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Hepato-Renal-Curative Effect of the Herbal Supplement of *Aloe vera* Linn Gel versus *Moringa oleifera* on Acetaminophen-Induced Dama ge on the Liver and Kidney of Wistar Rats (*Rattus novergicus*)

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Authors' contributions

This work was carried out in collaboration between both authors. Author COA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors HDK and COA managed the analyses of the study. Authors COA and HDK managed the literature searches. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Acetaminophen (APAP, paracetamol) is the most frequently used over-the counter analgesic and antipyretic drug. Conversely, its overdose leads to both liver and kidney damage. Several scientific reports have focused majorly on protective effects of medicinal plants on APAP – induced hepato-renal-toxicity. actually, there is a dearth of work on the hepato-renal-curative effects of the herbal drugs supplements on APAP induced toxicity.
Aims: In the present study, *Aloe vera* (ALOV) gel versus *Moringa oleifera* (MORN) leaf supplement effects was evaluated curatively against Acetaminophen (APAP) induced hepato- renal-toxicity.

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Study Design: This study was an experimental study in the Animal House of the Department of Pharmacology University of Port Harcourt. The work lasted for 7 days.
Methodology: Twenty adult wistar rats weighing 185-220 g were divided into four (4) groups of five (5) animals each and treated orally as follows: group 1(normal control) received distilled water (7days), group 2 received 1 g/kg acetaminophen (APAP) (2 days), whereas group 3-4 received APAP (2 days) followed by 500 mg/kg of ALOV and MORN supplements respectively for 5 days. At the end of the experiment, animals from different groups were anaesthesized, the liver and kidney tissues were dissected and blood collected subjected to different biochemical, antioxidants, and histopathological test.
Statistical Analysis: was done using One-Way Anova followed by Tukey's Post-hoc Test.
Results: APAP caused significant ($P<0.05$) decrease in creatinine with significant ($P<0.01$) increase and decrease in liver enzymes and renal catalase levels respectively in relation to normal control. Treatment of rats with the ALOV and MORN supplements attenuated the elevated liver and kidney biochemistry as well as improved histopathological alterations by APAP treatment.
Conclusion: The supplements demonstrated restorative ability. MORN and ALOV supplements extract can be suggested as a convincing remedy against APAP-induced hepato-renal-toxicity.

Keywords: Acetaminophen; toxicity; curative; Aloe vera; Moringa oleifera; supplement; gel; wistar rats.

ABBREVIATION

MORN: Moringa oleifera
ALOV: Aloe vera

1. INTRODUCTION

Liver and kidney are vital organs in the body entailed in the regulation of internal chemical environment Abdel-Azim SA et al. [1]. Therefore damage to these organs due to toxic agent is of serious consequences.

Acetaminophen (APAP) also known as paracetamol, is the most commonly used over-the counter analgesic and antipyretic medication. However, its abused leads to both liver and kidney damage Abere TA et al; Aboelhassan DM et al. [2,3]. APAP-induced toxicity is considered as one of the primary causes of acute liver failure; numerous scientific reports have focused majorly on APAP hepato-toxicity and renal-toxicity.

Toxicity of Acetaminophen as well as preventive, protective and curative effects of some herbal drugs had been widely reported. Several herbal drugs had been entwined in curing and protecting and attenuating acetaminophen toxicity on the liver and kidney damages Ali MD; [4]. Subsequently reliance on medicinal plants is progressively rising in developing countries Al-Quida MMA et al. [5,6].

Aloe vera (*Aloe barbadensis* Linn) is a succulent perennial cactus–like draught resisting plant which has been used for traditional medical uses for thousands of years. Clark DJ et al. [7] *Aloe vera* leaves comprises of the latex (a bitter yellow liquid beneath the epidermis of the leaf) and the gel (a colourless and tasteless substance) in the inner part of the leaf, both of them have many biologically active components, and possesses anti-oxidant, laxative, anti-bacterial, anti-fungal, antiviral and anti-tumor effects El-Badwi and Tayib [8]. It also possesses hypoglycemic, anticancer and gastro protective properties Elkott AF et al. [9].

Moringa oleifera is the most widely cultivated species in the genus moringa and only genus in the plant family *Moringaceae* Elmasry A et al. [10]. It has been praised for its health benefits for thousands of years Farreli SE [11]. It contains healthy antioxidants and bioactive plants Guengerish P [12]. Scientist has been able to investigate a fraction of the many outstanding health benefits. It is very nutritious, containing Protein, Vitamin A, VitaminB_2, Vitamin C, Iron, and magnesium. It is used as food preservative. It may lower blood pressure levels, reduce inflammation, lowers cholesterol, protects against drug toxicity Gulnaz H et al. [13].

Additionally, in the absence of reliable kidney and liver protective and curative drugs in modern medicine; herbal drugs play a major role in the treatment of hepatic and renal disorders. Moreover, scientific literatures have prescribed various medicinal plants/herbs such as *Aloe vera* and *Moringa oleifera* which had been extensively studied for their roles in curing and protecting the kidney and the liver due to the presence of hepato-renal-protective and curative activities Ali MD [5].
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There is paucity of literature on the comparison of hepato-renal-curative effects of these herbal drugs on acetaminophen-induced liver and kidney damage.

Therefore this study was designed to ascertain the hepato-renal-curative effect of *Aloe vera* gel versus *Moringa oleifera* supplements on acetaminophen induced liver and kidney damage.

2. MATERIALS AND METHODS

2.1 Procurement of Animals

Twenty (20) healthy male adult wistar rats weighing 185-220 g were obtained from the animal house of the Department of Pharmacology of the University of Port Harcourt.

The rats were maintained under 12 hour's light-dark cycle. Rats were housed in polypropylene cages and fed with finishers' marsh. They were allowed free access to regular tap water *ad libitum.*

Rats were acclimatized for one week before the start of the study. Handling of experimental animals was in accordance with the National Institute of Health Guide for care and use of Laboratory Animals Habibi G [14].

2.2 Plant Materials

The plants supplement are pure herbs.

Aloe vera gel (ALOV) was purchased from Forever Living Products.

Moringa oleifera leaves powder supplement was purchased from Chidi-Soky Pharmaceutical and Allied Products Limited, Port Harcourt, Nigeria.

2.3 Experimental Design

This is an experimental study carried out in the Animal house of Pharmacology Department faculty of Health science. University of Port Harcourt Nigeria. In this studies, standard drugs are administered to rats for a period of time before treatment with the test drugs are administered to alleviate the effect of the toxins in the liver and kidney of the experimental animals.

The standard drug here is the acetaminophen while test drugs are, ALOV and MORN supplements.

Twenty (20) adult wistar rats were divided into four groups having 5 rats each (n=5). The powder supplement and gel extracts of the herbal drugs were dissolved in distilled water.

The animals were fasted for twenty four hours, prior to the experiment under standard laboratory condition, but were allowed free access to water *ad libitum*. After 24 hours, Group A: Normal control group (NORC) received distilled water (5 ml/kg) orally from the 1st day of the experiment to the seventh day. Group B: Acetaminophen treated group which serves as negative control group received a single dose of acetaminophen (APAP) (1000mg/kg) dissolved in 5ml of distilled water orally for two days.

Group C: *Aloe vera* group C (APAP+ALOV) and Group D:(APAP+MORN), which served as curative groups were administered with Acetaminophen only on day 1 and Karthivashan G et al; Koroye OC et al. without the administration of the test drug and the test drug gel supplement administered without the toxin from day 3 to day 7 according to the method described by Juma KK et al. [15]. The weight of the animals was measured on the first, fourth, and seventh day of drugs and extracts administration respectively and dosage adjusted according to change in body weight.

Twenty-four hours after drugs administrations, the animals in each group were anaesthetized. Blood samples were collected after blood collection, animals were sacrificed, liver and kidney tissues removed for histopathological tests Karthivashan G et al.; Koroye OC et al. [16,17].

2.4 Biochemical Evaluation

All the rats were fasted for 12 hours at the end of the treatment period. The blood was collected by cardiac puncture using sterile disposable syringes under mild chloroform anesthesia. Sera were separated out by centrifuging at 3000rpm or 10 minutes to get serum for Biochemical parameters study. The animals were then sacrificed by cervical and homogenized for histopathological studies.

2.5 Liver Enzymes Assessment

Liver enzymes biochemical was assayed by collecting the sera. Liver enzymes assayed are; Alanine aminotransferase (ALT), alkaline phosphatase (ALP) and Aspartate aminotranferase (AST), other liver biochemical parameters measured include; Total Bilirubin (TB), Total protein (TP), and Albumin (Alb) levels using the Hitachi 902, Automatic Chemical Analyzer.

2.6 Kidney Assay Test

Kidney function assessments like Creatinine, Blood Urea Nitrogen (BUN), and cholesterol. Blood Electrolyte such as Bi-carbonate (CB), sodium (Na), potassium (K), chlorides (Cl) were measured using commercially available kits. Kidney specimens from all groups of rats were collected immediately after they were sacrificed. Tissues were fixed in 10% buffered normal saline, processed well and then embedded in paraffin wax. Tissue sections of 5 µm were obtained and stained with Hematoxylin and Eosin (H&E). The sections examinations were performed under a light microscope.

2.7 Histopathology

2.7.1 Hepatic histopathology test

The liver tissue was dissected out and fixed in the 10 % formalin, dehydrated in gradual ethanol cleared in Xylene and embedded in paraffin wax sectioned (50μm) with a rotary microtome and were stained with Haemotoxylin and eosine (H&E).

The liver sections were evaluated histologically with light microscope with camera attached to it. The liver sections were scored and evaluated to the severity of the hepatic injury.

2.8 Renal Histopathology Test

The kidney was freed from connective tissue coverings and gently removed, weighed and examined microscopically 3-5mm^2 thick pieces were excised from the organ and fixed in 10% formations solutions, dehydration in ascending grades of alcohol (ethanol), cleared in xylene and embedded in paraffin. 50μm thick sections were obtained and subsequently strained with eosine and haematoxylin and PAS and examined under light microscope Karthivashan G et al. [16].

2.9 Antioxidant Biomarkers

Hepatic and Renal Antioxidant: Glutathione (GSH), Superoxide Dismutase (SOD), Malondialdehyde (MDA) and Catalase (CAT) were determined using method described by Juma KK et al. [15].

2.10 Statistical Analysis

Statistical Analysis was conducted using Statistical package for Social Sciences (SPSS) version 20. (Chicago IL, USA) The mean value of data collected was represented as means, standard error of mean (S.E.M). The data were analyzed using one-way analysis of Variance (ANOVA) and the difference between the groups was determined using Tukey's Post Hoc test. The level of significance was set at 5%.

3. RESULTS

3.1 Effect of the Extracts on the Liver Marker Enzymes

The effect of the drugs on serum enzymes of APAP intoxicated rats is shown in Table 1.

There was significant rise in the AST, ALT and ALP enzyme in all treated rats; APAP+MORN, APAP+ALOV and APAP, ($P<0.05$) compared to NORC and significant ($P<0.05$) reduction on the liver enzymes of APAP+ ALOV and APAP+MORN compared to APAP group.

3.2 Effects of the Extracts on Bilirubin, Albumin and Total Protein

The effect of the drugs on other liver parameter of APAP intoxicated rats is shown in Table 2.

The administration of a single dose of APAP, (APAP+ALOV and APAP+ MORN) groups produced no significant ($P>0.05$) effects in Total bilirubin, Albumin and Total Protein, levels on the liver of the group administered with APAP compared to NORC group.

3.3 Effects of the Extracts on Kidney Markers

As shown in Table 3 APAP, Groups (APAP+ALOV) and (APAP+MORN) treated rats kidneys showed significant ($P<0.01$) rise in serum creatinine, when compare to normal control.

3.4 Effects of the Extracts on Kidney Electrolytes

Table 4 showed that, there was significant ($P< 0.05$) elevation in sodium level on the kidney biomarkers of the group administered with APAP+ALOV compared to normal control.

3.5 Effect of the Extracts on Kidney Histopathology

Renal histological results Plates 1-4 (A1b-D2b) showing the kidneys of rats treated with APAP and *Aloe* vera gel, *Moringa oleifera*, powder supplement extract.

Table 1. Effects of the extracts on liver enzymes

Groups	AST (U/L)	ALP (U/L)	ALT (U/L)
NORC	57.20±3.99	37.00±2.07	27.00±2.03
APAP	98.20±5.77**	58.40±2.38*	48.60±2.82*
APAP+ALOV	77.80±5.39*	44.40±4.80	56.80±0.86**
APAP+MORN	78.00±0.89*	58.60±2.73**	41.20±3.94

*Values are given as mean ± SEM for 5 rats in each group; experimental groups are compared with Group A. *p<0.05, **p<0.01 vs APAP group;* Keys: *AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, ALP- Akaline phosphatase*

Table 2. Effects on other liver marker

Groups	TP(g/L)	ALB (g/L)	TB (g/L)
NORC	63.40±3.54	38.40±0.98	5.34±0.25
APAP	65.40±2.2	37.80±0.6	7.60±0.57
APAP+ALOV	65.00±1.64	38.40±1.21	7.14±0.65
APAP+MORN	60.40±1.50	34.20±2.18	7.02±0.21

*Values are given as mean ± SEM for 5 rats in each group; experimental groups are compared with Group A. *p<0.05, **p<0.01 vs APAP group; Keys ⇨ TP- total protein, ALB- albumin, TB- total bilirubin*

Table 3. Effects of the extracts on kidney markers

Groups	Urea	Creatinine	Cholesterol
NORC	2.74±0.13	98.40±4.70	42.00±2.78
APAP	4.68±0.22	130.00±6.16*	49.20±1.24
APAP+ALOV	5.22±0.07	142.20±1.24**	49.40±1.57
APAP+MORN	4.30±0.19	130.60±2.79**	42.60±1.69

*Values are given as mean ± SEM for 5 rats in each group; experimental groups are compared with Group A. *p<0.05, **p<0.01 vs APAP group*

The histological investigation of the kidney section of the normal control group as illustrated in Plate 1 (NORC), showed histologically normal kidney and renal tubules. APAP group (B1b) produced k severe distortion of the renal tubules, and shrinkage of glomeruli as illustrated in Plate 2.

APAP+ALOV as shown in Plate 3 (C1b) indicated distorted kidney with distorted renal tubules (RT) with some preserved features and APAP+MORN Plate 4 (D) and distorted glomeruli (G) with sparsely distributed preserved glomeruli as illustrated in Plate 4 (D1b)

3.6 Effect of the Extracts on Liver Histology

The histological investigation of the liver tissue of normal control group as illustrated in plate 5 (A1b) showed normal liver showing good hepatocytes with central vein (CV) containing blood cells as well as normal hepatic sinusoids.

Acetaminophen group produced alteration of liver architecture, vacuolation of hepatocytes, sinusoids, central vein and portal triad as illustrated in Plate 6 (B1b).

Group (APAP+ ALOV) liver tissue of treated rats as illustrated in Plate 7 (C2b)) showed mildly distorted liver tissue with few vacuoles/ widened sinusoids, the greater part of the micrograph is occupied by normal liver histology.

Liver tissue of group (APAP+MORN) (treated rats group as illustrated in Plate 8 (D2b) showed generalized vacuolated tissue with small vacuoles, micro and macrovesicular steatosis showing area of normal hepatocytes.

4. DISCUSSION

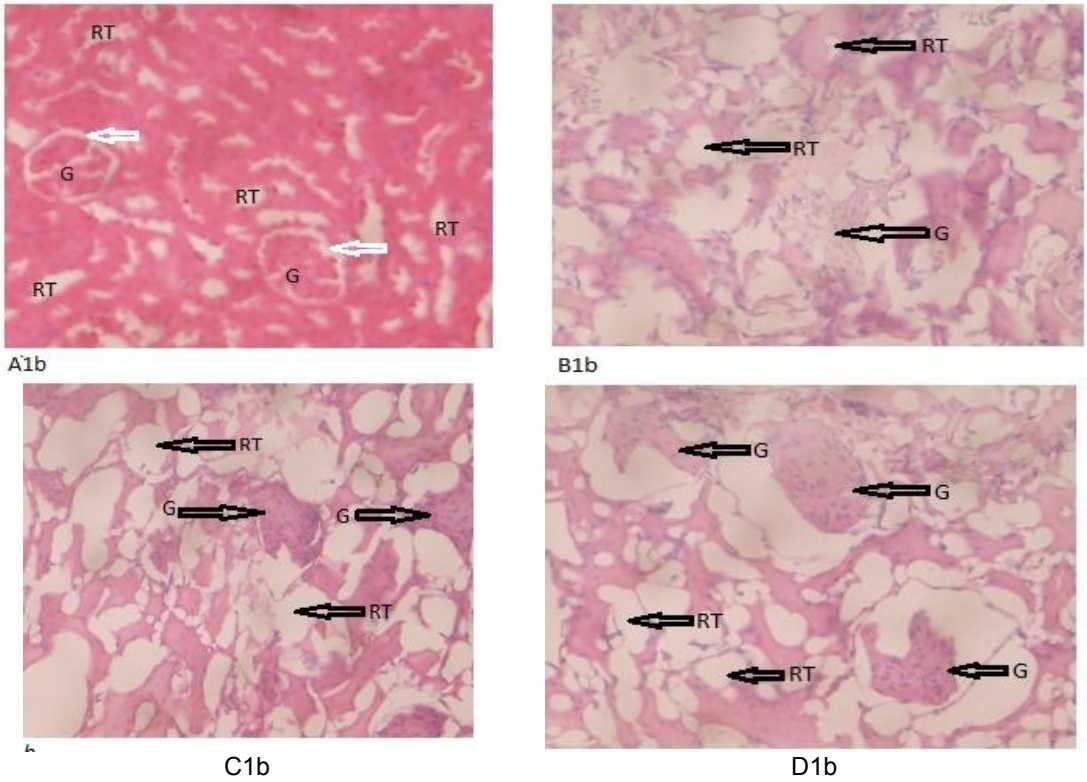
Liver and kidney are imperative organs in the body entailed in the regulation of internal chemical environment. Therefore damage to these organs due to toxic agent is of serious consequences.

Following acetaminophen intake, majority of the drug is metabolized by sulphation and glucuronidation to unreactive metabolites Ali, MD [4]. Abused of Acetaminophen, cause large

Table 4. Effects of the extracts on kidney electrolytes

Groups	Sodium	Potassium	Chloride	CB (µmol/l)
NORC	113.80±4.15	5.42±0.27	26.20±3.31	4.36±0.42
APAP	142.20±8.38	7.58±10.44	26.80±1.02	3.98±0.42
APAP+ALOV	151.00±4.35**	7.48±0.59	25.60±1.33	4.78±0.54
APAP+MORN	130.00±2.61	4.88±0.25	28.40±0.75	4.48±0.13

*Values are given as mean ± SEM for 5 rats in each group; experimental groups are compared with Group A. *p<0.05, **p<0.01 vs APAP group; CB- Bicarbonate*

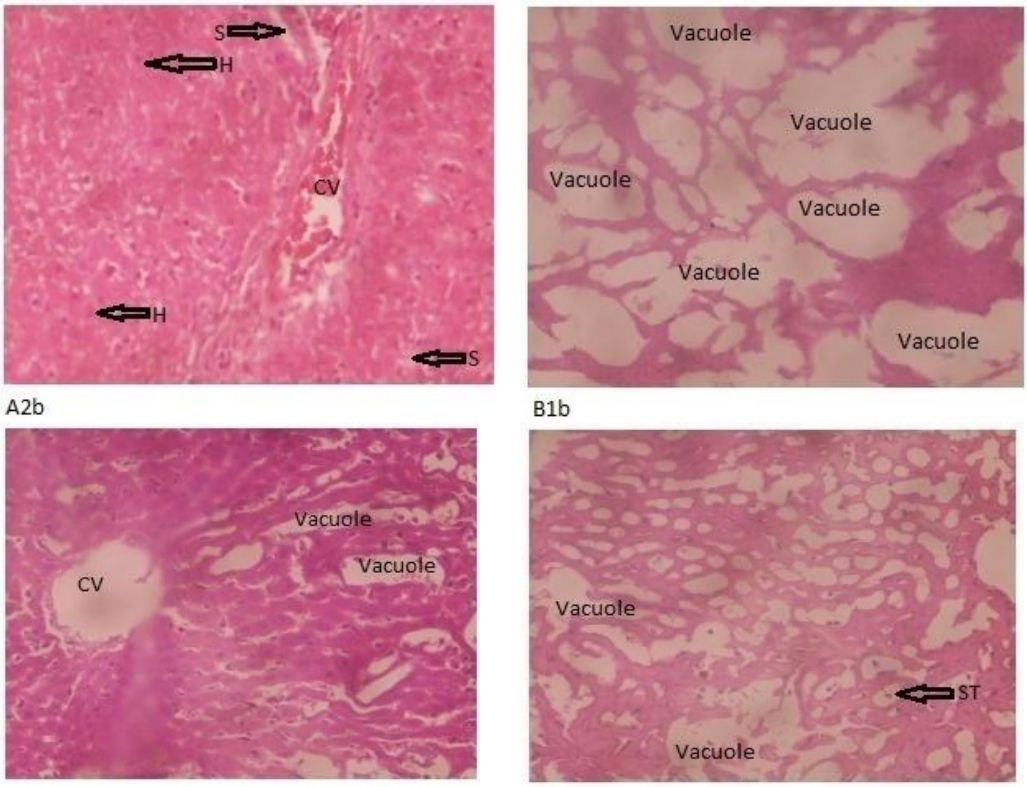


Plates 1-4. Histopathological photomicrographs of Kidney tissues of rats treated with acetaminophen before different extracts treatment (x400). (A1b) Normal control, (Bib) Acetaminophen (negative control), (C1b) *Aloe vera*, (\D1b) *Moringa oleifera*

amount of APAP to generate cytochrome P450 enzymes Cyp2e1 in rats leading in the formation of reactive metabolite N-acetyl P-benzoquinoeimine (NAPQI), thereby resulting to the saturation of the hepatic glucoronide and sulphate then increase the P450 sulphate conjugation pathway triggering the oxidation pathway Lee WW; Maduka H et al. [18,19].

Damage to or effect on target organs often results in increase in investigational chemistry parameters such as ALP, AST, ALT (liver) Urea and creatinine (kidney) increase in levels of the serum creatinine and urea had been considered as index of assessing renal-toxicity. Severity of the kidney damage is caused by the paracetamol Mahmoud MF et al. [20]. In the present study, the ability of two herbal drugs to protect or cure drug-induced hepto-renal toxicity was assessed.

In this work, acetaminophen administration resulted in the elevated increase in ALP, AST and ALT, TB and TB levels. The rise in the levels of alanine amino transferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities in the serum were used to measure liver damage while rise in the blood urea nitrogen and creatinine were used to measure the level of damage to the kidney. Therefore, serum hepatic biomarkers analysis is important for identification of liver damage Masoud RE [21].



Plates 5-8. histopathological photomicrographs of liver tissues of rats treated with acetaminophen before different extracts treatment (x400). (A1b) Normal control, (Bib) Acetaminophen (negative control), (C2b) *Aloe vera*, (D2b) *Moringa oleifera*

In this work, high level of AST and ALT was shown which indicated that AST and ALT were released into circulation indicating liver damage. Rise in AST and ALT (is a more specific marker of liver damage) showing cellular leakage and loss of functional cohesion of parenchyma cell in the liver.

Acetaminophen overdose or abuse results in permanent obliteration of liver cells in turn resulting in alarming and absolute high elevation in serum level of enzymes ALT, ALP, and AST Mathew C et al. [22]. This is in agreement with Juma KK et al; Michael MC [15,23] who reported that paracetamol intoxication produced a significant increase in AST, ALT ALP. In our work, APAP administration (1000mg/kg) caused acute liver injury in rats, characterized by an increase in serum activity of transaminase and phosphatases (AST, ALT and ALP).

This is also similar to Mingzhi and Hongbo; Mohammad SI et al. [24,25] who reported that acetaminophen administration produced a significant rise in liver enzymes and this leakage of enzymes is due to hepatotoxicity which caused the alteration of the activity of the liver function.

When there is damage of cell, cytoplasmic transaminase will be released thereby leading to the damage of the liver structure cohesion, because these are normally located on the cytoplasm, mitochondrial and microsome released into the circulation after cellular damage Odo, GE et al. [26] or due to the alteration to the cell membrane permeability, increase anabolism and reduction in breaking down of aminotransferase. This is also in agreement with Okokon JE et al; Onwubuariri TC [27,28] whofound out that serum levels of both ALT and AST were elevated almost four folds in acetaminophen treated group in relation to control. Decrease in serum, plasma level of total protein, albumin is also the evidence of chronic liver damage.

Similar to our work, Owolabi and Ogunnaike [29] reported that acute acetaminophen toxicity induced remarkable elevation on plasma ALT, AST and ALP action and significantly decrease in plasma level of total protein and albumin of rats. It is also in agreement with Owolabi J et al. [30] who revealed that acetaminophen induced toxic injury of the liver of rats as seen by significant decrease in albumin level. This indicated the decrease in capacity of hepatic to synthesize protein and consequently liver weight.

The liver and kidney have the capacity to rejuvenate when left alone after acute toxicity Oyagbemi AA et al; Pathan MM et al. [31,32], subsequently, a single dose before curative treatment was administered before treatment.

In (APAP+ALOV), ALP was reduced. The present result is in agreement with Samuhasanector and Kajornvutaide [33] which revealed that *Aloe vera* is non toxic to the vital organs as it did not display alteration for all biochemistry values suggesting that *Aloe vera* might possess immune system amendment effect, which is an evidence of the cure of cellular and tissue damage under APAP condition.

Alternatively, APAP+ALOV did not show the expected result as compared to normal control, no significant different was seen when this group is compared to APAP group. This is in agreement with Sanchez M et al. [34] who reported that *Aloe vera* did not show the expected decrease in serum activities of AST and ALT as compared to APAP group. This may be due to the advert effect of APAP administration which had impaired the activity of glutathione-mediated detoxification as well as free radical suppressure activity. This was not in line with Lee WW [18], who reported that serum ALP was significantly decreased in rabbit, mice, rats and humans who were given *Aloe vera* juice.

The *Aloe vera* treatment result as contrarily to the expected result did not show decrease in ALT when compared to group B. This is consistent with the reported work of Senders P [35] who reported improvement in liver enzymes after *Aloe vera* administration. In APAP+ MORN group, the levels of AST and ALP were significantly ameliorated in comparison with APAP. Thus indicating that moringa possessed antioxidants properties which were able to improve the elevated state of the liver enzymes. Similar to the present work Stevens CO et al; Subramaya S etal; Toppo R et al. [36,37,38] reported that the extract can be toxic if overdose and the extract is drug dependent. The drug ameliorative feature can be as a result of the state of health of the hepatocytes and its response depends on the active effect of the hepato-protective drugs. Therefore, *Moringa oleifera* might have produced synergic anti toxicity or effects to alter the consequences of cellular activities thereby helping the liver to improve their state of health.

Administration of drugs in APAP+ALOV produced significant effects on the level of serum creatinine compared to normal control. There was also significant effect in the sodium electrolytes. This result is in agreement with Tumer TB [39] who reported electrolytes imbalanced after *Aloe vera* treatment. This could be as a result of drug interactions. No significant effect as compared to Acetaminophen group. This is in agreement with Samuhasanector and Kajornvutaide [33] who reported that there was no significant alteration in terms of biochemical effect on the rats.

APAP+MORN produced no significant related effects on the kidney cholesterol level when compared to normal control and APAP groups. This is dose dependent. APAP+MORN produced no significant related effects on the kidney electrolytes when compared to APAP group. Contrarily, Wang X et al. [40] reported significant lowering of blood electrolytes when compared with APAP.

Rats treated with (APAP+ALOV*)* produced CAT closer to the normal control indicating free radical scavenging property. This is in agreement with Werawatgano D et al. [41] who reported improved in hepatic GSH in *Aloe vera*- treated group when compared with APAP group.

Rats treated with (APAP+MORN) produced hepatic CAT concentration closer to the normal control indicating free radical foraging property. Significant rise in CAT and SOD compared to APAP group, showed improvement in liver biomarker indicating present of antioxidant which acts as hepato-protective effect. This is slightly similar to Owolabi and Ogunnaike [29] who reported improvement in hepatic antioxidant after *Moringa oleifera* administration to APAP intoxicated rats liver but dissimilar with GSH which in this result remain no significant when compared to APAP group. This may be as a result of diminished GSH after over utilization in free radical scavenging after APAP intoxication.

However, administration in APAP+ALOV showed significant rise in CAT, SOD. This result suggested that *Aloe vera* is renal-protective. This is similar to Samuhasanector and Kajornvutaide [33] who also reported improvement in renal antioxidant after *Aloe vera* administrations

APAP+MORN treated group produced significant increase in renal SOD, decrease in renal MDA and renal GSH.

The photomicrographs of the renal tissues of the experimental animals when illustrated histologically in PlateS 1-4 (A1b- D2b) as presented in the figures. The kidney of the control groups shows glomerular surrounded with bowman capsules and renal tubules of control groups as illustrated by A1b (Plate 1).

Hence, in kidney sections APAP as illustrated in Plate 2 caused severe changes in renal cells, distorted renal tubules and glomerular. This is similar to Karthivashan G et al. [16] who reported toxic effects of APAP on the kidney. This report also agreed with Lee WW [18] who reported that kidney sections of APAP treated group caused severe alterations in renal cells. Work of Ali MD [4] also reported disorganized glomerulus, dilated and inflammatory tubules

(APAP+ ALOV), the kidney micrograph showed distorted renal tubule, distorted glomeruli (plate 3). This is dissimilar to Tumer TB et al. [39] who reported that *Aloe vera* appear to be significantly nephrotoxic causing severe renal damage as well as chronic infiltration of the tissues.

Plate 4 (APAP +MORN) showed distorted renal tubules, distorted glomeruli with some preserved features. This result to some extent agreed with Lee WW [18] reported that kidney sections of the group treated with acetaminophen causes severe changes to the kidney but the treatment with *Moringa oleifera* help to retain the normal kidney architecture to almost normal features.

The hepatic tissues of the experimental animals are illustrated histologically in the photomicrographs presented in Plates 5-8 (Aib-D2b). Plate 5 illustrated histologically normal liver showing: hepatocytes (H) that are histologically good. There was present of central vein (CV) containing blood cells, hepatic sinusoids; that are histologically normal. In the APAP treated group, the liver tissue as illustrated in Plate 6 showed distorted and destroyed liver with vacuolation. This is in consistent with Juma KK [15] who reported ballooning and degeneration as well as sinusoidal congestion of the liver 24 hours after APAP administration. This also agreed with Mingzhi and Hongbo [24] who reported that in paracetamol treated group, there was distortion of liver architecture, there were also vacuolation of hepatocytes, infiltration with inflammatory cells, Cellular protein after covalent bonding of acetaminophen and its metabolites might trigger some series of events which resulted to liver damage. This is in line with the present result which showed vacuolated hepatocytes, distorted liver and sinusoidal.

The liver architecture of the group administered with *Aloe vera* as shown in plate 3 showed mildly distorted liver tissue, few vacuoles, greater part occupied by normal hepatocytes. This improvement in liver architecture is in line with Werawatgano D et al. [41] who reported improved histopathological architecture in liver tissue of rats treated with *Aloe vera*. Thus this improvement of liver architecture indicated reduction in oxidative stress; diminish in liver injury thereby restoring the hepatic GSH.

Liver section of rats treated in APAP+MORN group as shown in plate 3 showed small vacuole and few normal hepatocytes. This agreed with Stevens CO et al. [36] which reported that *Moringa oleifera* could produce synergistic antitoxicity effect to complement the liver. It provides prophylactic effects against the consequences of hepatocytes or helps improve the state of the liver. The work of Yadav A et al. [42] also reported that *Moringa oleifera* administration also mitigate the massive changes in hepatic and renal tissues.

5. CONCLUSION

ALOV and MORN supplements extracts remediated the liver and kidneys from APAP toxicity through enhancement of the endogenous antioxidant enzymatic level to counteract the oxidative stress environment (ROS). Biochemical results and histological findings, ALOV and MORN supplements extract suggested as convincing remedy against APAP-induced hepato-renal-toxicity. Thus, further extensive investigation of these supplements against APAP-induced hepato-renal in combination is encouraged.

The study concluded that *Aloe vera* gel and *Moringa oleifera* supplement extracts were comparable to each other in the liver and kidney damage caused by acetaminophen abused.

CONSENT

It is not applicable

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author.

COMPETING INTERESTS

Authors have declared that no competing interests exist

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