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Original Research Article

The Ameliorative Effect of *Andrographis paniculata* on Aspirin-Induced Ulcerogenic and Hepatic Damage in Wistar Rats

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Abstract: The study investigated the anti-ulcerogenic and hepatoprotective potential of the methanolic extract of *Andrographis paniculata* in Wistar albino rats with aspirin-induced ulcer and liver damage. The study measured the following parameters: AST, ALT, ALP, and MDA. A total of 50 rats (weighing about 150-300g) were divided into 5 groups of 10 rats each. Group 1 (Normal control), group 2 (Positive control) were given normal saline(10ml/kg), Group 3(Test 1) and Group 4(Test 2) received 200 mg/kg and 400 mg/kg of the extract, respectively, and group 5 (standard), received 30mg/kg of Omeprazole for 7days. On day 7, rats in groups 2, 3, 4, 5 were fasted for 24hrs and, on the 8th day, were induced with 10mg/kg of Aspirin orally. The animals were sacrificed on day 9 under chloroform anaesthesia, and blood was collected via cardiac puncture for liver function assay. Parts of the liver and the GIT of the rats was harvested and fixed in 10% chlorororm for histological studies while the liver and GIT were homogenized for lipid peroxidation assay. The study discovered that Serum AST, ALT and ALP. levels were significantly increased ($p < 0.05$) in positive control compared to the normal control. However, pretreatments with *Andrographis paniculata* (200mg/kg and 400 mg/kg) in test1 and 2 significantly decreased the activities of serum AST, ALT, and ALP, compared to those in group 2 (positive control). In addition, treatment with. The activity of the GIT SOD was decreased in positive compared to normal control. Test 1 and 2 pretreated with *Andrographis paniculata* (200mg and 400 mg/kg) respectively demonstrated significant increase in the activities of MDA compared to positive control. From the Histology of the GIT Positive control shows Sections areas of ulcerated epithelium with atrophic gastric glands compared to Test 1 and 2 which shows gastric mucosa with the disappearance of the original gastric glands and other epithelium replacements and healing by fibrous respectively. In conclusion, the methanolic extract of *Andrographis paniculata* demonstrated antioxidant properties that conferred hepatoprotective and anti-ulcerogenic effects in the aspirin-induced ulcer and liver damage model in Wistar albino rats. The higher dose of the extract (400 mg/kg) exhibited more pronounced protective effects compared to the lower dose (200 mg/kg).

Keywords: *Andrographis paniculata*, anti-ulcerogenic, hepato-protective and Omeprazole.

INTRODUCTION

Medicinal plants are indispensable for primary healthcare because to their easy accessibility, high tolerance, compatibility, and reasonable cost. Research suggests that there are over 80,000 plant species that are utilised for medical purposes globally. It has been found that 75-80% of people in developing countries and 25% of citizens in industrialised nations rely on medicinal plants for their healthcare needs [9]. *Andrographis paniculata*, commonly referred to as Kalmegh or King of Bitters, is a plant that is abundant in South-Eastern Asia, specifically in countries such as Pakistan, Indonesia,

India, and Sri Lanka. Studies [25], have shown that *Andrographis paniculata* has a wide range of pharmacological actions. These actions encompass properties such as reducing inflammation, lowering blood sugar levels, fighting viruses, combating malaria, inhibiting the growth of cancer cells, boosting the immune system, and preventing the development of cancer. This plant possesses a distinctive composition and interactions that render it a potent therapeutic and preventative agent. It has been found to regulate numerous metabolic pathways and signal transmission. Aspirin, a widely available non-prescription medicine and inhibitor of COX enzymes, possesses distinct risks and benefits that are not present in other COX inhibitors. Aspirin has multiple benefits. *Andrographis paniculata*, often known as Kalmegh, is a medicinal plant that has been widely researched for its various pharmacological qualities. The primary bioactive compound found in this plant is andrographolide, which belongs to the class of diterpenoid lactones.The leaves of the plant contain the maximum amount of andrographolide, with a concentration of up to 2.39% [12], as indicated by recent studies. Conversely, the seeds possess the minimal quantity of this chemical. *Andrographis paniculata* contains not only andrographolide, but also additional phytochemicals such as 14-deoxy-11,12-dihydroandrographolide (andrographolide D) and Andrographon.

The plant also possesses a diverse range of flavonoids, including 5,7,2',3'-tetramethoxyflavanone, with other flavonoids, diterpenoids, and polyphenols [12]. In addition, a total of six novel compounds have been extracted from the above-ground sections of *Andrographis paniculata*, highlighting the extensive range of phytochemicals present in this medicinal plant [12]. Extensive research has been conducted on the different pharmacological qualities of *Andrographis paniculata*, a medicinal plant that is commonly utilised in traditional medicine. *Andrographis paniculata* contains a significant bioactive ingredient called andrographolide, which is classified as a diterpenoid lactone. Recent research has shown that *Andrographis paniculata* extract and its main component, andrographolide, have strong anti-inflammatory effects. Some of the main mechanisms that reduce inflammation include: inhibiting the expression of intercellular adhesion molecule-1 (ICAM-1) in monocytes activated by tumour necrosis factor-α (TNF-α) (Xia *et al*., 2004), suppressing the production of inducible nitric oxide synthase (iNOS) in RAW264.7 macrophage cells [3], and decreasing the expression of cyclooxygenase-2 (COX-2) in neutrophils and microglial cells [8-22]. The anti-inflammatory activities of *Andrographis paniculata* and its main compound, andrographolide, have been widely studied in laboratory and animal experiments, demonstrating the potential of this medicinal plant in treating inflammatory disorders. *Andrographis paniculata* exhibits a range of medicinal qualities, such as anti-inflammatory, antioxidant, and immunomodulatory effects. These properties make it a highly interesting option for the creation of natural medicinal medicines.

Oxidative stress, which refers to an unevenness between the creation of free radicals and the body's ability to counteract them with antioxidants, has a significant impact on multiple physiological processes [15]. Reactive oxygen species (ROS) are radicals that include oxygen and have unpaired electrons, which leads to oxidative stress. This group frequently encompasses molecules that contain oxygen, such as hydrogen peroxide (H2O2), singlet oxygen (1O2), superoxide (O2•−), and oxygen-containing radicals like hydroxyl (OH•) [19]. The presence of ROS and reactive nitrogen species has wide-ranging effects on several components of hepatocytes, including proteins, lipids, DNA, and other cellular constituents. This ultimately results in both structural and functional changes in the liver [10]. These alterations can have significant ramifications for liver well-being and general physiological operation.

Antioxidants have a vital function in counteracting the harmful effects of free radicals and enhancing overall well-being. They are commonly known as "free-radical scavengers" [31]. Research conducted by Chiou *et al*., in [3], has demonstrated that antioxidants can effectively decelerate the advancement of age-related macular degeneration.

The proper functioning of physiological processes depends on maintaining a delicate balance between the production of reactive oxygen species (ROS) through cellular activities and their removal by antioxidant defence mechanisms. Oxidative stress arises from an imbalance that promotes the creation of reactive oxygen species (ROS), which can potentially harm cellular structures. Oxidative stress has been linked to several disorders, including as cancer [20-26]. In order to mitigate the harmful consequences of oxidative stress, it is essential to enhance the body's antioxidant defence mechanisms. A promising approach that has shown promise is the use of plant-derived bioactive compounds, which have been widely employed in conventional healthcare for the management of oxidative stress-related disorders [14-18].

Reactive oxygen species consist of several molecules, including non-radical species like hydrogen peroxide (H2O2), singlet oxygen (1O2), and superoxide (O2•−), as well as oxygen-containing radicals like hydroxyl (OH•−). The presence of ROS and reactive nitrogen species can have a significant impact on many cellular components in hepatocytes, such as proteins, lipids, and DNA. This can result in structural and functional changes in the liver [10-27]. Researchers are studying ways to improve the body's ability to defend against harmful oxidative stress by investigating the use of plant-based natural products. The goal is to develop new treatments for diseases related to oxidative stress [21-26].

MATERIALS AND METHODS

Chemicals: All reagents and chemicals were sourced from reputable suppliers and were of analytical quality

Plant Collection and Extraction

Professor Ching F. Poh and Professor Ajibesin Kolawole obtained the *Andrographis paniculata* plant in Benin, Edo State. The plant was identified and validated by Professor Kolawole. After drying in the air for three weeks, the leaves were pulverized into a fine powder and stored in an airtight container for extraction. This revised version ensures precision and correctness in the gathering and manipulation of the plant.

Animal and Diet

Fifty healthy male Wistar albino rats, weighing between 110-200g, were acquired from the Animal House of the former Faculty of Pharmacy at the University of Benin, Benin, Edo State. The rats were kept in polypropylene cages with good ventilation in the animal house experimentation room of the Department of Pharmacology, Faculty of Basic Medical Sciences, College of Health Sciences, Niger Delta University. The housing conditions were kept at a constant temperature, with a relative humidity ranging from 45% to 55%, and a light/dark cycle of 12 hours each. Before the experiment, the animals had a 2-week acclimatisation period. Throughout this period, the rats were given unrestricted access to conventional laboratory animal diet in pellet form and water.

Experimental Design

The study employed a sample of 50 healthy male Wistar albino rats, which were randomly allocated into five groups, each consisting of 10 rats. The animals underwent pretreatment for a duration of 8 days in the following manner:

Group 1 (Normal Control): Given a typical laboratory food and purified water.

Group 2 (Positive Control) was administered a typical laboratory food, purified water, and a dose of 20 mg/kg body weight of Aspirin.

Group 3 (Test 1) was administered a diet consisting of ordinary laboratory food, distilled water, a methanolic extract of *Andrographis paniculata* at a dosage of 200 mg/kg body weight, and Aspirin at a dosage of 20 mg/kg body weight.

Group 4 (Test 2) was administered a diet consisting of a conventional laboratory food, distilled water, 400 mg/kg body weight of a methanolic extract derived from *Andrographis paniculata*, and 20 mg/kg body weight of Aspirin.

Group 5 (Standard) received a laboratory food that complies with federal standards, purified water, Omeprazole at a dosage of 20 mg/kg body weight, and Aspirin at a dosage of 30 mg/kg body weight. On the eighth day of the experiment, the animals in Groups 2, 3, 4, and 5 were given Aspirin orally at a dosage of 200 mg/kg body weight. They were then slaughtered after 24 hours. The new edition guarantees precision in the specifics about the categorization, pre-treatment, and application of the test compounds to the experimental animals.

Collection of Samples

On the ninth day of the experiment, the animals were rendered unconscious using chloroform and then euthanized. Cardiac puncture was performed on each rat to collect blood samples using 5 mL syringes. The blood was collected in simple sample bottles to facilitate the process of clotting. The serum was isolated from the entire blood by centrifuging at 4,000 revolutions per minute for 10 minutes after coagulation. The serum that had been isolated was then gathered for biochemical examination.

Ethics

The Niger Delta University's ethical committee approved animal protocols in accordance with the National Institutes of Health's Principles of Laboratory Animal Care, and the animals received compassionate care in line with the National Academy of Sciences' "Guide for the Care and Use of Laboratory Animals (1996)".

Biochemical Parameters

The following biochemical parameters were determined spectrophotometrically using the respective kits and instructions provided in the biochemical kit manual.

Estimations of Biochemical Parameters

Serum Parameters

The research involved euthanizing animals and collecting blood for biochemical analysis. Serum was isolated for determining liver function parameters using enzymatic kits from Accurex Biomedical Limited Pvt. Ltd., India, following manufacturer's instructions. The serum was used to determine aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatases (ALP).

Determination of Markers of Oxidative Stress

The concentration of MDA was determined using a method developed by Hunter *et al*., in [6] and later improved by Gutteridge and Wilkins in [7].

Statistical Analysis: The data was analyzed using ANOVA using SPSS, with significance considered when p-values were less than 0.05.

RESULTS

The findings of this study have been summarized in Tables 1, 2, and 3. Table 1 displays the average body weight of the rats before the pretreatment with *Andrographis paniculata* and before the sacrifice of the aspirin-induced Wistar Albino rats. Table 2 presents the mean and standard deviation concentrations of ALP (Alkaline Phosphatase), AST (Aspartate Aminotransferase), ALT (Alanine Aminotransferase), and MDA (Malondialdehyde) in Wistar Albino rats following the pretreatment with *Andrographis paniculata* extract. Table 3 showcases the ulcer index and percentage protection after the 9-day pretreatment with *Andrographis paniculata*.

Table 1: Mean body weight of the male Wistar rats given *Andrographis paniculata*

TREATMENT	Body weight
Normal control	360.77±21.32[a]
Positive control with 200mg/kg aspirin	155.185±19.183[b]
Test 1 with 200mg/kg extract and 200mg/kg aspirin	223.239±34.209[c]
Test 2 with 400mg/kg extract and 200mg/kg aspirin	199.511±28.281[d]
Test 3 with 30mg/kg of Omeprazole and 200mg/kg aspirin	206.06±33.68[d]

Table 2: Mean serum liver enzymes and MDA values of the male Wistar rats given *Andrographis paniculata*

GROUP	ALT(IU/L)	AST(IU/L)	ALP(IU/L)	MDA (U/mg protein)
Normal control	78.99± 3.22[a]	72.66 ± 4.53[a]	111.50 ± 1.18[a]	16.30 ± 3.74[a]
Positive control +Aspirin 200mg/kg	159.82 ± 12.97[b]	167.04 ± 15.34[b]	204.32 ± 1.34[b]	39.81 ± 2.4[b]
Test 1 (A.P 200mg/kg +aspirin 200mg/kg)	117.73 ± 13.99[c]	111.88 ± 9.12[c]	142.69 ± 3.20[c]	22.62 ± 3.77[c]
Test 2 (A.P+ Aspirin 400mg/kg +200mg/kg)	95.26 ± 31.09d	96,23 ± 5.41[c]	126.13 ± 2.27[c]	18.66 ± 2.91[d]
Test 3 (+Omeprazole 30mg/kg +Aspirin 200mg/kg)	100.79 ± 8.24[c]	98.09 ± 7.58[c]	113.16 ± 2.95[d]	18.05 ± 4.7[d]

Values are expressed as MEAN ± SD (Standard deviation). Values with different superscripts from control are significantly at ($p<0.05$).

The results presented in Table 3.2 indicated that the administration of Aspirin led to a significant increase ($p<0.05$) in ALT (159.81 ± 12.97), AST (167.04), and ALP (204.32) activities in the positive control group compared to the normal control animals. However, treatment with *Andrographis paniculata* at doses of 200 mg and 400 mg notably resulted in a significant decrease in ALT (117.72 ± 14.0 and 95.26 ± 3.1), AST (111.88 ± 9.2 and 96.23 ± 5.4), and ALP (142.69 ± 3.2 and 126.13 ± 2.3) activities compared to the positive control group. Additionally, treatment with Omeprazole at 30 mg/kg also led to a significant decrease ($p<0.05$) in serum ALT (100.79 ± 8.24), AST (98.00 ± 7.58), and ALP (113.16 ± 2.95) levels compared to the positive control group. In the positive control group, the administration of Aspirin resulted in a notable increase ($p<0.05$) in the level of MDA (39.81 ± 2.4) compared to the control animals (group 1). Conversely, treatment with *Andrographis paniculata* at doses of 200 mg and 400 mg/kg led to a significant decrease ($p<0.05$) in MDA levels (22.62 ± 3.77 and 18.66 ± 2.91) compared to the positive control group. Similarly, treatment with Omeprazole at a dose of 30 mg/kg resulted in a significant decrease ($p<0.05$) in the level of MDA (18.05 ± 4.7) compared to the positive control group.

Table 3: Ulcer index and percentage protective activity of *andrographis paniculata* in GIT of wistar rat

GROUP	PERCENTAGE PROTECTION
GROUP 1 Normal control	**100%**
GROUP 2 Positive control	**0%**
GROUP 3 Test group 1 with 200mg/kg extract	**13.85%**
GROUP 4 Test group 2 with 400mg/kg extract	**22.29%**
GROUP 5 Standard group with 30mg/kg of Omeprazole	**26.20%**

The administration of aspirin at a dose of 200 mg/kg caused ulceration of the gastrointestinal tract (GIT) lining, which was used as an index to evaluate the percentage of inhibition by the extract. The results obtained showed that the administration of the *Andrographis paniculata* extract at doses of 200 mg/kg and 400 mg/kg resulted in a percentage inhibition of 13.85% and 22.29%, respectively. In comparison, the group treated with the standard drug, omeprazole, showed a percentage inhibition of 26.20%.These findings suggest that the *Andrographis paniculata* extract exhibited a

dose-dependent protective effect against the aspirin-induced gastric ulceration, with the higher dose (400 mg/kg) providing a more substantial inhibition of ulcer formation. However, the standard drug omeprazole demonstrated a higher percentage of inhibition compared to the extract, indicating its superior gastroprotective efficacy. The results highlight the potential of *Andrographis paniculata* extract to mitigate the gastric ulcerogenic effects of aspirin, though further research is needed to fully elucidate its mechanisms of action and optimize its gastroprotective properties.

Histopathology of the Liver

Transverse Section of the liver Stained with haematoxylin and eosin X400magnification.

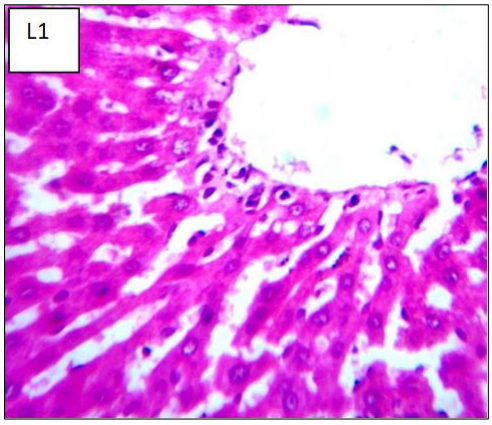


Plate 1(Liver Section of Group 1): Normal control rats show liver with normal central vein, sinusoids and hepatocytes consistent with histology of the liver.

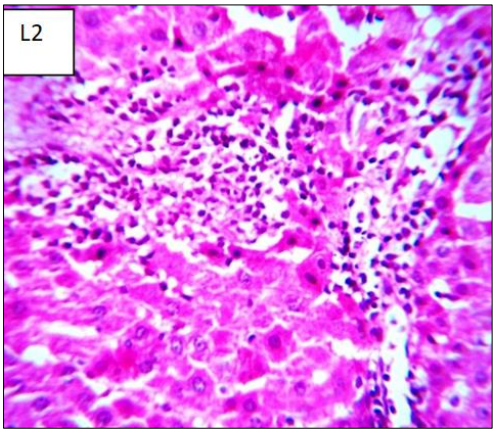


Plate 2(Liver Section of Positive Control Group 2): Section shows total obliteration of the central (right) and infiltration, inflammatory into the liver parenchyma with island abnormal cells.

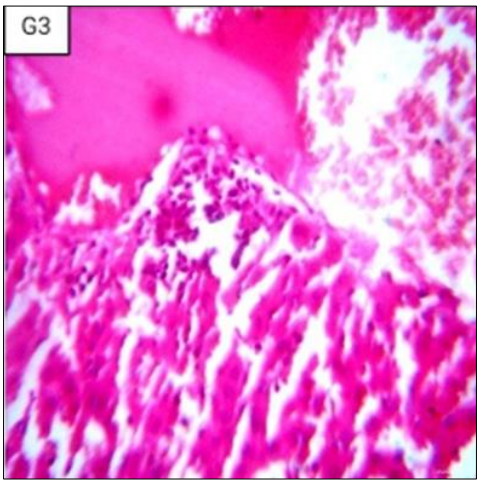


Plate 3(Liver section of aspirin + *Andrographis Paniculata* 200mg/kg Group 3): Section shows abnormal liver with inflammation of the blood vessel and congestion of the central vein.

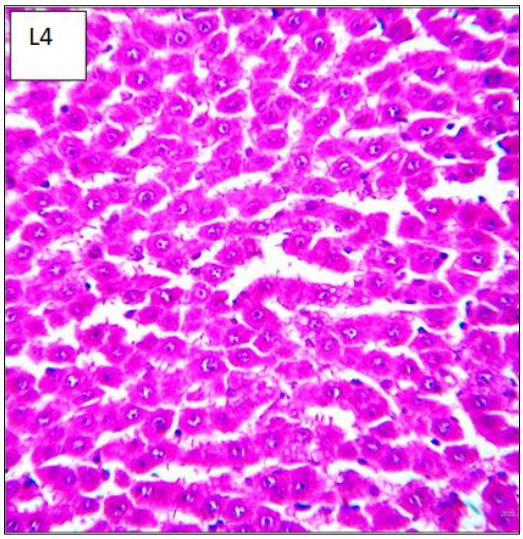


Plate 4(Liver section of aspirin + *Andro*graphis *paniculata* 400mg/kg Group 4): Section shows normal histology of the liver.

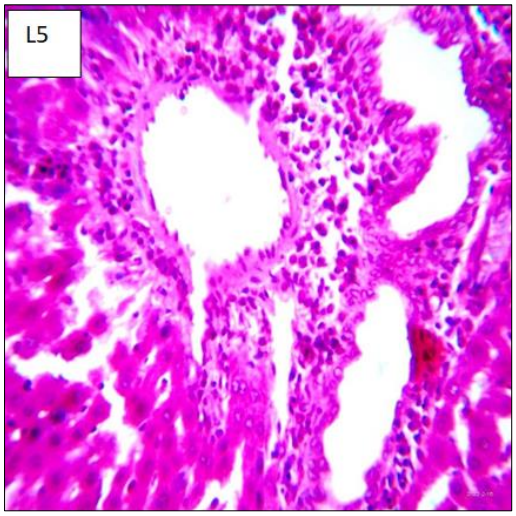


Plate 5(Liver section of aspirin + 30mg/kg Omeprazole Group 5): Section shows central necrosis and hypertrophic sinusoids at different zones while the right section shows a central vein with normal radiating sinusoids.

Plate 3.2: Photomicrograph of stomach of an adult Wistar rat stained with haematoxylin and Eosin technique.

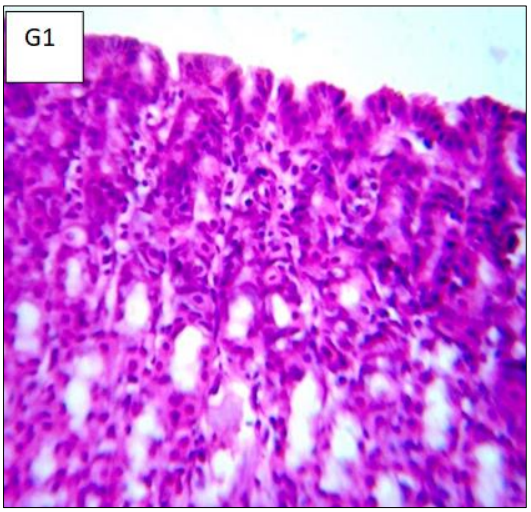


Plate 6(Normal Control): shows a transverse section of the stomach with normal gastric pits and mucosa and abundant gastric glands consistent with histology of the stomach. X400.

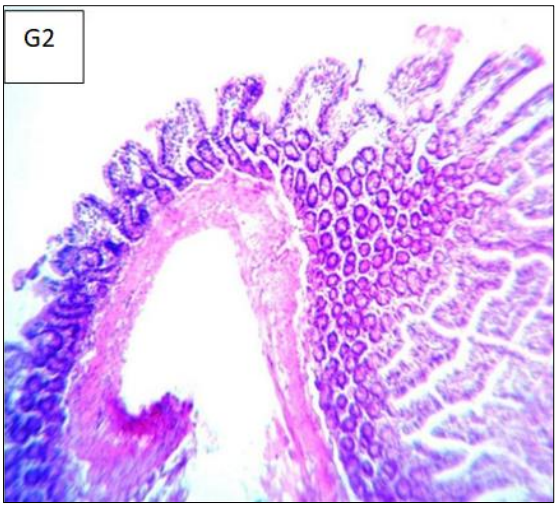


Plate 7(Positive Control): Transverse section of haematoxylin and eosin-stained slides x 400 magnification. Sections areas of ulcerated epithelium with atrophic gastric glands.

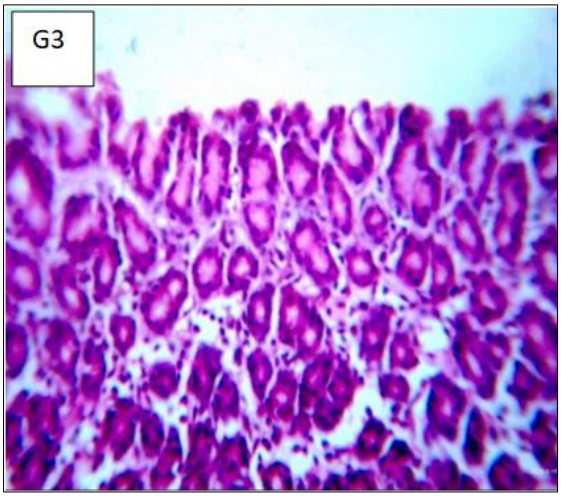


Plate 8(Test Group I): Transverse section of haematoxylin and eosin-stained slides x 400magnification. The section shows gastric mucosa with the disappearance of the original gastric glands and other epithelium replacements

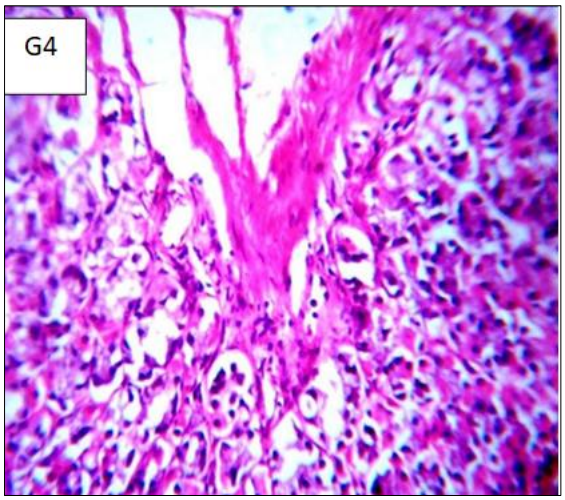
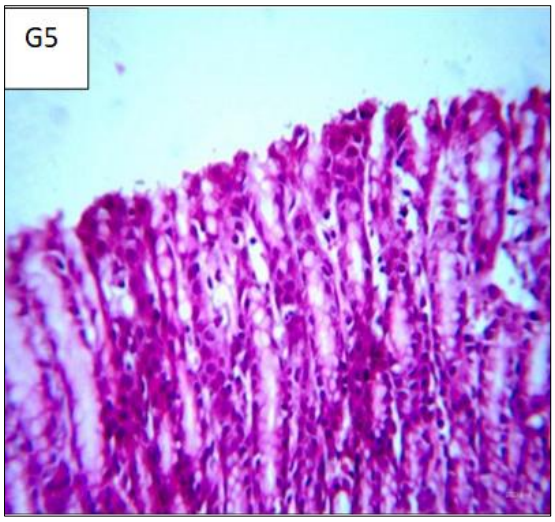


Plate 9 (Test Group II) Transverse section of haematoxylin and eosin-stained slides x 400magnification. The section shows healing by fibrous.



G10. (Standard Control) Transverse section of haematoxylin and eosin-stained slides x 400magnification. The section shows regenerating epithelium with tall gastric glands displaying normal columnar epithelium.

DISCUSSION

Gastric ulcer is a major global health issue, impacting around 14.5 million individuals globally and resulting in nearly 4.08 million fatalities each year [1]. This condition is frequently caused by the production of free radicals and oxidative stress. Andrographis paniculata is a commonly utilised medicinal herb that is utilised as a supplemental treatment for a range of gastrointestinal ailments, such as gastric difficulties [29].

High doses of aspirin are administered to experimental rats in order to develop ulcers. Prior studies have indicated that non-steroidal anti-inflammatory medicines (NSAIDs), like aspirin, reduce the activity of antioxidant enzymes in the stomach of rats, leading to the development of gastric ulcers. This is caused by the overwhelming impact of free radicals on the cellular antioxidant defence systems, leading to oxidative damage in the stomach. High-dose therapy with aspirin is often linked to mild antinotrand, which can result in severe apparent, acute, or chronic liver damage [34].

Results obtained from the ulcer index of the GIT showed that administration of aspirin 200mg/kg caused ulceration in the GIT of the rats when compared with normal control. Administration of the extract (200 and 400mg/kg) significantly protected the rats from aspirin induced ulceration of GIT. It gave a percentage inhibition of 13.85% and 22.29% respectively while the Omeprazole group (standard) gave a percentage inhibition of 26.29% compared to positive control.

The hepatoprotective efficacy of *Andrographis paniculata* was assessed using a model of hepatotoxicity produced by aspirin. The findings demonstrated that the introduction of aspirin at a dosage of 200 mg/kg led to a notable elevation in the serum concentrations of the liver enzymes AST, ALT, and ALP in the positive control group, as compared to the normal control group. The elevation in liver enzyme levels suggests hepatic injury, most likely caused by the release of these enzymes from the injured liver into the bloodstream. Nevertheless, administering the methanolic extract of *Andrographis paniculata* at doses of 200 mg/kg and 400 mg/kg (Test 1 and Test 2 groups, respectively) prior to treatment significantly decreased the heightened levels of AST, ALT, and ALP in comparison to the positive control group. This decrease indicates that *Andrographis paniculata* has hepatoprotective effects. Similarly, the group that got pretreatment with Omeprazole, known as the standard group, similarly exhibited a reduction in the levels of these liver enzymes when compared to the positive control group. The antioxidant capabilities of *Andrographis paniculata* are responsible for its potential to improve liver damage. Oxidative stress caused by free radicals has been linked to several illnesses. Potential antioxidant treatments should involve natural compounds that scavenge free radicals or enhance the activity of antioxidant enzymes [30]. The study revealed that a greater dosage of *Andrographis paniculata* (400 mg/kg) demonstrated a more significant hepatoprotective activity compared to the lower dose (200 mg/kg), demonstrating a dose-dependent impact. The findings demonstrated that the use of Aspirin resulted in an elevation in the concentration of Malondialdehyde in liver tissue. Groups 3 and 4, which were given pretreatment doses of 200 mg/kg and 400 mg/kg of Andrographis paniculata, respectively, exhibited a notable reduction in SOD activity compared to the positive control. This substantial reduction was also directly proportional to the dosage. Group 5, which received a pre-treatment of 30 mg/kg of Omeprazole, likewise showed a noteworthy decrease in MDA activity compared to the positive control. This discovery is consistent with the investigation carried out by Naito *et al*., [17]. In addition, *Andrographis paniculata* at doses of 200 mg/kg and 400 mg/kg showed a percentage inhibition of 13.85% and 22.29%, respectively, in the ulcer index compared to the positive control. On the other hand, prior administration of Omeprazole led to a 26.20% inhibition rate, as compared to the positive control.

The presence of flavonoids and xanthones in the extract of *Andrographis paniculata* indicates its ability to prevent ulcers caused by Aspirin by exerting antioxidant effects. These results align with the discoveries made by Nagalekshmi *et al*., [16].

The findings in this study are supported by the histological report depicted in the photomicrographs above. The positive control group (Plate 7) has ulcerated epithelium with atrophic gastric glands. This report demonstrates the erosion of the inner lining of the gastrointestinal (GIT) wall and the depletion of gland cells responsible for digestion caused by aspirin. This is in contrast to the histology observed in Plate 6 (Normal control), which shows intact gastric pits, mucosa, and plentiful gastric glands, consistent with the normal histology of the GIT. The administration of a 200mg/kg dose of the methanol extract of *Andrographis paniculata* in Plate 8 (Group 3) resulted in the gastric mucosa showing the absence of the original gastric glands and the replacement of the epithelium. The histology report for Plate 9 (Group 4), conducted with a dosage of 400mg/kg of methanol extract, reveals fibrous repair, indicating the replacement of ulcerated tissues. When omeprazole is given at a dose of 30mg/kg, it leads to the formation of new epithelial cells in the stomach. These cells have tall gastric glands and exhibit a normal columnar shape. The extent of cellular damage was diminished in comparison to Plate 7 (positive control Group 2), consequently approximating the values observed in group 1. The research also revealed that aspirin caused cellular damage to the liver tissues through oxidative stress, similar to the histopathology shown in Plate 1 (Normal control Group 1). This plate displayed a liver with a normal central vein, sinusoids, and hepatocytes, which is compatible with the liver's histology. At a dose of 200mg/kg, the administration of a methanol extract from *Andrographis paniculata* in Plate 3 (Group 3) resulted in the presence of an aberrant liver, characterised by inflammation of the blood vessels and congestion of the central vein. In addition, the histopathology report for Plate 4 (Group 4), which received a dosage of 400mg/kg of methanol extract, indicates that the liver exhibits normal histology. The degree of cellular damage was diminished in comparison to Plate 2 (positive control Group 2), whereas Plate 5 (Group 5) exhibited central necrosis and hypertrophic sinusoids in distinct areas. In the right part, a central vein with typical radiating sinusoids was observed. The histological findings presented in the discussion are consistent with previous studies on aspirin-induced gastric ulceration and the protective effects of natural compounds. A study by Lien *et al*., [13], on the Gastroprotective Effect of Anisomeles indica on Aspirin-Induced Gastric Ulceration in Rats reported similar histological observations, where aspirin administration caused severe disruption and heavy infiltration of inflammatory cells in the gastric epithelium. This aligns with the description of the positive control group (Plate 7) in the current study. Another study on the Effectiveness of Sechium edule Jacq. Swartz Extract Changes in the Histopathology of Aspirin-Induced Rat Gastritis Model [28], also demonstrated that aspirin-induced gastritis led to mild inflammatory infiltration, which was improved by the administration of Sechium edule extract, similar to the findings with *Andrographis paniculata* in the current study. The histological changes observed in the liver, such as inflammation of blood vessels and congestion of the central vein, are consistent with the known hepatotoxic effects of aspirin, as reported in the literature [32-4]. While the current study found that *Andrographis paniculata* exhibited dose-dependent protective effects on the gastric mucosa, a study on Aspirin-Induced Gastric Injury in the Rat: Histologic Changes and Protection by Sucralfate [5], reported that sucralfate, rather than the herbal extract, significantly decreased aspirin-induced deep mucosal erosions. The current study suggests that the higher dose of Andrographis paniculata (400 mg/kg) showed better hepatoprotective effects compared to the lower dose (200 mg/kg). However, some studies have reported that high doses of certain herbal extracts may actually exacerbate liver damage, and the optimal dose should be carefully determined.

CONCLUSION

The results of the present experimental study indicate that the methanolic extract of Andrographis paniculata possesses antioxidant compounds responsible for its anti-ulcerogenic and hepatoprotective effects against aspirin-induced ulcers and liver damage. The study findings demonstrate that the protective effects of the *Andrographis paniculata* extract are dose-dependent, with higher concentrations (400 mg/kg) exhibiting more pronounced anti-ulcer and hepatoprotective activities compared to the lower dose (200 mg/kg). The antioxidant properties of the Andrographis paniculata extract appear to be the key mechanism underlying its ability to mitigate the harmful effects of aspirin on the gastric lining and liver. The extract was able to significantly reduce the elevated levels of liver enzymes (AST, ALT, ALP) and lipid peroxidation (MDA) induced by aspirin administration, in the liver. These results suggest that *Andrographis paniculata* could be a promising natural therapeutic option for addressing gastric ulcers and liver dysfunction caused by oxidative stress, with the higher doses exhibiting more potent protective effects. Further research is warranted to fully elucidate the underlying mechanisms and optimize the therapeutic potential of this medicinal plant.

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