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Original Research Article

The Protective Effects of *Andrographis paniculata* against Cardiac Damage Induced by Diclofenac in Wistar Albino Rats

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Abstract: This study aimed to evaluate the potential preventative effects of *Andrographis paniculata* on cardiac damage produced by diclofenac in Wistar albino rats. The rats were randomly assigned to five groups: Group 1, which served as the normal control and was given only feed; Group 2, which served as the positive control and was given feed along with 100 mg/kg body weight diclofenac; Group 3, which received feed along with 100 mg/kg body weight diclofenac and 200 mg/kg extract; Group 4, which received feed along with 100 mg/kg body weight diclofenac and 400 mg/kg extract; and Group 5, which received feed along with 100 mg/kg body weight diclofenac and 200 mg/kg vitamin E. The oral administration of the extract was conducted over a period of 14 days, following which the animals were slaughtered on the 15th day in order to facilitate subsequent analysis. The findings indicated that administering *Andrographis paniculata* extract to the experimental groups led to a statistically significant increase in bodyweight for group 3 (167.33 ± 21.33) and group 4 (173.33 ± 17.63), as compared to the normal and positive control groups ($p<0.05$). The research findings demonstrated a clear association between diclofenac administration and cardiac damage, with a statistically significant elevation in blood concentrations of total cholesterol, triglycerides, low-density lipoprotein, and malondialdehyde. Pretreatment with Andrographis paniculata resulted in a modulation of the decrease in levels of serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and malondialdehyde (MDA) in group 2 compared to group 1. However, the administration of Vitamin E led to a significant decrease in serum total cholesterol (TC) level, triglyceride (TG), low-density lipoprotein (LDL) level, and malondialdehyde (MDA) levels, as well as an increase in serum high-density lipoprotein (HDL) level, superoxide dismutase (SOD), and catalase (CAT) activity compared to the positive control. The histological examination demonstrated the presence of coronary artery congestion, infiltration of inflammatory cells predominantly composed of lymphocytes, and acute myocarditis. However, the administration of an extract derived from the *Andrographis paniculata* plant prior to therapy demonstrated a significant improvement in the cardiac tissues when compared to the positive control. The ongoing study has revealed that the extract obtained from *Andrographis paniculata* possesses potential qualities that can protect the cardiovascular system and may be a beneficial natural antioxidant agent.

Keywords: Vitamin E, *Andrographis paniculata*, diclofenac, cardioprotective, lipoprotein.

INTRODUCTION

Andrographis paniculata, also known as the king of bitters or green chiretta, is taxonomically categorised as an annual herbaceous plant belonging to the Acanthaceae family. The species is native to India and Sri Lanka. Based on the research undertaken by Benoy *et al*., (2012), the plant in question is cultivated on a large scale across many regions in southern and southeastern Asia, encompassing Cambodia, the

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Caribbean islands, Indonesia, Laos, Malaysia, Myanmar, and Sri Lanka. The places under consideration exhibit specific phytogeographical and edaphic zones, which create favourable environments for the proliferation of this particular plant species (Mishra *et al.*, 2007). The plant under consideration is frequently noticed as a branching, upright, herbaceous annual species that flourishes in hedgerows encompassing several terrains, including plains, hill slopes, waste grounds, farms, damp environments, seashores, and roadsides. Moreover, it possesses the capacity to be cultivated inside a horticultural environment. Moist, shaded environments, such as forests and wastelands, are commonly regarded as favourable conditions for attaining optimal growth and development. The genus under investigation has been documented to possess a reported species count of 19 (Bhattacharya *et al*., 2012), 40 (Boopathi 2000), or 44 (Parixit *et al*., 2012). The exact taxonomic count of species belonging to the *Andrographis* genus has yet to be definitively established.

Throughout the course of history, the use of the leaves and roots of *Andrographis paniculata* has been widely observed in Asia and Europe as a therapeutic intervention for a multitude of health conditions. The study undertaken by Chopra in 1980 established the utilisation of the entire plant for the treatment of several disorders, including dyspepsia, cardiovascular diseases, influenza, diarrhoea, malaria, and respiratory infections. Furthermore, throughout history, it has been utilised as a remedy for snake bites and venomous stings inflicted by diverse bug species. According to Abhishek (2010), The preliminary analysis of the phytochemical content of *Andrographis paniculata* has revealed the existence of andrographolide, diterpene, lactone, and flavonoids.

Diclofenac is categorised as a nonsteroidal anti-inflammatory drug (NSAID). The mechanism of action entails the suppression of a certain endogenous chemical synthesis within the human body, which is accountable for the production of pain, heightened temperature, and inflammatory reactions. The study conducted by Lapi *et al*., (2013) has proven a correlation between the incidence of oxidative stress and the detrimental effects of nonsteroidal anti-inflammatory medicines (NSAIDs). Symptoms suggestive of an overdose encompass lethargy, fatigue, nausea, vomiting, epigastric discomfort, gastrointestinal bleeding, and predominantly, heart impairment.

According to a study conducted by Newman and Cragg (2016), a majority of the global population, specifically over 60%, depends on the utilisation of medicinal plants in order to address their healthcare requirements. Furthermore, a significant majority, approximately 80%, of inhabitants residing in underdeveloped countries rely on these plants to meet their healthcare needs. The utilisation of botanical resources as a means to alleviate health concerns and improve overall wellness is a lengthy and diverse therapeutic approach that spans across numerous cultures and historical periods. The utilisation of medicinal plants holds considerable importance in the realm of African traditional medicine. According to Brown and Wright (2016), medicinal plants are frequently recommended by traditional healers in Nigeria due to their perceived efficacy, ease of access, and cost-effectiveness. There exists a substantial body of evidence documenting the historical pedigree of numerous pharmaceutical drugs, which may be traced back to their origins in herbal remedies and their subsequent administration by medical experts. Prominent examples include opium, aspirin, digitalis, and quinine. In their study, Sarkar *et al*., (2015) found that a significant proportion, above 80%, of the bioactive compounds utilised in contemporary medicine are sourced from higher plants. Furthermore, a notable correlation may be demonstrated between the present-day therapeutic applications of these compounds and their past use.

A significant proportion of regularly used nonsteroidal anti-inflammatory drugs (NSAIDs) have potentially life-threatening adverse effects. Based on extant literature, the utilisation of pharmaceuticals falling under this particular categorization has the capacity to present hazards to individuals who are in a state of prime physical well-being, those with pre-existing cardiovascular ailments, or neonates. The findings of Olsen *et al*., (2011), Herman (2009), and Cheetham *et al*., (2008) indicate that... Additionally, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been linked to notable detrimental consequences, including the emergence of gastrointestinal ulcers or bleeding, compromised liver and kidney function, hypersensitivity reactions, myocardial infarction, and sudden cardiac mortality. (Tras and Elmas, 2012; Ray *et al*., 2009; O'Malley, 2006; Singh *et al*., 2006) have been cited in the text. The sources referenced in the text consist of Olsen *et al*., (2011), Herman (2009), and Cheetham *et al*., (2008). Furthermore, there exists empirical evidence indicating that the utilisation of nonsteroidal anti-inflammatory drugs (NSAIDs) may lead to notable deleterious consequences, including myocardial infarction, sudden cardiac death, hepatic and renal impairment, gastric ulcers, and haemorrhage. (Tras and Elmas, 2012; Ray *et al*., 2009; O'Malley, 2006; Singh *et al*., 2006) have been cited in this context.

The objective of this study was to investigate the potential cardioprotective effects of *Andrographis paniculata* against diclofenac-induced heart injury.

MATERIALS AND METHODS

Animals and diet

A total of fifty male Wistar albino rats, with weights ranging from 117g to 202g, were selected as subjects for the present investigation. The animals were purchased from the Department of Pharmacology at the University of Port Harcourt, located in Rivers State, Nigeria. The rats were housed in conventional cages and

underwent a period of acclimatisation in the animal facility located inside the Department of Pharmacology at Niger Delta University. This acclimatisation period lasted for two weeks, during which the rats were provided with unrestricted access to pelleted chicken feed and water. Chemicals and reagents The chemicals used in the experiment include distilled water, chloroform, methanol, normal saline, formaldehyde, 0.1M Tris-HCl buffer with a pH of 7.4, Tween 80, thiobarbituric acid, 30% trichloroacetic acid, and diclofenac. The kits provided are manufactured by Randox Laboratories Ltd., located in Co. Antrim, United Kingdom. The chemicals utilised in this study were sourced from Sigma-Aldrich Ltd., U.S.A. and PerkinElmer, USA. All additional reagents and chemicals were sourced from reputable suppliers and were of analytical quality. The compilation of extracts and the methodology employed for their extraction Professor Ching F. Poh procured *Andrograhis paniculata*, a plant referred to as the "king of bitters," from the Niger Delta University's Department of Pharmacology. Professor Kolawole Ajibesin from the Department of Pharmacognosy at Niger Delta University conducted the plant's identification and authentication. The freshly harvested leaves of *Andrographis paniculata* were gathered and placed in a sanitary and arid tray, where they were subjected to a drying process under shaded conditions for a duration of three weeks. The leaves were dried in the shade and subsequently pulverised into a fine powder using an electric blender. The resulting powder was carefully weighed, yielding a mass of 0.6 kilogrammes, and subsequently stored in a securely sealed container. A quantity of 0.6 kilogrammes of powdered leaves was immersed in 3.2 litres of methanol for a duration of 48 hours in order to facilitate the extraction process. The methanol extract was obtained and subsequently subjected to filtration and concentration under reduced pressure using a rotary vacuum evaporator operating at a temperature of 50°C and a rotation speed of 40 revolutions per minute. The methanol extract was quantified (65.95g) and stored in a refrigerator at a temperature of 4 oC for subsequent use.

EXPERIMENTAL DESIGN

Fifty rats were used in this research and grouped into five of 10 rats each as follows:

Group 1: (Normal control), Feed Only
Group 2: (Positive control), Feed + 100mg/kg body weight body weight of diclofenac
Group 3: Feed + 100mg/kg body weight of diclofenac + 200mg/kg body weight of the extract
Group 4: Feed + 100mg/kg body weight of diclofenac + 400mg/kg body weight of the extract
Group 5: (Standard group) Feed + 100mg/kg body weight of diclofenac + 200mg/kg body weight of vitamin E

The process of gathering samples and conducting biochemical analyses

The methods described by Hoff *et al*., (2000) were followed in order to carry out the procedures for sacrifice as well as the collection of blood and serum samples. On the fifteenth day of the study, following the administration of general anaesthesia (chloroform) for euthanasia purposes, the animals were dissected and blood samples were obtained using a heart puncture using a 5 ml syringe. The collected blood was then transferred into appropriately marked, plain sample bottles. The liquid portions of the samples were utilised for the purpose of conducting biochemical analysis. The serum was subjected to centrifugation at a speed of 4000 revolutions per minute (rpm) for a duration of 10 minutes. The experiment was conducted using serum. The cardiac tissues were collected and subsequently immersed in a solution of 10% acetone for the purpose of histological examination. The biochemical parameters refer to the measurable quantities used to assess and analyse various biochemical processes within living organisms. These parameters provide valuable insights into The quantification of lipid peroxidation by malondialdehyde (MDA) was determined using the Adam-Vizi and Seregi (1982) methodology. Superoxide dismutase was evaluated using a kinetic approach, following the criteria outlined by Marklund in 1982. The measurement of total serum cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) was conducted using Randox test kits in accordance with the procedure provided by the manufacturers. The LDL cholesterol concentration was determined using the Friedewald *et al*., method, which involves subtracting the sum of the HDL cholesterol and triglyceride concentrations from the total cholesterol concentration (TC).

The present study aims to conduct a comprehensive statistical analysis in order to examine the data and draw meaningful conclusions. All measurements were reported as the mean value plus or minus the standard deviation. The statistical significance was assessed using GraphPad InStat software, specifically employing a one-way analysis of variance (ANOVA) with a Turkey-Kramer multiple comparison test. The statistical significance of the values was determined at a significance level of $p < 0.05$.

The present study evaluated the biochemical and histological analyses of the ethanol extract of *Andrographis paniculata* in Wistar albino rats with diclofenac -induced cardiomyopathy. A preliminary investigation was conducted to analyse the phytochemical composition. The initial phytochemical analysis indicated the existence of tannins, saponins, alkaloids, phytosterols, proteins, terpenoids, flavonoids, and glycosides in the sample (Sinha *et al*., 2020).

The body weight

A reduction in body weight was observed in rats treated with diclofenac at the conclusion of the study, in comparison to the control group. The administration of

Andrographis paniculata at doses of 200 and 400 mg/kg body weight resulted in a significant increase in body weight in comparison to the control group treated with diclofenac, as indicated in Table 1.

The investigation of biochemical parameters

The serum markers under investigation in this study are Superoxide Dismutase (SOD), Catalase (CAT), and Lactate Dehydrogenase (LDH).

The administration of diclofenac results in an increase in the concentration of LDH and a significant reduction ($p < 0.05$) in the levels of SOD and CAT. These biomarkers are recognised as specific indicators of heart injury caused by oxidative stress, as compared to the standard condition ($p < 0.05$). The treated groups exhibited a statistically significant reduction ($p < 0.05$) in LDH levels and an increase ($p < 0.05$) in SOD and CAT levels, as compared to the positive control (refer to Table 2).

The lipid profile is a diagnostic tool used in clinical settings to assess an individual's lipid levels.

The biochemical evaluation of the lipid profile in rats treated with diclofenac revealed a significant elevation ($p < 0.05$) in triglyceride and cholesterol levels, as well as LDL and lipid peroxidation (MDA) levels in the heart. Additionally, a substantial reduction ($p < 0.05$) in HDL levels was observed when compared to the normal control group. The administration of *Andrographis paniculata* extract at doses of 200 and 400 mg/kg prior to treatment resulted in a noteworthy reduction in triglyceride, cholesterol, LDL, and lipid peroxidation (MDA) levels, as well as a substantial increase in HDL levels, in comparison to the positive control ($p < 0.05$) According to Table 3.

Table 1: Effects of diclofenac and *Andrographis paniculata* on the mean body weights of the male albino wistar rats

TREATMENT	Mean wt of rats on day 1 (g)	Mean wt of rats on day 15 (g)
Normal control with normal saline	142.75±15.39[a]	161.33 ± 9.88[d]
Positive Control with 10mg/kg Diclofenac	133.75±7.58 [b]	154.08 ± 20.63[e]
Test group 1 with 200mg/kg extract and 10mg/kg Diclofenac	155.75 ± 3.77 [c]	167.33 ± 21.33[d]
Test group 2 with 400mg/kg extract and 10mg/kg Diclofenac	155.75 ±10.41 [c]	173.33 ± 17.63[d]
Test group 3 with 200mg/kg Vitamin E and 10mg/kg Diclofenac	157.5± 9.02 [c]	186.17 ± 13.86[e]

Values are represented as Mean ± SD. Value with different superscripts from control are statistically different at $p<0.05$

Table 2: Effect of ethanol extract of *Andrographis paniculata* leaf on CAT, SOD and LDH levels in rats by diclofenac induced cardiac damage

Treatment	CATALASE (ŋmoles/min/ml)	SOD (ŋmoles/min/ml)	LDH (mg/ml)
Group 1 Normal control with Normal saline	1.51 ± 0.17[a]	9.43E-03 ± 2.76E-03[a]	10.6 ± 0.1[a]
Group 2 Positive Control with 10mg/kg Diclofenac	0.21 ± 0.07[b]	1.29E-02 ± 5.77E-04 [b]	16.8 ± 0.1[b]
Group 3 Test group 1 with 200mg/kg extract and 10mg/kg Diclofenac	0.39 ± 0.1[c]	1.22E-02 ± 6.35E-04 [c]	13.6 ± 0.2[c]
Group 4 Test group 2 with 400mg/kg extract and 10mg/kg diclofenac	0.89 ± 0.1[d]	1.7E-02 ± 6.35E-04 [d]	11.4 ± 0.2[d]
Group 5 Test group 3 with 200mg/kg Vitamin E and 10mg/kg diclofenac	0.96 ± 0.1[e]	1.74E-02 ± 5.77E-04[e]	11.2 ± 0.1[e]

Data expressed as MEAN ± SD (Standard deviation), values with different superscript from control are statistically different at $p < 0.05$.

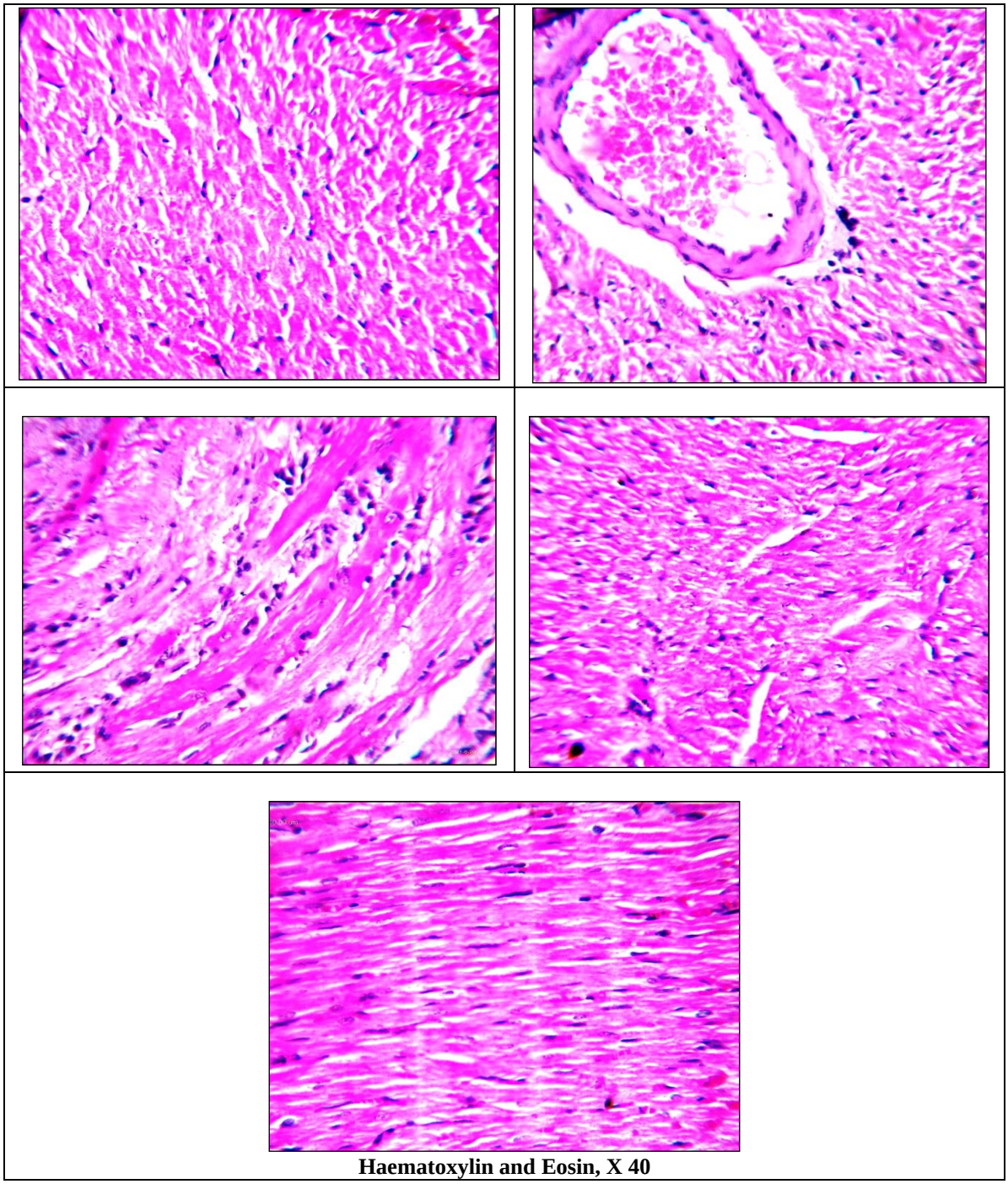
Table 3: The protective role of *Andrographis paniculata* on diclofenac-induced albino rats

Treatment	Total cholesterol(mg/ml)	Triglycerides (mg/ml)	HDL (mg/ml)	LDL (mg/ml)	MDA (µmole/ml)
Group 1 Normal control with saline water	139.66 ± 1.38[a]	70.47 ± 1.14[a]	117.42 ± 0.74[a]	8.14 ± 1.74 [a]	1.63E-5 ± 3E-7 [a]
Group 2 Positive control with 10mg/ kg diclofenac	148.93 ± 0.65[b]	167.74±0.43[b]	44.14 ± 2.07 [b]	71.24±1.93[b]	8.17E.6 ± 1.42E-6[b]
Group 3 Test group 1 with 200mg/kg extract and 10mg/kg diclofenac	146.06 ± 1.10 [c]	117.89±2.79[c]	56.67 ± 1.54 [c]	61.10±1.93[c]	1.46E-5 ± 1.77E-6[c]
Group 4 Test group 2 with 400mg/kg extract and 10mg/kg diclofenac	144.72 ± 0.65[d]	114.85±1.19[d]	63.60 ± 1.40 [d]	59.49±0.56[d]	9.26E-6 ± 1.91E-7[d]
Group 5 Test group 3 with 200mg/kg vitamin E and 10mg/kg diclofenac	141.36 ± 1.49 [e]	107.37±2.51[e]	113.25 ± 0.77[e]	9.99 ± 0.97 [e]	2.68E-5 ± 8.5E-7[e]

Data expressed as Mean ± SD (standard deviation), values with different superscript from control are satisfactorily different at $P < 0.05$

Histopathological changes on Diclofenac-induced cardiac damage

The heart sections obtained from diclofenac treated animals showed congestion of the coronary artery and thickening of the membrane with striation of the epithelium and mild peri-vascular infiltration of inflammatory cells predominantly lymphocytes. Animals pretreated with extract of *Andrographis paniculata* at 200 and 400 mg/kg showed improvement in the cell integrity evidenced by absence of necrosis, less vacuolization of the cytoplasm and maintenance of normal integrity of the cardiac muscles, Fig 1.



Haematoxylin and Eosin, X 40

Fig 1: Histopathological images of heart pretreated with ethanol extract of *Andrographis paniculata* by diclofenac induced cardiac toxicity. A: Normal control, B: Positive control, C: Test group – 200 mg/kg, D: Test group – 400 mg/kg, E: Vit E Standard group – 200mg/kg

DISCUSSION

Diclofenac is a well-recognised member of the class of nonsteroidal anti-inflammatory drugs (NSAIDs), which are extensively used both as over-the-counter and prescribed therapeutic interventions for a variety of ailments. These include pain management, rheumatoid arthritis, osteoarthritis, musculoskeletal diseases, and

other concurrent conditions. Crofford (2013) and Lanas *et al*., (2015) are two academic sources that have been referenced. In contrast, the administration of diclofenac has been associated with adverse effects such as the development of ulcers, bleeding, and renal dysfunction, as well as an elevated susceptibility to cardiovascular events including heart attack and stroke (Soyun *et al.*, 2013). According to the study conducted by Gonzalez-Ponce *et al*., (2018), the association between the adverse effects of diclofenac and the occurrence of oxidative stress has been established. *Andrographis paniculata* is an herb that shows promise in the management of cardiovascular ailments. According to the study conducted by Okhuarobo *et al*., in 2014 and Tan *et al*., (2018), the presence of andrographolide in *Andrographis paniculata* has been documented, and it is known to play a role in bolstering antioxidant mechanisms. The mechanism of action involves the direct neutralisation of free radicals. Additionally, it exerts an indirect influence by safeguarding the integrity of mitochondria, impeding the activity of pro-oxidant enzymes, and/or stimulating the activation of antioxidant enzymes (Li *et al.,* 2018). The diagnostic biochemical blood biomarkers associated with cardiotoxicity include triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol, malondialdehyde (MDA) as a measure of lipid peroxidation, lactate dehydrogenase (LDH), and levels of antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD). According to a study conducted by Andersson *et al.*, in 2014, deviations from normal levels of biomarkers such as triglycerides, HDL, LDL, total cholesterol, LDH, MDA, SOD, and CAT have been identified as potential indicators of tissue damage and can serve as predictive factors for the occurrence of early coronary heart diseases. Catalase (CAT), superoxide dismutase (SOD), and lactate dehydrogenase (LDH) are essential enzymes involved in the antioxidant defence system. Previous studies conducted by Cooper *et al*., (2005) demonstrated that the treatment of diclofenac resulted in a considerable reduction in the levels of superoxide dismutase (SOD) and catalase (CAT), while concurrently increasing the level of lactate dehydrogenase (LDH) in the cardiac tissue of albino rats. In the present study, it was observed that the groups receiving A. *paniculata* exhibited a significant elevation in the levels of superoxide dismutase (SOD) and catalase (CAT) as compared to the positive control group. This increase was particularly evident in groups 3 and 4. Furthermore, a significant reduction in LDH levels was observed in groups 3 and 4, which were treated with *A. paniculata*, as compared to the positive control group (group 2). Table 2 is presented in the following section. According to a previous study conducted by Feron (2009), many conditions, such as tissue injury, necrosis, hypoxia, hemolysis, and malignancies, have been identified as potential factors that could lead to an elevation in lactate dehydrogenase (LDH) levels. The efficacy of the *A. paniculata* extract exhibited a correlation with dosage, as seen by the data presented in Table 2. Rat groups 3 and 4 exhibited a concentration-dependent way in which the levels of SOD and CAT experienced a significant increase. The LDH level exhibited a notable reduction in rat groups 3 and 4, which corresponded to the administered concentrations of 200 mg/kg and 400 mg/kg, respectively. The present investigation demonstrates that the methanol extract of *A. paniculata* exhibits a notable reduction in LDH levels and an increase in CAT and SOD activity, as indicated in table 2. These findings suggest that the extract possesses antioxidant properties that contribute to its cardio-protective effects. A previous study conducted by Peopples *et al*., (2019) posited that oxidative stress has a significant role in the progression of several cardiovascular conditions, such as atherosclerosis, heart failure, cardiac arrhythmia, and myocardial ischemia-reperfusion injury. Malondialdehyde (MDA) is a well-established indicator of lipid peroxidation. The findings depicted in Table 3 indicate a considerable elevation in MDA levels among the rats in the positive control group compared to those in the normal control group. According to Andersson *et al*., (2014), the observed rise in MDA levels can be linked to prior injury in the cardiac tissues. The findings of the study indicated that the combination of *Andrographis paniculata* and Vitamin E resulted in a significant reduction in the serum concentration of malondialdehyde (MDA). Cholesterol is a lipid compound that is naturally synthesised in the body. It plays a crucial role in the construction of cellular membranes and the production of various hormones and vitamins. However, elevated levels of cholesterol have been associated with an increased susceptibility to cardiovascular illnesses (Bechthold *et al*., 2019). The study found that the levels of TC, TG, LDL, and MDA were much higher in the positive control groups compared to treatment groups 3 and 4. However, there was a noticeable drop in HDL levels in the positive control groups compared to groups 3 and 4 that were given A. *panicualta.* Table 3 is shown in the following section. The toxic effect of the medicine, which leads to hepatobiliary diseases and poor cholesterol metabolism, may be to blame for the increase in serum levels of total cholesterol and triglycerides, as well as the decrease in serum levels of HDL-cholesterol. The research by Maity *et al*., (2012) and Arhoghro *et al*., (2023), which found that diclofenac-treated rats had significant increases in blood cholesterol and triglyceride levels, is consistent with the findings of this study. According to Berman *et al*., (2019), elevated levels of total cholesterol, TG, and LDL and reduced levels of HDL cholesterol are associated with an increased risk of cardiovascular illnesses. The current study investigated the effects of pretreatment with *Andrographis paniculata* on various lipid parameters. The results show that *Andrographis paniculata* pretreatment effectively controlled the activities by decreasing the levels of total cholesterol, triglycerides, and LDL cholesterol, bringing them closer to normal values. Additionally, *Andrographis paniculata* pretreatment elevated the levels of HDL cholesterol, likewise towards normal levels (Berman *et al*., 2019). Previous studies have shown evidence that an increased

level of total cholesterol, namely LDL-C, contributes to the development of atherosclerosis through the accumulation of cholesterol and fatty acids in the artery wall. Conversely, HDL-C is believed to have a positive effect by facilitating the transportation of cholesterol back to the liver (Glasser *et al*., 2016). Elevated concentrations of blood lipoproteins have been identified as significant risk factors for cardiovascular disease (CVD), calcific aortic valve stenosis, and stroke, as noted by Willeit *et al*., (2018). The histopathological analysis of the albino rats, as seen in Figure 2, reveals transverse congestion of the coronary artery and thickening of the membrane, accompanied by striation of the epithelium. Additionally, there is a slight peri-vascular infiltration of inflammatory cells, primarily lymphocytes. The present study has shown evidence of cellular injury to cardiac tissues resulting from oxidative stress triggered by diclofenac. This is supported by the histopathological findings depicted in Figure 1, slide A (Group 1), which exhibit characteristics compatible with the typical histological appearance of healthy cardiac tissue. The administration of a methanol extract of *A. paniculata* at a dose of 200 mg/kg resulted in the observation of considerable inflammatory cell infiltration and the presence of exuberant lesions consisting of Anitschkow cells. Nevertheless, the histological analysis of slide D (group 4), which received a dosage of 400 mg/kg of methanol extract of *A. paniculata*, and slide E (group 5), which received a dosage of 200 mg/kg of vitamin E, revealed no detrimental pathological findings. The observations and findings from these slides were consistent with those from slide A. In conclusion, it can be inferred that the information provided supports the notion that the current investigation has revealed that the administration of *Andrographis paniculata* is a good approach to mitigating the heart harm induced by diclofenac, owing to its natural antioxidant properties. The cardio-protective properties of *Andrographis paniculata* were confirmed by the observed reductions in LDH, triglycerides, LDL, and MDA levels, as well as the increases in HDL, SOD, and CAT levels after pretreatment with *Andrographis paniculata.*

Compliance with ethical standards

Acknowledgments

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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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