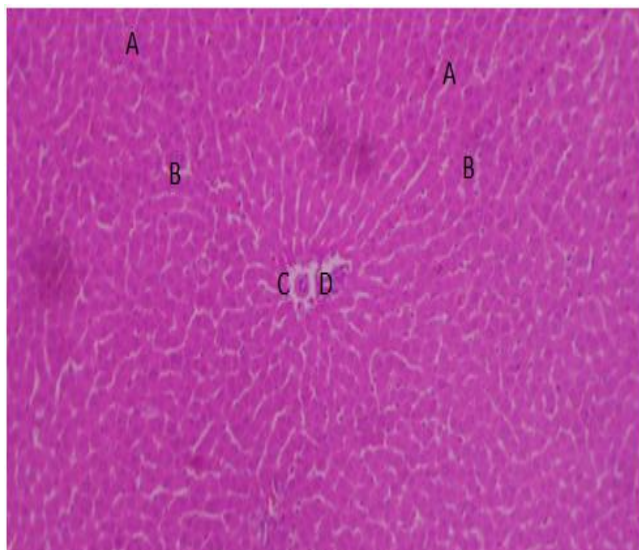


Figure-1. Liver section of rat Control (Group 1) composed of: A, hepatocytes, B, sinusoids, C, hepatic artery and D, bile duct (H&E x 100).

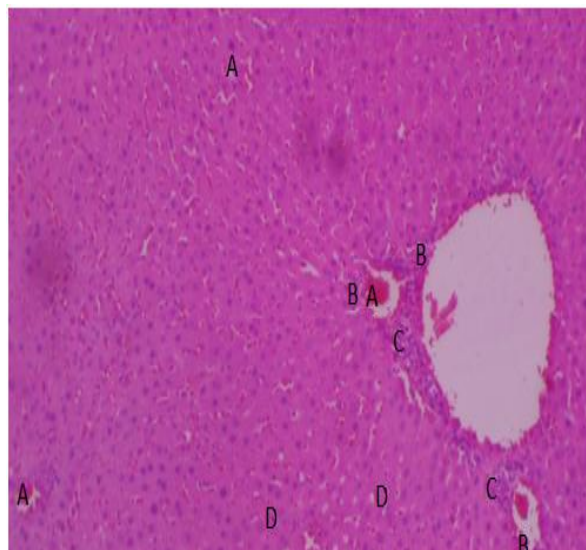


Figure-2. Liver section of rat given SA only (Group 2) showing: A, moderate vascular congestion, B, vascular ulceration, C, heavy periportal infiltrates of inflammatory cells and D, moderate Kupffer cell activation (H&E x 100).

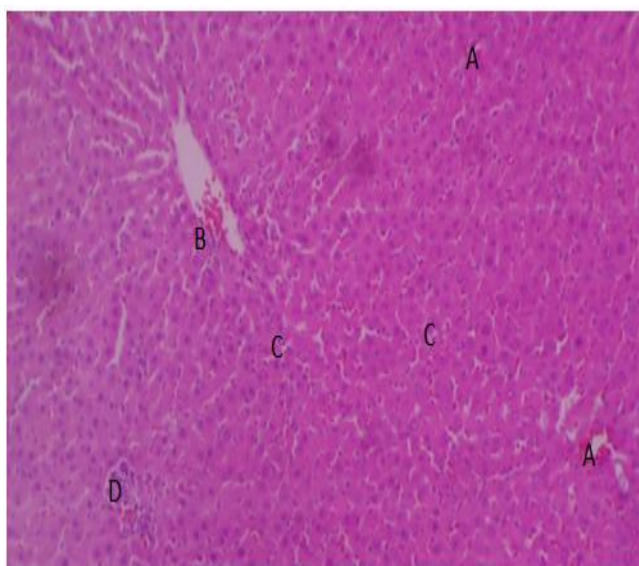


Figure-3. Liver section of rat given SA followed by 100mg/kg stem extract after 14 days (Group 3) showing: A, moderate vascular congestion, B, focal vascular ulceration, C, moderate Kupffer cell activation and D, mild periportal infiltrates of inflammatory cells (H&E x 100).

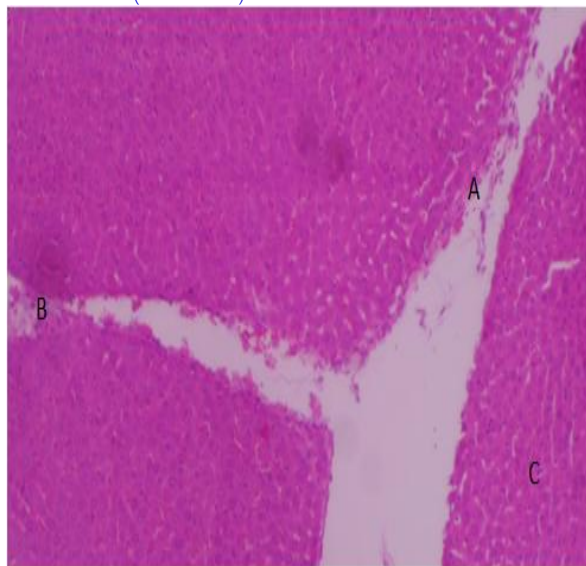


Figure-4. Liver section of rat given SA plus 200mg/kg stem extract after 14 days (Group 4) showing: A, mild vascular congestion, B, vascular stenosis, C, moderate Kupffer cell activation (H&E x 100).

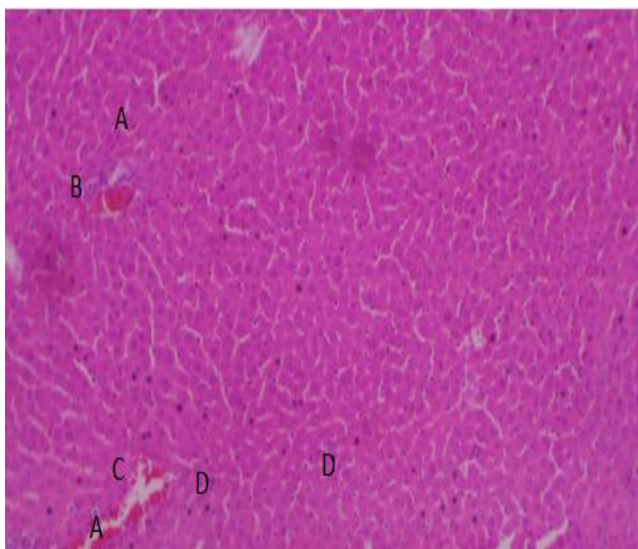


Figure-5. Liver section of rat given SA plus 400mg/kg stem extract after 14 days (Group 5) showing: A, vascular congestion, B, periportal infiltrates of inflammatory cells, C, vascular ulceration and D, moderate Kupffer cell activation (H&E x 100).

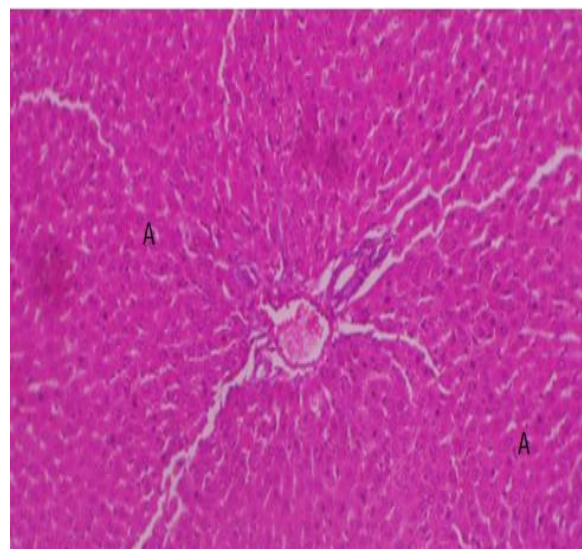


Figure-6. Liver section of rat given SA plus 100mg/kg stem extract simultaneously for 14 days (Group 6) showing: A, mild Kupffer cell activation (H&E x 100).

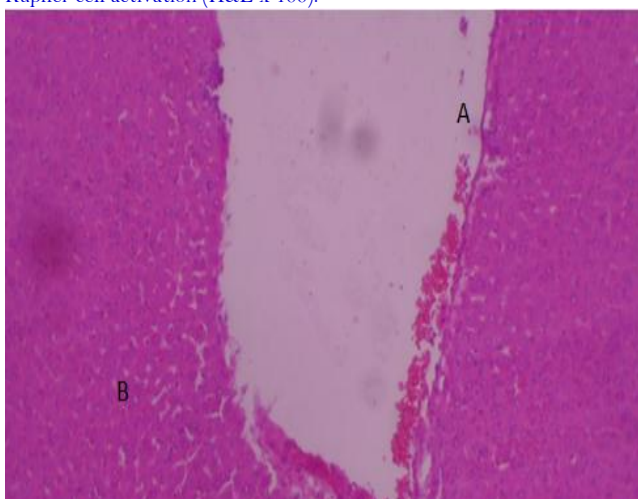


Figure-7. Liver section of rat given SA plus 200mg/kg stem extract simultaneously for 14 days (Group 7) showing: A, marked vasodilatation and B, mild Kupffer cell activation (H&E x 100).

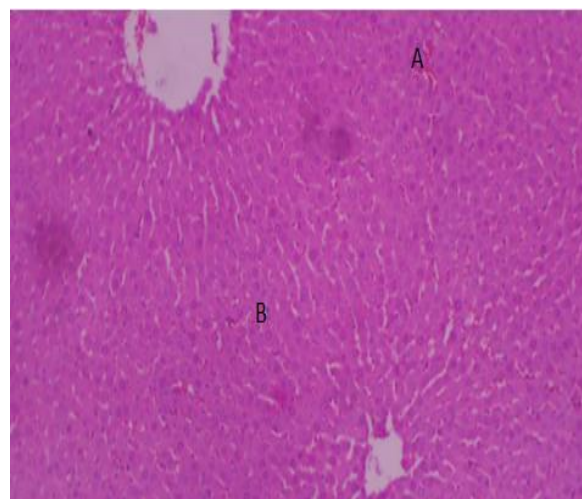


Figure-8. Liver section of rat given SA plus 400mg/kg stem extract simultaneously for 14 days (Group 8) showing: A, mild vascular congestion and B, mild Kupffer cell activation (H&E x 100).

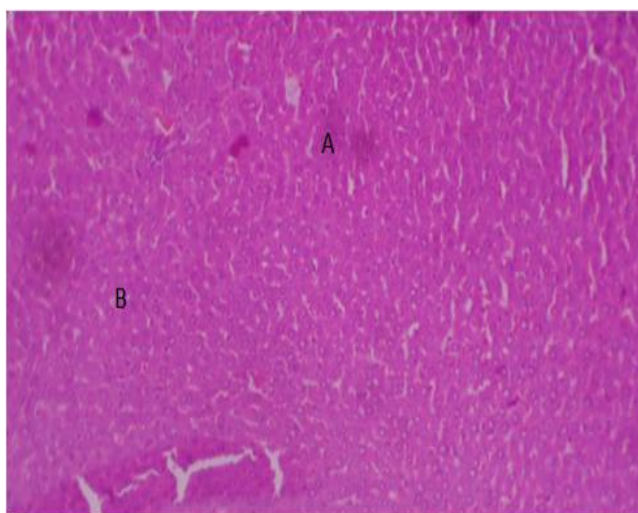


Figure-9. Liver section of rat given 100mg/kg stem extract only for 14 days (Group 9) showing: A, normal hepatocytes and B, mild Kupffer cell activation (H&E x 100).

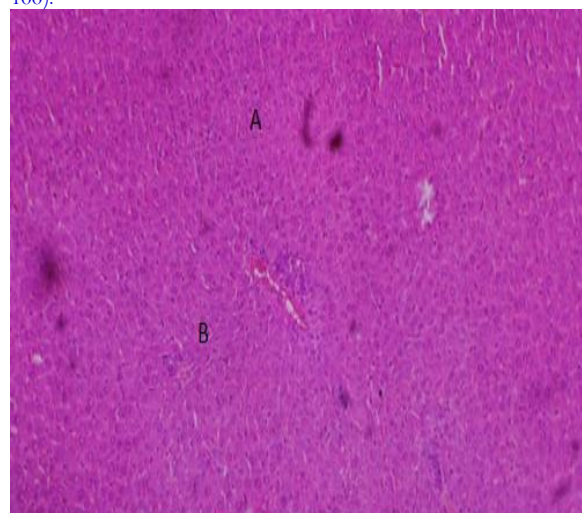


Figure-10. Liver section of rat given 200mg/kg stem extract only for 14 days (Group 10) showing: A, normal hepatocytes and B, Kupffer cell activation (H&E x 100).

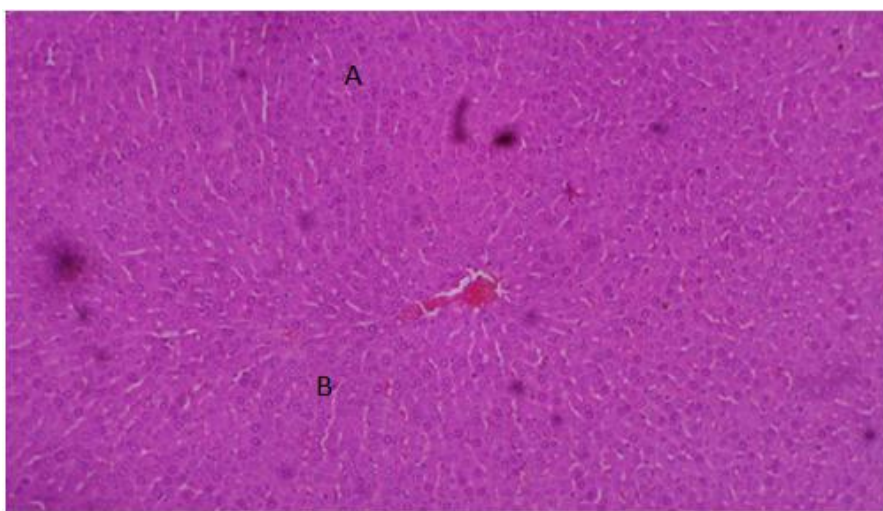


Figure-11. Liver section of rat given 400mg/kg stem extract only for 14 days (Group 11) showing: A, normal hepatocytes and B, Kupffer cell activation (H&E x 100).

4. DISCUSSION

The liver is an important organ for drug and xenobiotic toxicity (including arsenic toxicity) because most orally ingested xenobiotics and drugs pass through the liver where some are metabolized into toxic intermediates [35-37]. Assessment of liver function is done by evaluating the levels of some biomarkers in the blood and in the liver. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) belong to the transaminase family of enzymes. ALT catalyzes the transfer of amino group from L-alanine to α -ketoglutarate forming pyruvate and L-glutamate. On the other hand, AST catalyzes the transfer of amino group from L-aspartate to α -ketoglutarate forming oxaloacetate and L-glutamate in a reaction referred to as transamination reaction [38]. They are largely found in the liver and small amounts are also found in some other tissues of the body [39-43]. An injury to the liver which may be due to exposure to toxic substances, leads to an elevation in blood levels of AST and ALT. The levels of these enzymes in the blood are therefore directly related to the extent of the tissue damage [43-46].

In the present study, administration of sodium arsenite alone produced significant elevations in serum AST and ALT levels when compared with control. This may be attributed to damaged structural integrity of the liver orchestrated by sodium arsenite, culminating in the leakage of these enzymes into the blood stream. This indicates that sodium arsenite induced hepatocellular necrosis in the exposed experimental animals [47] and it is consistent with findings from previous studies [48, 49].

Treatment with ethanol stem bark extract of *Irvingia gabonensis* O'Rorke baill both simultaneously and two weeks after (post-treatment) produced significant decreases in AST levels when compared group 2 (administered sodium arsenite only). Similarly, treatment with ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill both simultaneously and two weeks after (post-treatment) produced significant decreases in ALT levels in dose-dependent manner when compared with group 2 (administered sodium arsenite only). However, administration of ethanol stem bark extract of *Irvingia gabonensis* O'Rorke baill alone at different doses produced significant increases in AST and ALT levels, when compared with control. This suggests a slight hepatotoxicity of the ethanol stem bark extract when administered singly.

Alkaline phosphatases are enzymes that catalyze the hydrolysis of organic phosphate in several molecules like nucleotides, proteins and alkaloids at alkaline pH, hence the name alkaline phosphatase [50]. Tissue-nonspecific alkaline phosphatases (TNSALPs) occur in several tissues but are particularly high in concentration in skeletal, hepatic and renal tissues as well as intestinal wall and placenta [51, 52]. Elevation of serum ALP activity indicates the presence of diseases such as liver and bone diseases [53]. Elevated serum ALP levels may also be indicative of bile duct obstruction [52]. Serum ALP activity may also be elevated due to primary neoplasm at site other than liver and non-neoplastic hepatobiliary diseases, such as in xenobiotic-induced hepatotoxicity [54].

Gamma-glutamyltransferase (GGT) is a cell-surface protein that catalyzes the extracellular catabolism of glutathione, in the main mammalian cells [55, 56]. It is produced in several tissues but a higher percentage of GGT in serum is derived from the liver [57]. The determination of serum GGT activity is a well established diagnostic test for hepatobiliary diseases, and it's used as a sensitive marker of liver damage. Elevated serum GGT activity is associated with diseases of the liver, biliary system and pancreas [58, 59]. High level of GGT has been reported to be a marker of metabolic syndrome [60]. Documented evidence has shown that the liver (the primary source of circulating GGT) is a major target organ for the development of metabolic syndrome. A high level of GGT is closely associated with hepatic steatosis [61-64] which in turn is strongly associated with metabolic syndrome [65-69]. Furthermore, GGT is an early predictive biomarker for various hepatic diseases and life-threatening cancers alongside other disease conditions such as atherosclerosis, heart failure, arterial stiffness and plaque and gestational diabetes [56].

In the present study, administration of sodium arsenite alone produced significant elevations in serum ALP and GGT levels when compared with control. However, treatment with ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill both simultaneously and two weeks after (post-treatment) produced significant decreases in serum ALP and GGT levels when compared with group 2 (administered sodium arsenite only). Paradoxically, administration of ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill alone produced significant increases in serum ALP and GGT levels when compared with control. This is also suggestive of the possible hepatotoxic effects of the ethanol stem bark extract when administered singly on sub-chronic basis.

Bilirubin is the end product of haemoglobin breakdown [47] and serves as a biomarker of liver and blood disorders. Serum bilirubin is a mixture of α , β , γ and δ fragments which are unconjugated, singly conjugated, doubly conjugated and covalently bound to albumin, respectively. Conjugated bilirubin is also referred to as direct bilirubin [70]. An elevated serum bilirubin level indicates the presence of liver disease and conjugated hyperbilirubinemia (high levels of serum conjugated bilirubin) occurs in disease conditions such as hepatocellular damage, viral hepatitis and toxic or ischemic liver injury [47, 71-73].

In the present study, administration of sodium arsenite alone produced significant and non-significant increases in serum total bilirubin (TBIL) and direct bilirubin (DBIL) concentrations when compared with the control. This suggests the interference with the transport function of the liver by sodium arsenite [47].

Treatment with ethanol stem bark extract of *Irvingia gabonensis* O'Rorke baill both simultaneously and 14 days after (post-treatment) produced significant decreases in serum TBIL concentrations when compared with group 2 (administered sodium arsenite only). On the other hand, post-treatment with the ethanol stem bark extract led to no significant differences in serum DBIL concentrations whereas simultaneous treatment produced significant decreases in serum DBIL concentrations. Furthermore, administration of ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill alone produced non-significant differences in serum TBIL concentrations and significant increases in DBIL concentrations when compared with control.

Histopathological assessment of liver tissues showed that there were no visible lesions in the liver of the animals in the control group. In contrast, exposure to sodium arsenite alone produced vascular congestion and ulceration, infiltration of inflammatory cells and moderate Kupffer cell activation. On administration of graded doses of ethanol stem bark extract, 14 days later and simultaneously, there was mild amelioration of the hepatitis with the first modality and a better amelioration with the simultaneous treatment. This is consistent with findings from previous studies on the hepatotoxicity of sodium arsenite [74, 75].

Generally, co-administration of sodium arsenite and ethanol stem bark extract of *Irvingia gabonensis* O'Rorke Baill showed potential protective effect of the extract. However, administration of the ethanol stem bark extract alone at various doses indicated a potential toxicity of the same extract when compared with control, which was a common trend in almost all the assayed parameters. It is therefore possible that sodium arsenite exerted antagonistic effect on the ethanol stem bark extract which manifested as protective effect when compared to group

2, administered sodium arsenite only. Other studies have also reported the antagonistic effects of different established toxicants when co-administered. Aliyu and co-workers had reported the suppressive activities of ethanol on the effect of sodium arsenite in Wistar albino rats Muhammad, et al. [76]. Ubani-Rex, et al. [77] have also reported antagonistic effects between the heavy metals, copper and lead in *Clarias gariepinus* [77]. Similar findings were reported by Montvydienė and Marčiulionienė [78] in a study using *Lepidium sativum*.

5. CONCLUSION

The findings from this study suggest that ethanol stem bark extract of *Iringia gabonensis* O'Rorke Baill may possess some medicinal properties against sodium arsenite-induced hepatotoxicity in Wistar rats. However, the possible mechanisms responsible for the observed slight hepatotoxic effect of the extract when administered alone need to be unraveled.

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Competing Interests: The authors declare that they have no competing interests.

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