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ETHANOL INDUCED NEPHROTIC DAMAGE IN MALE WISTAR RATS: THE ANTIULCEROGENIC AND NEPHROPROTECTIVE PROPERTIES OF THE METHANOLIC LEAF EXTRACT OF ANDROGRAPHIS PANICULATA

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ABSTRACT

This study investigated the Nephroprotective property of methanol leave extract of Andrographis paniculata by ethanol induced Nephrotic damage in wistar male rats, by measuring serum urea, creatinine and bilirubin and antioxidant activities of Superoxide dismutase (SOD) and Catalase. 50 healthy male rats weighing about (150-250kg) were divided into five (5) groups of ten rats each. Group 1 (Normal control) and group 2 (positive control) received normal saline (10ml/kg), Group 3 and group 4 recieved 200mg/kg body weight and 400 mg/kg body weight of the extract respectively and group 5 (Standard Control) recieved 30mg/kg body weight Omeprazole orally for days 7. On the eighth day, groups 2, 3, 4, and 5 were given 10ml/kg of ethanol orally. After 24 hours, the animals were euthanized using chloroform anaesthesia and blood was collected through cardiac puncture for kidney function and antioxidant tests. Sections of the kidneys and gastrointestinal tract were also collected and preserved in 10% formalin for histopathological analysis. This study shows that Administration of ethanol caused a significant decrease ($p < 0.5$) in CAT and SOD activities in the positive control group compared to the normal control group. Treatment with extract at dose 200mg/kg body weight and 400 mg/kg body weight remarkably elevated ($p < 0.5$) in SOD and CAT activities respectively compared to positive control. The administration of ethanol caused a significant increase ($p< 0.05$) in serum urea, creatinine and Bilirubin activities in the positive control group compared to the normal control group.. Treatment with Omeprazole at dose 30mg/kg body weight significantly decreased ($p < 0.05$) urea, creatinine and bilirubin compared to the positive control group. Therefore from this present study it can be drawn that methanol leave extract of Andrographis paniculata showed a mitigating effect which indicates that the extract has protective effects on the kidney against ethanol induced Nephrotic damage.

KEYWORDS: Neprotic damage, Omeprazole, Andrographis paniculata . Creatinine, Bilirubin.

INTRODUCTION

Andrographis paniculata, commonly known as the 'king of bitter,' is a significant medicinal plant used in traditional herbal medicine across various countries.[11] The plant is rich in bioactive compounds, with andrographolide being the principal component known for its anticancer, anti-inflammatory, anti-angiogenic, antivenom, antidiabetic, and antimalarial properties.[4] It has been historically used for treating fever, herpes, sore throat, upper respiratory infections, and other chronic and infectious diseases The leaves and roots are key sources of active principles, with andrographolide being the major active component.[12]

Moreover, bitter diterpenoids and flavonoids have been extracted from several parts of the plant, enhancing its therapeutic characteristics. Recent research has identified various compounds in Andrographis paniculata, including andrographolide, deoxyandrographolide-19ß-D-glucoside, neo-andrographolide, apigenin-7,4'-di-O-methyl ether, and 5-hydroxy-7,8,2',3'-tetramethoxy flavone. Flavonoids, diterpenoids, and polyphenols have also been extracted from this plant, showcasing its diverse chemical composition.[14] Flavonoids, andrographolide diterpenoids, and polyphenols extracted from Andrographis paniculata have garnered significant attention for their potential health benefits.[3] identified

flavonoids like 5,7,2',3'-tetramethoxyflavanone along with various other flavonoids from the entire plant of A. paniculata. These compounds contribute to the plant's pharmacological properties and therapeutic potential. Furthermore,[13] discovered six novel compounds from the aerial parts of A. paniculata, expanding the understanding of the plant's chemical composition and bioactive constituents. These newly identified compounds may hold promise for future research into the medicinal applications of Andrographis paniculata. The kidney, a vital organ with excretory functions, plays a crucial role in various physiological processes beyond waste elimination. Studies have shown that after ethanol consumption, the kidneys are involved in processing ethanol and its metabolites, leading to their excretion in urine. The kidney's role extends to maintaining electrolyte balance, counter-regulating complex disturbances like phosphate and potassium levels, and participating in enzymatic reactions and immunization processes. Recent research by[2] highlights the multifaceted functions of the kidney, emphasizing its significance in maintaining homeostasis. Although certain investigations, such as the one conducted byl,[5] indicate that prolonged consumption of ethanol alone may not directly cause damage to the kidneys.

It is crucial to note that regular alcohol consumption can elevate blood pressure, posing a risk factor for renal damage. Furthermore, research has shown that consuming an excessive amount of ethanol can cause harmful consequences for the kidneys, resulting in both structural and functional abnormalities.

Notably, in fetal alcohol syndrome, children exposed to ethanol prenatally may exhibit kidney-related issues. Research conducted by.[17] has found that alcohol-fed rats experience decreased kidney function, interstitial edoema, and renal hypertrophy. Additionally, there are changes in enzyme activity inside the kidney.

MATERIALS AND METHODS

Animals

Fifty healthy male Wistar rats, weighing between 150-250g, were procured from the Animal House at the former Faculty of Pharmacy, University of Benin, Edo State. These rats were housed in well-ventilated polypropylene cages located in the animal farm experimentation room within the Department of Pharmacology, Faculty of Basic Medical Sciences, College of Health Sciences, Niger Delta University. The rats were maintained under standard conditions of room temperature, with a relative humidity ranging between 45-55%, and subjected to a 12:12 hour light/dark cycle. Prior to the commencement of the experiment, a two-week acclimatization period was observed to allow the rats to adjust to their new environment. Throughout the study, the rats were provided with a standard laboratory animal feed in the form of pelletized feeds and had access to water ad libitum, ensuring their nutritional needs were met adequately

Collection of Extract/Extract procedure

Andrographis paniculata plants were meticulously collected in Benin, Edo State by Professor Ching F. Poh from the Department of Pharmacology, Faculty of Basic Clinical Sciences, College of Health Sciences at Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State. The botanical identification and authentication of the plant were expertly conducted by Professor Ajibesin Kolawole from the Department of Pharmacognosy, Faculty of Pharmacy at Niger Delta University in Wilberforce Island, Amassoma, Bayelsa State. Upon collection, the fresh Andrographis paniculata plants were carefully laid out in a clean, dry tray and allowed to undergo a controlled shade-drying process for a period of three weeks. Subsequently, the leaves were finely powdered using a dry hand grinder and stored in a sealed container in preparation for the extraction process. The powdered Andrographis paniculata leaves were accurately weighed (604g) and subjected to extraction using 3 liters of methanol over a 48-hour period. The resulting methanol extract was meticulously collected, filtered, and then concentrated under reduced pressure at 50°C and 40rpm utilizing a Rotary Vacuum Evaporator. The obtained residue was precisely weighed (65.9g) and stored in a refrigerator at 4°C to maintain its integrity for future utilization in research and experimentation.

Experimental Design and Procedure

Fifty healthy male Wister rats we're divided into 5 groups and were pretreated for 7 days as follows

Group 1 (10 normal rats): Feed + distilled water

Group 2 (positive control consisting of 10 rats): Feed + distilled water+ 10ml/kg of Ethanol Group 3 (Test group 1 consisting of 10 rats): Feed + distilled water+200mg/kg body weight of methanoic extract of Andrographis paniculata+10ml/kg body weight of Ethanol

Group 4 (Test group 2 consisting of 10rats): Feed + distilled water+400mg/kg body weight of methanolic extract of Andrographis paniculata +10ml/kg body weight of Ethanol.

Group 5 (standard group consisting of 7 rats): Feed + distilled water+ 30mg/kg of Omeprazole+ 10ml/kg of Ethanol.

Sample Collection and Biochemical analysis

On the 9th day of the study, the animals were anesthetized with chloroform and subsequently euthanized. Subsequently, blood samples were obtained from each rat by performing a heart puncture using a 5ml syringe. The blood that was gathered was put into sample container without any additives in order to facilitate the process of clotting.

Following coagulation, the serum was carefully separated from the whole blood by centrifugation at 4000rpm for 10 minutes. The isolated serum samples were then collected for further biochemical analysis to assess various parameters.

Biochemical assay

Determination of antioxidant enzymes

The tissues were promptly excised, rinsed with cold normal saline, dried gently, and then weighed accurately. Subsequently, a 10% (w/v) tissue homogenate was meticulously prepared using a mortar and pestle in a 10mM potassium phosphate buffer at pH 7.4, supplemented with 30mM KCl. The homogenate was subsequently subjected to centrifugation at 1000 x g for 10 minutes at 4°C using a refrigerated centrifuge to efficiently remove cellular debris and nuclei.

The resulting supernatants, devoid of debris, were utilized for the assessment of antioxidant activities, ensuring the integrity and accuracy of the biochemical analyses.

Ethics

The ethical council of Niger Delta University Amassoma, Bayelsa State, Nigeria approved all animal protocols, in accordance with the National Institutes of Health's Principles of Laboratory Animal Care [NRC 1985]. The animals were provided with humane care in accordance with the standards set forth in the "Guide for the Care and Use of Laboratory Animals (1996)" established by the National Academy of Sciences.

Biochemical investigations

Renal function Test

Determination of serum Urea by Berthelot's Enzymatic Method

Determination of serum creatinine by Jaffe colorimetric –kinetic Method

Determination of bilirubin D

etermination of Markers of Oxidative stress.

This was by measuring Malondialdehyde (MDA)[19] and superoxide dismutase (SOD)[20] catalase[19] as well as reduced Glutathione GSH[21]

Preparation of homogenate

Homogenate of the kidneys were treated with the non-ionic detergent Triton X-IOO (1% final concentration) and was allowed to stand on ice for 30 minutes to completely release the enzyme (Cu-Zn SOD).

Statistical analysis

Results obtained were subjected to statistical analysis. All values were expressed as the mean ± S.D and data were analyzed using one-way ANOVA. Values were considered statistically significant at $P < 0.05$.

RESULTS

The mean body weight (g) of Wistar rats in ethanol induced toxicity after treatment with Andrographis paniculata The result in table (3.1) indicates that, when compared to normal and positive control, pretreatment with Andrographis paniculata caused a significant ($p<0.05$) increase in the body and their recorded values were (236.77±21.30), (209.54±21.50), (202.96±41.28) and (223.33±22.95), (182.95±14.19), (183.98±33.41). (Table 1). The findings presented in Table 3.1 demonstrate a notable impact of pretreatment with Andrographis paniculata on body weight compared to both the normal and positive control groups. The recorded values for the body weight were as follows: (236.77±21.30), (209.54±21.50), (202.96±41.28), and (223.33±22.95) for the experimental groups, while the normal and positive control groups exhibited values of (182.95±14.19) and (183.98±33.41) respectively, as outlined in Table 1. This significant difference ($p<0.05$) underscores the potential influence of Andrographis paniculata on body weight regulation, highlighting its impact in the experimental setting.

Effects of andrographis paniculata on ethanol induced nephrotic damage in wistar rats

The results presented in Table 3.2 indicate a significant impact of different treatments on catalase (CAT) and superoxide dismutase (SOD) activities in the experimental groups. The administration of ethanol led to a notable decrease ($p < 0.5$) in CAT (0.51±0.03) and SOD (1.91±1.05) activities in the positive control group compared to the normal control group. In contrast, treatment with Andrographis paniculata at doses of 200mg/kg and 400 mg/kg resulted in a remarkable increase in SOD (3.07±0.05 and 3.15±0.07, respectively) and CAT (1.28±0.02and 1.36±0.02, respectively) activities compared to the positive control group. Additionally, treatment with Omeprazole at 30mg/kg also significantly elevated SOD (3.8±0.04) and CAT (1.38±0.02) activities in comparison to the positive control group, as outlined in Table 2. These findings underscore the potential antioxidant effects of Andrographis paniculata and Omeprazole in enhancing the antioxidant enzyme activities in the experimental setting.

Protective role of andrographis paniculata on ethanol induced wistar rats

The results presented in Table 3.3 highlight the impact of different treatments on urea, creatinine, and bilirubin activities in the experimental groups. Administration of ethanol led to a significant increase ($p < 0.05$) in urea (111.17±1.43), creatinine (0.92±0.04), and bilirubin (1.12±0.08) levels in the positive control group compared to the normal control animals.In contrast, treatment with Andrographis paniculata at doses of 200mg/kg and 400mg/kg resulted in a significant reduction in urea (97.50±3.34 and 90.15±3.22), creatinine (0.61±0.05 and 0.55±0.04), and bilirubin (0.79±0.06 and 0.64±0.07) activities compared to the positive control group, indicating a potential protective effect against ethanol-induced changes. Furthermore, treatment with omeprazole at a dose of 30mg/kg also demonstrated a noticeable decrease ($p < 0.05$) in these parameters compared to the positive control group, as outlined in Table 3. These findings suggest the potential of Andrographis paniculata and omeprazole in mitigating the adverse effects of ethanol on urea, creatinine, and

bilirubin levels, highlighting their therapeutic potential in this experimental context.

Table 1: Effect of ethanol and Andrographis Paniculata on the mean body weight (g) of Wistar rat.

Experimental groups	DAY 1 MEAN±SD	DAY8 MEAN±SD
Group 1: Normal control (with normal saline)	236.77±21.30[a]	223.33±22.95[a]
Group 2: positive control	209.54±21.50[b]	182.95±14.19[b]
Group 3: Test 1(with 200mg/kg extract	190.29±21.44[c]	165.99±21.04[c]
Group 4: Test 2 (with 400mg/kg extract	209.07±33.41[b]	183.98±33.41[b]
Group 5: Standard (with 30mg/kg of omeprazole + 10 ml /kg ethanol)	202.96±41.28[b]	177.07±41.28[b]

The data is presented as the mean ± standard deviation (SD). Values with a different superscript from the control group are statistically significant at $p < 0.05$.

Table 2: The mean antioxidant activities of kidney and GIT homogenate in ethanol induced nephrotic damage in wistar rats.

Experimental group	Catalase (Units/mg protein)	Sod (Kidney) (Units/mg protein)	Sod (Git) (Units/mg protein)
Group 1: Normal control (with Normal saline)	1.82±0.09[a]	4.80 ± 1.01[a]	4.81± 0.04[a]
Group 2: positive control (with Normal saline +10 ml /kg ethanol	0.51±0.03[b]	1.91 ± 1.05[b]	2.92 ± 0.01[b]
Group 3: Test 1(with 200mg/kg extract +10 ml /kg ethanol)	1.28±0.08[c]	3.07±0.05[c]	3.19 ±0.06[c]
Group 4: Test 2 (with 400mg/kg extract +10 ml /kg ethanol)	1.36±0.02[c]	3.15±0.07[c]	3.20 ± 0.02[c]
Group 5: Standard (with 30mg/kg of omeprazole + 10 ml /kg ethanol)	1.38±0.02[c]	3.8±0.04[c]	3.18 ±0.04[c]

The data is presented as the mean ± standard deviation (SD). Values with a different superscript from the control group are statistically significant at $p < 0.05$.

Table 3: Mean renal function levels in ethanol induced nephrotic damage in wistar rats.

Experimental group	Urea(mg/dl)	Creatinine (mg/dl)	Bilirubin(mg/dl)
Group 1: Normal control (With normal saline)	81.27±4.27[a]	0.42±0.04[a]	0. 05±0.06[a]
Group 2: positive control (With normal saline 10 ml/kg ethanol)	111.17±1.43[b]	0.92±0.04[b]	1.12±0.08[b]
Group 3: Test 1(With 200mg/kg of extract +10ml/kg ethanol)	97.50±3.34[c]	0.61±0.05[c]	0.79±0.06[c]
Group 4: Test2 (with 400mg/kg of extract + 10ml/kg ethanol Group 5: Standard (30mg/kg of Omeprazole 10 mg/ml ethanol)	90.15±3.22[d] 96.89±1.61[b]	0.55±0.04[d] 0.54±0.01[d]	0.64±0.07[d] 0.54±0.01[e]

The data is presented as the mean ± standard deviation (SD). Values with a different superscript from the control group are statistically significant at $p < 0.05$.

Histopathology of kidney

Photomicrograph of kidney tissue of an adult male wistar rat stained with haematoxylin and Eosin technique X400magnification.

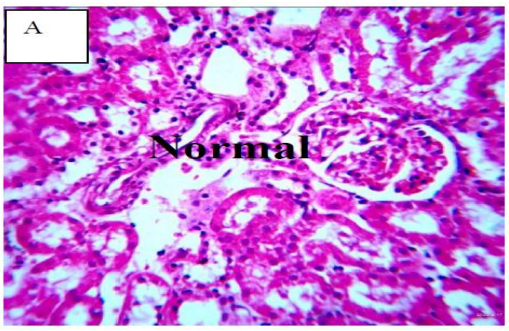

Fig. A: Kidney section of group 1: normal control rats) shows the photomicrograph of Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows normal histology of the kidney, features consistent with histology of the kidney.

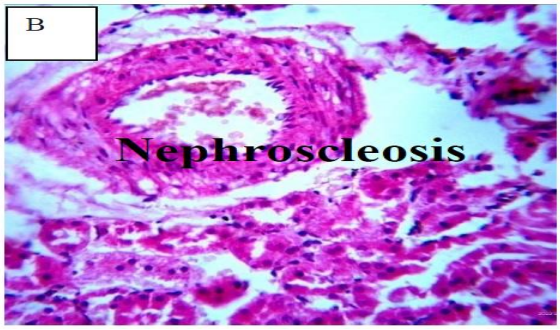

Fig. B: (Kidney section of Positive treated rats group 2) Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. This section show mark intimal proliferation and fibrosis with narrowing of the lumen of the blood vessel. Conclusions: nephrosclerosis. Normal A Nephroscleosis.

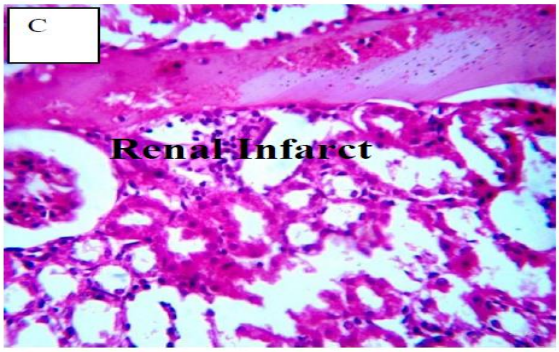

Fig. C: (Kidney section of ethanol + Andrographis paniculata 200mg/kg Group 3). Shows Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows a specialized area of ischemic necrosis.

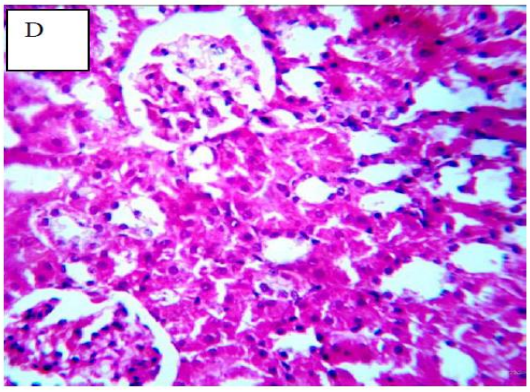

Fig. D: (Kidney section of ethanol + Andrographis paniculata 400mg/kg Group 4) Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows normal histology of the kidney.

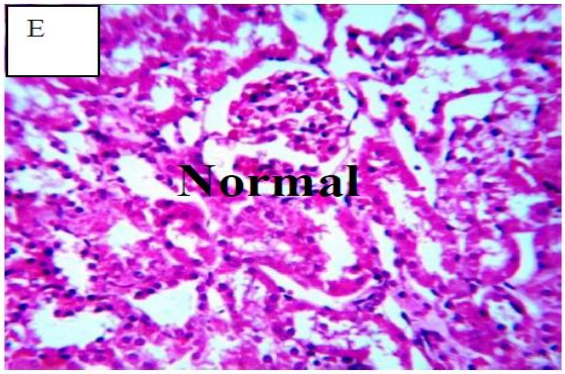

Fig. E: (Kidney section of ethanol + Omeprazole Standard Control group 5) Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows normal histology of the kidney.

Histopathology of GIT

Figure 3.1 Photomicrograph of gastrointestinal tract tissue of an adult male wister rat stained with haemztoxylin and Eosin technique. Transverse section of haematoxylin and Eosin stained slides X400 magnification.

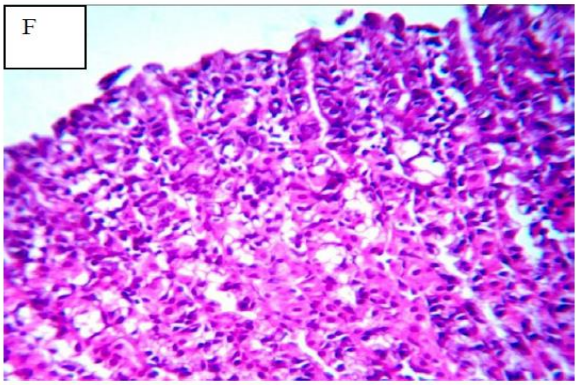

Fig. F: Shows transverse section of the gastrointestinal tract with normal gastric pits and mucosa and abundant gastric glands consistent with normal histology of the gastrointestinal tract. X400mag.

Conclusion: Normal histology

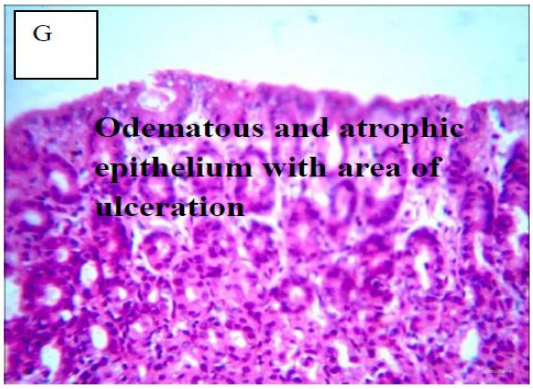

Fig. G: Transverse section of haematoxylin and eosin stained slides x 400magnification. Sections shows hyperplasic and edematous gastric glands with area of ulceration.

Conclusion: Atrophic gastritis and ulceration of the epithelium

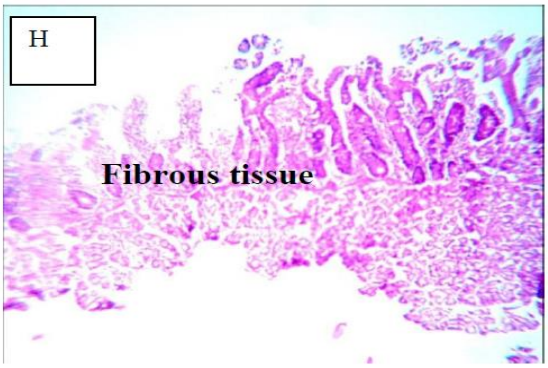

Fig. H: Transverse section of haematoxylin and eosin stained slides x 400magnification. Section left show healing by fibrous and right shows regenerating epithelium with tall gastric glands displaying normal columnar epithelium.

Conclusion: Epithelial regeneration

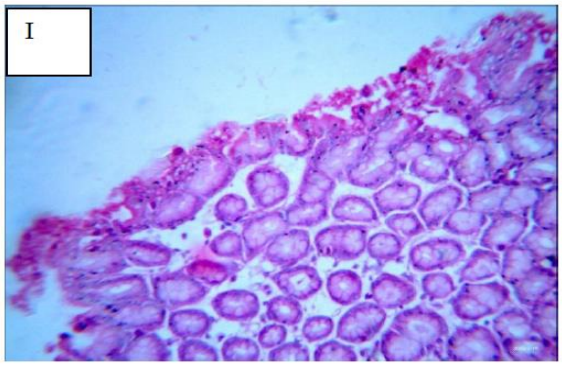

Fig. I: Transverse section of haematoxylin and eosin stained slides x 400magnification. Section right show healing by fibrous and left shows regenerating epithelium with gastric glands displaying normal columnar epithelium.

Conclusion: Epithelial regeneration

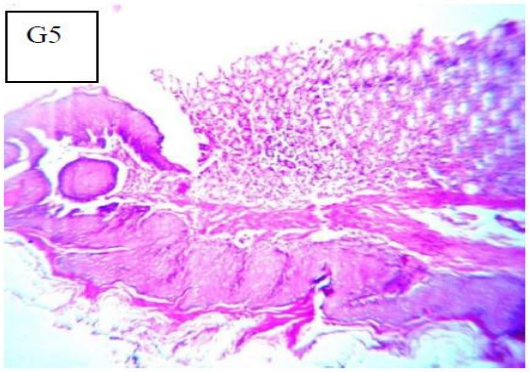

Fig. I: Transverse section of haematoxylin and eosin stained slides x 400magnification. Section shows sharply delineated margin and scar formation. The margin of the ulcer is I G5 accentuated by hyperplasia of the bordering epithelium (left) while right shows a pyloric ring with surface consisting of nuclear fragments and inflammatory cells.

Conclusion: Gastric ulcer

DISCUSSION

One prevalent gastrointestinal tract (GIT) condition that is quite concerning to people is gastric ulcers. Gastrointestinal bleeding, perforation, and erosion of the mucosal wall are characteristic of this condition, which is caused by an imbalance between aggressive forces (such as acid, pepsin, and Helicobacter pylori) and defensive factors (such as mucin, prostaglandin, bicarbonate, nitric oxide, mucosal blood flow, and growth factors).[16] Numerous factors contribute to this illness, such as Helicobacter pylori, overuse of non-steroidal anti-inflammatory medicines (NSAIDs), smoking, stress, long-term alcohol consumption, abnormal metabolism of the prostaglandin E series, and poor eating habits.[17] Administering ethanol orally is detrimentalto the gastrointestinal system since it directly impacts its intestinal mucosa by destroying its protective barrier and causing significant alterations in the microvasculature within a short period of time after ingestion. There have been attempts to find new, less expensive medications with fewer side effects, even though treating stomach ulcers with antibiotics, prostaglandin analogues, proton pump inhibitors (omeprazole), and H2 receptor blockers (cimetidine, ranitidine, and famotidine) lowers the mortality rate of stomach ulcers.[6] Plants and other substances from nature are crucial sources for preventing and treating stomach ulcers.[8] It has been demonstrated that andrographis paniculata has antioxidant properties. It is possible that this plant extract's gastroprotective effects are due to its antioxidant radicals, which work by directly scavenging free radicals. Antioxidants prevent ethanol-induced stomach damage, shield cells from oxidative stress-induced cellular damage, and strengthen the body's defences against degenerative diseases. Superoxide dismutase (SOD) and catalase are two components of the enzymatic antioxidant defence system, which guards the host cells from excessive free radical exposure.[15] This study evaluated the amelorative effects of methanol leaves extract of Andrographis paniculata on ethanol induced ulcerogenic and nephrotic damage in wistar rat. The experimental results showed that A. Paniculata extract has an effective antisecretory and antiulcer activity against ethanol-induced gastric mucosa injury, Administration of 10 ml/kg of alcohol significantly ($p<0.05$) reduced catalase (0.51±0.03) and SOD (1.91 ± 1.05) activities in the positive control group

compared with the normal group. However, Pretreatment with 200 mg/kg and 400 mg/kg methanolic extract of Andrographis Paniculata showed a significantly elevated catalase (1.28±0.08) and SOD (3.07 ± 0.05) activities compared to the positive control group. Pretreatment with Omeprazole at 200mg/kg also remarkably elevated SOD (3.15±0.07) and CAT (1.36±0.02) activities compared to the positive control group. The administration of ethanol also caused a significant increase ($p< 0.05$) urea (111.17±1.43), creatinine (0.92±0.04) and Bilirubin (1.12±0.08) in the positive control group compared to the normal control group. However, pretreatment with 200 mg/kg body weight and 400 mg/kg body weight caused a significant reduction in catalase, SOD and bilirubin levels compared to positive control group. The administration of Omeprazole also significantly increased the levels of Catalase and SOD, and reduced the levels of urea, creatinine and bilirubin compared with the positive control group. This result is in agreement with Recent research that has continued to explore the gastroprotective effects of Andrographis paniculata and its key component, andrographolide, on gastric ulcer development. Research has demonstrated the therapeutic and preventive properties of Andrographis paniculata in treating stomach ulcers caused by aspirin. This highlights its potential as a natural remedy[9] Additionally, investigations into the protective effects of andrographolide against NSAID-induced gastric damage have shown promising results, indicating its role in mitigating ulcer development.[1][23]

This protective potential of Andrographis Paniculata could be due to its phytochemicals which possess antioxidant properties. Flavonoids, andrographolide diterpenoids, and polyphenols were obtained from the whole plant of A. paniculata.[3] On the contrary, some studies have raised questions about the efficacy of herbal remedies like Andrographis paniculata in treating gastric ulcers. While traditional medicine often relies on plant-based treatments, the experimental evidence supporting their effectiveness can be limited.[11][23]

This study investigated the histopathology of methanol leaf extract of Andrographis paniculata on ethanol induced ulcerogenic and nephrotic damage Plate A: (Kidney section of group 1: normal control rats) shows the photomicrograph of Transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows normal histology of the kidney. This shows the normal features consistent with histology of the kidney. Plate B, (Kidney section of Positive control) the section shows marked intimal proliferation and fibrosis with narrowing of the lumen of the blood vessel. There was a clear indication of nephrosclerosis as a result of ethanol exposure without treatment.

Plate C: (Kidney section of 200mg/kg body weight treated Group) shows transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. This image showed a section specialized area of ischemic necrosis. Plate D: (Kidney section of 400mg/kg body weight treated group) transverse section of the kidney stained with haematoxylin and eosin x 400 magnification. Section shows normal histology of the kidney due to the effect of the high dose of the extract Plate E: (Kidney section of Omeprazole treated group) transverse section of the kidney stained with hematoxylin and eosin x400 magnification. This section shows normal histology of the kidney.

Histopathological report on the wistar rats' gastrointestinal tracts are shown in Fig.2. Plate F: group 1 (normal control) shows the transverse section of the gastrointestinal tract with normal gastric pits and mucosa and abundant gastric glands consistent with histology of the gastrointestinal tract indicating normal histology. Plate G: group 2 (positive control) shows distortion of the gastrointestinal tract morphology, and ulcerations induced by ethanol. The transverse section shows hyperplasic and edematous gastric glands with area of ulceration, indicating that there is atrophic gastritis and ulceration of the epithelium due to the untreated effect of ethanol.

Plate H: group 3, Section left show healing by fibrous and right shows regenerating epithelium with tall gastric glands displaying normal columnar epithelium. I: group 4, show healing by fibrous and left shows regenerating epithelium with gastric glands displaying normal columnar epithelium. Both of the group show epithelial regeneration due to the protective effect of Andrographis paniculata.

I: (Standard group) the margin of the ulcer is accentuated by hyperplasia of the bordering epithelium (left) while right shows a pyloric ring with surface consisting of nuclear fragments and inflammatory cells indicating healing process of omeprazole on gastric ulcer. This result is consistent with studies by other researchers. The effect of leaf extract of Andrographis paniculata on the histopathology of ethanol induced ulcerogenic and nephrotic damage is shown to be dose dependent. This histopathological analysis further confirms the potential therapeutic effects of A. Paniculata extract in protecting the gastric and renal tissues from ethanol-induced damage.

In conclusion, this study demonstrates that methanol leaf extract of Andrographis Paniculata possesses potent antiulcer and nephroprotective effects against ethanol-induced damage in Wistar rats. The antioxidant properties of this plant extract, as evidenced by the elevated catalase and SOD activities, play a key role in its protective mechanisms. This study provides valuable insights into the potential of natural products, such as A. Paniculata, as alternative and effective treatments for gastric ulcers. Further research is warranted to elucidate the specific phytochemicals responsible for these beneficial effects and to explore the underlying

mechanisms of action. Overall, the findings of this study contribute to the growing body of evidence supporting the use of natural products in the management of gastric ulcer and related gastrointestinal disorders.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

Statement of ethical approval

The study protocol was approved by the Ethical and Research Committee of Niger Delta University, Bayelsa State, Nigeria. The ethical principles for medical research involving animal subjects as outlined in the Helsinki declaration in 1975 and subsequent revisions were strictly followed in the course of this study

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