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Research Article

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The Protective Activity of *Bridelia ferruginea* against Cardiac Injury Induced by Diclofenac in Wistar Albino Rats

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Abstract *Bridelia ferruginea* is an indigenous medicinal plant in Nigeria belonging to the *Euphorbiaceae* family and is used for diverse medicinal purposes. The present study aimed to determine the cardiac protective property of methanol extract of *Bridelia ferruginea* against diclofenac-induced cardiac damage in wistar albino rats. Fifty (50) wistar rats (weighing about 150-200kg) were used for this research and divided into 5 groups of 10 rats each as follows: Group 1: Feed Only (Normal control); Group 2: Feed + 100mg/kg body weight diclofenac (Positive control); Group 3: Feed + 100mg/kg body weight diclofenac + 200mg/kg extract; Group 4: Feed + 100mg/kg body weight diclofenac + 400mg/kg extract; Group 5: Feed + 100mg/kg body weight diclofenac + 200mg/kg body weight vitamin E. The extract was administered intra-peritoneally with food and distilled water for 15 days. Afterward, the animals were sacrificed under chloroform anesthesia, and blood was collected via cardiac puncture for cardiac function and antioxidant assays. Total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDH), Malondialdehyde (MDA), antioxidant status (Superoxide dismutase, SOD, catalase, CAT), and lactate dehydrogenase (LDL) were determined. The results of this research showed that serum activities of superoxide dismutase, SOD (129.41E-02 ± 5.44E-04) catalase, and CAT (1.01 ± 0.24) were significantly decreased ($p < 0.05$) in group2. However, treatment with *Bridelia ferruginea* (200 and 400 mg/kg) significantly increased serum activities of SOD (128.06E-02 ± 1.86E-04 and 134.71E-02 ± 1.26E-04) and CAT (1.18 ± 3.4 and 1.52 ± 0.28) compared to group 2. Treatment with Vitamin E at a dose of 200mg/kg also caused a significant increase in SOD (148.92E-02 ± 2.13E-04) and CAT (1.59.66 ± 1.3) compared to group 2. In group 2, there was also increased activity of LDH (238.17 ± 5.12)
compared to group 1 animals (170.30 ± 4.42). However, treatment with *Bridelia ferruginea* (200 and 400 mg/kg) and vitamin E significantly decreased the activity of LDH ($p < 0.05$) (206.15 ± 5.41 and 181.97 ± 3.17) compared to group 2. Total cholesterol (203.72 ± 9.83), triglyceride (25.27 ± 1.20), LDL (48.80 ± 1.67), and MDA (62.79E.06 ± 1.67E-06) levels were significantly increased ($p < 0.05$) while HDL (38.22 ± 4.99) decreased significantly in the positive control group 2 treated animals. However, treatments with *Bridelia ferruginea*

(200 and 400 mg/kg) significantly decreased the activity of total cholesterol (105.24 ± 5.39 and 76.07 ± 4.33), triglyceride (23.09 ± 2.86 and 18.08 ± 0.25), LDL (23.46 ± 8.73 and 20.14 ± 6.80) and MDA (53.42 ± 1.86 and 49.62 ± 1.67) while HDL (61.80 ± 2.40 and 46.78 ± 7.69) level were increased significantly. Treatment with Vitamin E at a dose of 200mg/kg also caused a significant decrease ($p < 0.05$) in the total cholesterol (112.18 ± 12.71), triglyceride (12.17 ± 1.41), LDL (11.32 ± 3.92) and MDA (44.82 ± 1.32) and a significant increase in HDL (88.68 ± 9.43). The current study's findings suggest that the methanolic extract of *Bridelia ferruginea* may have antioxidant properties that protect the heart against diclofenac-induced cardiac injury.

Keywords *Bridelia ferruginea, Vitamin E, Cardio-protective,diclofenac, Lactate dehydrogenase, lipid peroxidation.*

Introduction

Newman and Cragg (2016) reported that a significant proportion of the global population, over 60%, and a substantial majority, approximately 80%, of those residing in developing countries depend on medicinal plants to fulfil their healthcare requirements. The utilisation of botanical resources for the purpose of alleviating health conditions and promoting overall well-being is a longstanding and multifaceted therapeutic approach that spans across various cultures and time periods. Medicinal plants have been a noteworthy component of African traditional medicine. In Nigeria, medicinal plants are frequently recommended by traditional healers owing to their efficacy, availability, and cost-effectiveness (Brown & Wright, 2016). Many pharmaceutical drugs that are commonly prescribed by doctors today have a well-documented historical background as herbal remedies. Notable examples include opium, aspirin, digitalis, and quinine. According to Sarkar et al. (2015), a significant proportion, specifically over 80%, of the active compounds utilised in contemporary medicine are sourced from higher plants. Furthermore, there exists a notable correlation between the present therapeutic applications of these chemicals and their historical utilisation.

A significant proportion of nonsteroidal anti-inflammatory drugs (NSAIDs) often employed exhibit potentially fatal side effects. Based on available studies, the use of pharmaceuticals within this particular category may potentially present hazards to individuals who are in good health, those with pre-existing heart issues, or neonates. (Olsen et al., 2011; Herman, 2009; Cheetham et al., 2008) In addition, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been linked to notable detrimental consequences, including the emergence of gastrointestinal ulcers or bleeding, compromised hepatic and renal function, hypersensitivity reactions, myocardial infarction, and sudden cardiac mortalit (Tras and Elmas 2012; Ray et al., 2009; O'Malley, 2006; Singh et al 2006; Olsen et al., 2011; Herman, 2009; Cheetham et al., 2008). Furthermore, there have been reports indicating that the use of nonsteroidal anti-inflammatory drugs (NSAIDs) may lead to notable detrimental consequences, including myocardial infarction, sudden cardiac death, hepatic and renal impairment, gastric ulcers, and haemorrhaging (Tras and Elmas 2012; Ray et al., 2009; O'Malley,2006; Singh et al 2006).

Bridelia ferruginea, an indigenous plant species of Nigeria, belongs to the taxonomic family *Euphorbiaceae* and is recognised for its therapeutic properties. Under favourable conditions, this particular plant species has a twisted and contorted growth pattern, resembling a shrub but with the potential to attain the stature of a tree. In Nigeria, the plant often referred to as Kirni or Kizni in Hausa, Maren in Fulani, Iralodan in Yoruba, and Ola in Igbo has been well recognised (Rashid et al., 2000). The savannah is typically regarded as its natural environment. The bark of this species is commonly characterised by its scaly, rough texture and dark grey coloration. *Bridelia ferruginea* possesses various medical uses. According to Kolawole et al. (2006), it has been observed that the aqueous extract has a hypoglycemic effect, and the indigenous population uses the leaves for the management of diabetes. Additionally, it has the potential to serve as a vermifuge and purgative agent. According to Orafidiya et al. (1990), the conventional gargle called ogunefu is prepared by combining lime juice with bark extract. Additionally, the bark extract is used as a coagulant for milk. According to the results of Owoseni et al. (2009), *Bridelia ferruginea* bark extract is not very good at stopping the growth of bacteria because it can't target all strains that cause upper respiratory tract infections and related gastrointestinal problems. The plant's leaf and bark both have significant concentrations of phytochemical compounds, according to a study by Owoseni et al. (2009).

Chemicals and Reagents

The materials used in this study include distilled water, chloroform, methanol, Tween 80, as well as various test kits such as the lipid peroxidation (TBARS) test kit, superoxide dismutase (SOD) test kit, catalase test kit, Randox triglyceride test kit, Randox HDL test kit, Randox LDH test kit, and Randox total cholesterol test kit. The chemicals and reagents used in this study were of standard analytical grade.

A collection of extract/extraction procedures

The study involved the collection of fresh leaves from the plant species *Bridelia ferruginea* in the geographical area of Amassoma, situated inside Bayelsa State, Nigeria. The plant specimen was recognised and subsequently submitted to the Herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Niger Delta University, situated at Wilberforce Island, Bayelsa State, Nigeria, under the direction of Professor K. Ajibeshin. The foliage was detached from its stalks and subjected to a three-week period of natural drying at ambient temperature. The dry leaves were pulverised into a fine powder using a blender. In order to achieve adequate homogenization and extraction, a quantity of one kilogramme of powdered leaf material was subjected to a steeping process in 4.6 litres of methanol for a duration of 72 hours, during which continuous agitation (shaking) was maintained. The filtrate underwent concentration at reduced pressure using a rotary vacuum evaporator operating at a temperature of 50°C and a rotation speed of 40 rpm. Prior to this, the mixture was filtered into a 1000 ml beaker using a glass filter and filter paper. In order to obtain a final quantity of 56.4 grammes of paste, the concentrated solution underwent a process of evaporation until complete dryness was achieved. This evaporation process was carried out over a period of three consecutive days, utilising a water bath maintained at a temperature of 40 degrees Celsius. In order to determine the specific concentrations administered to each rat, the residue was weighed accordingly.

A total of fifty male Wistar albino rats, considered to be in good health, were allocated into five groups, each containing ten rats per cage. These rats were subjected to pre-treatment for a duration of fifteen days, according to the following protocols:

Group 1 (Normal rats): feed + distilled water.

Group 2 (Positive control): feed + distilled water +10mg/kg bodyweight of diclofenac.

Group 3 (Test group I): Feed+ distilled water + 10mg/kg bodyweight of diclofenac + 200mg/kg body weight of methanolic extract of *Bridelia ferruginea.*

Group 4 (Test group II): Feed+ distilled water +10mg/kg bodyweight of diclofenac + 400mg/kg body weight of methanolic extract of *Bridelia ferruginea.*

Group 5 (Standard group): Feed+ distilled water +10mg/kg bodyweight of diclofenac + 200mg/kg of Vitamin E.

On the 15th day of research, animals were sacrificed. Blood was drawn and placed in simple vials for biochemical analysis. For histopathological investigation, the kidneys were removed and preserved in 10% formalin.

Sample Collection and Biochemical Analysis

The rats were subjected to a final weighing at the conclusion of the experiment, followed by a 24-hour period of fasting. Subsequently, the rats were euthanized using chloroform anaesthesia. The blood of each animal was obtained by a heart puncture procedure using a sterile needle and syringe. Subsequently, the acquired blood samples were subjected to centrifugation at a speed of 3000 revolutions per minute (rpm) for a duration of 10 minutes. The liquid portion of the sample was utilised for the purpose of conducting biochemical analysis. The cardiac organ was surgically removed by a central abdominal incision, subsequently weighed, and then immersed in a solution of 10% neutral buffered formalin for the purpose of conducting histological analysis. The cardiac organ was extracted and subjected to a cold saline wash prior to the creation of 10% tissue homogenates in a 0.1M Tris-HCL buffer with a pH of 7.4.The kinetic methodology, as recommended by the Deutsche Gesellschaft fur Klinische Chemie, was used for the quantification of Lactate dehydrogenase (LDH) concentrations in the serum. The cardiac tissue homogenate was generated by utilising a phosphate buffer with a concentration of 0.05 M and a pH value of 7.4. The homogenization procedure was conducted for a duration of 10 minutes using a tissue homogenizer working at a rotational speed of 3000 revolutions per minute (rpm). The determination of lipid peroxidation malondialdehyde (MDA), total serum cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) levels

should be conducted in accordance with the instructions supplied by the manufacturer of the Randox test kits. Friedewald et al. (1972) calculated the LDL cholesterol concentration by subtracting the sum of HDL cholesterol and triglyceride values from the total cholesterol concentration (TC). The concentration of VLDL-cholesterol was determined by dividing the triglyceride level by a factor of five..

The serum sample was employed for the estimation of Lactate dehydrogenase (LDH) using a kinetic methodology, in accordance with the guidelines provided by the Deutsche Gesellschaft fur Klinische Chemie. Heart tissue homogenate was prepared using a 0.05 M phosphate buffer with a pH of 7.4. The homogenization process was carried out for a duration of 10 minutes using a tissue homogenizer operating at a speed of 3000 rpm. The quantity of lipid peroxidation, namely malondialdehyde (MDA), was then measured. The total serum cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured using Randox test kits, following the protocol provided by the manufacturer. Friedewald et al. (1972) proposed a method for estimating the concentration of LDL cholesterol by subtracting the combined values of HDL cholesterol and triglycerides from the total cholesterol concentration (TC).

Statistical Analysis

All data were expressed as Mean ± Standard deviation. The data obtained were analyzed using Two-way Analysis of Variance (ANOVA) using SPSS (Statistical Package for Social Sciences) Version 20. The means were separated and compared by post-Hoc and Turkey method. $P < 0.05$ was considered as statistically significant.

Results

A study was conducted to investigate the biochemical and histological impacts of a Methanol extract derived from the leaves of *Bridellia ferruginea* on diclofenac-induced cardiomyopathy in Wistar albino rats. The initial analysis of phytochemical constituents revealed the presence of tannins, saponins, alkaloids, flavonoids, and glycosides, while anthraquinones, sterols, and phenols were not detected.

General observation

In contrast to the standard control group, the rats in the diclofenac-treated group exhibited symptoms of illness and lethargy. The aforementioned observations exhibited a notable decrease in the groups subjected to treatment with *Bridellia ferruginea* leaf extract in comparison to the control group treated with diclofenac.

Body weight

Body weight gain was measured in all groups, including diclofenac-treated rats and normal control rats; extracts of *Bridellia ferruginea* leaf at 200 and 400 mg/kg body weight also showed a significant increase in body weight gain when compared to the diclofenac control group (Table 1)

Biochemical study

Serum Lipid Profile and lipid peroxidation

Triglycerides, cholesterol, LDL, VLDL, and lipid peroxidation (MDA) levels all increased significantly in diclofenac-treated rats, according to biochemical analysis. When compared to the normal control, it exhibited a substantial drop in HDL levels. In comparison to the positive control, the administration of *Bridellia ferruginea* leaf extract at doses of 200 and 400 mg/kg prior to treatment exhibited a notable reduction in triglycerides, cholesterol, LDL, VLDL, and lipid peroxidation (MDA), along with a significant elevation in HDL levels ($p<0.05$). (Table3).

When compared to the normal control group, there was a considerable rise in Superoxide Dismutase (SOD) Catalase activities and LDH diclofenac-treated rats (positive control group). When compared to the positive control, pretreatment with *Bridellia ferruginea* leaf extract at 200 and 400 mg/kg resulted in a significant decrease in SOD, Catalase, and LDH levels (p0.05). (Table 2). $p<0.05$. (Table 2).

Table 1: Effect of methanol extract of *Bridellia ferruginea* leaf on body weight (g) by diclofenac induced cardiomyopathy

Experimental groups	Mean wt of Rats			Mean wt gain
	Day 1	Day 7	Day 14	
Normal control	234.33±8.6[a]	242.33±7.2[b]	249.67±8.4[c]	15.34±11.2[a]
Positive control (distilled water + Diclofenac)	258.33±9.4 [a]	268.00±10.1[b]	277.67±9.2[c]	19.34±9.1[a]
Test group 2 (400mg/kg extract + 10 mg/kg Diclofenac)	286.33±11.3[a]	296.67±9.7[b]	308.33±10.2[c]	22.00±8.7[a]
Standard (Vitamin E + Diclofenac)	283.00±6.9[a]	292.33±7.4[b]	301.67±6.3 [c]	18.67±10.3[a]

Data are expressed as the mean ± SD (n = 10). Means within the same row carrying same superscripts are not significantly different at ($p < 0.05$).

Table 2: Effect of ethanol extract of *Bridellia ferruginea* leaf on Catalase, LDH and SOD levels in rats by diclofenac induced cardiomyopathy.

Experimental group	Catalase (Units/ml)	LDH(Units/ml)	SOD (units/ml)
Normal control	2.54±1.96[a]	170.30±4.42[a]	165.41 ± 2.84[a]
Positive control (Diclofenac + distilled water)	1.01±0.24[b]	238.17±5.12[d]	129.41 ± 5.44 [b]
Test group 1 (200mg/kg extract) +Diclofenac)	1.18±3.4[b]	206.15±5.41[b]	128.06±1.86[b]
Test group 2 (400mg/kg extract) +Diclofenac)	1.52±0.28[c]	181.97±3.17[c]	134.71 ± 1.26
Standard (Vitamin E+Diclofenac)	1.59.66±1.38[c]	192.67±4.99[b]	148.92±2.13[d]

Data are expressed as the mean ± SD (n = 10). Means within the same column (in each parameter) carrying different superscripts (a, b, c, d, e) is significantly different ($p < 0.05$).

Table 3: Effect of ethanol extract of *Bridellia ferruginea* leaf on Total CHOL, TG, HDL, LDL and MDA levels in rats by diclofenac induced cardiomyopathy.

Experimental groups	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	MDA (Units/ml)
Normal control	182.87±35.91[a]	10.65±1.35[a]	159.83±29.09[a]	12.39±5.89[a]	42.24 ± 1.52[a]
Positive control (distilled water + Diclofenac)	203.72±9.83[d]	25.37±1.20[b]	38.22±4.99[d]	48.80±1.67[c]	62.79 ± 1.67[d]
Test group 1 (200mg/kg extract + 10 mg/kg Diclofenac)	105.24±5.39[b]	23.09±2.86[b]	61.80±2.40[b]	23.46±8.73[b]	53.42±1.86[b]
Test group 2 (400mg/kg extract + 10 mg/kg Diclofenac)	76.07±4.33[c]	18.08±0.25[c]	46.78±7.69[c]	20.14±6.80[b]	49.62 ± 2.53[c]
Standard (Vitamin E + Diclofenac)	112.18±12.71[b]	12.17±1.41[a]	88.68±9.43[e]	11.32±3.92[a]	44.82±1.32[e]

Data are expressed as the mean ± SD (n = 10). Means within the same column (in each parameter) carrying different superscripts (a, b, c, d, e) are significantly different at ($p < 0.05$).

Histopathological changes on Diclofenac-induced cardiomyopathy

In contrast to the control group (Figure 1), the heart sections collected from animals treated with diclofenac (Figure 2) exhibited notable instances of necrosis, the accumulation of acute inflammatory cells, and disturbed vascular gaps. The administration of *Bridelia ferruginea* extract at doses of 200 and 400 mg/kg to animals resulted in notable enhancements in cellular integrity, as indicated by the lack of necrosis, reduced cytoplasmic vacuolization, and the preservation of normal cardiac muscle architecture, as depicted in figures 2 and 4.

The lack of necrosis, decreased cytoplasmic vacuolization, and preservation of the typical cardiac muscle structure are signs of improved cellular integrity as a result of vitamin E use prior to therapy (see figure 5).

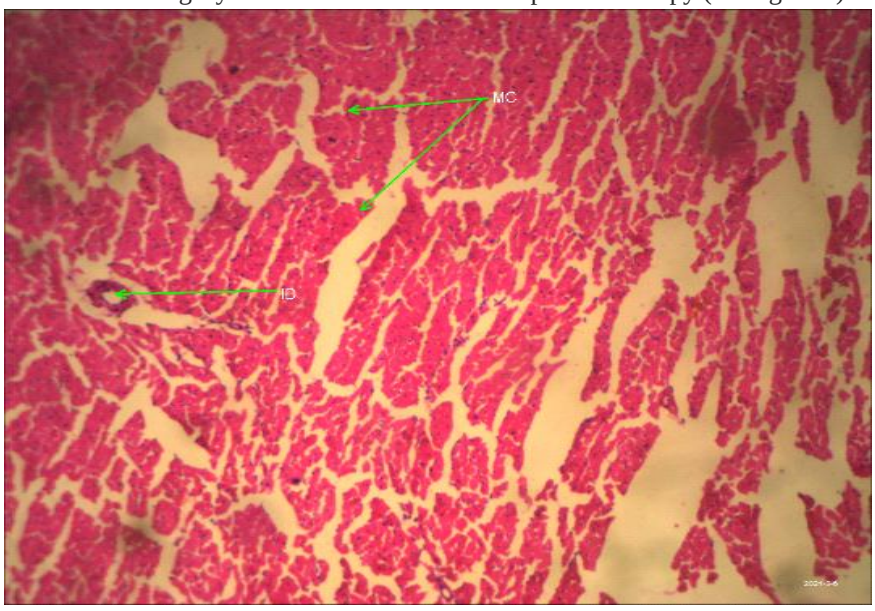

Figure 1: (cardiac section of group 1: Normal Control animals) shows normal cardiac cell

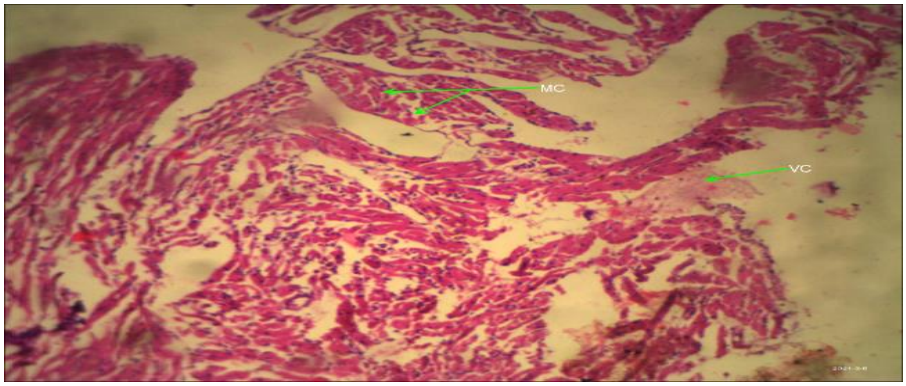

Figure 2: (Cardiac section of positive control group 2). Shows distortion of cardiac cell arrangement which indicates cellular damage of the cardiac tissues

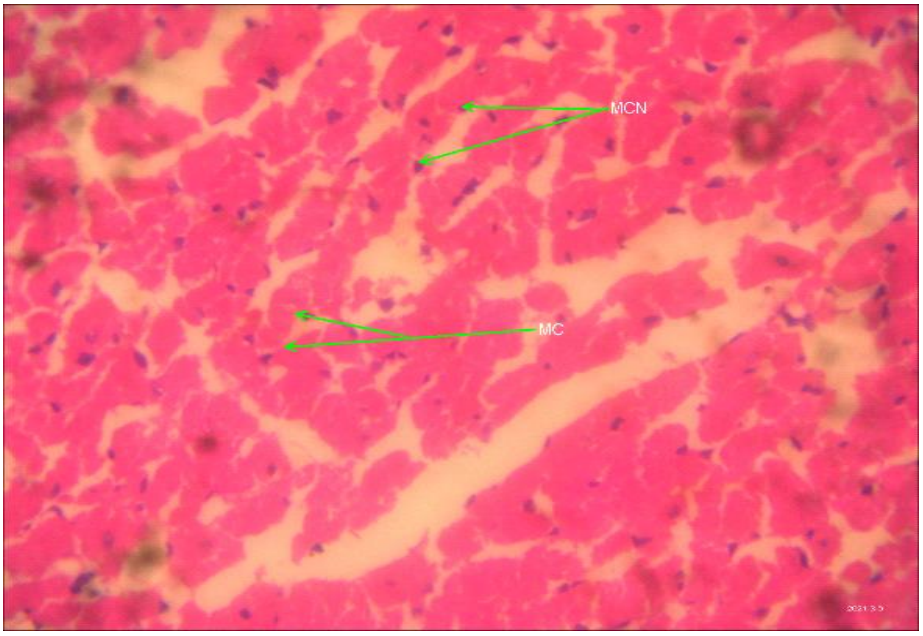

Figure 3: (Bridelia ferruginea 200mg/kg + diclofenac group 3) shows a well differentiated heart histology with a mild distortion.

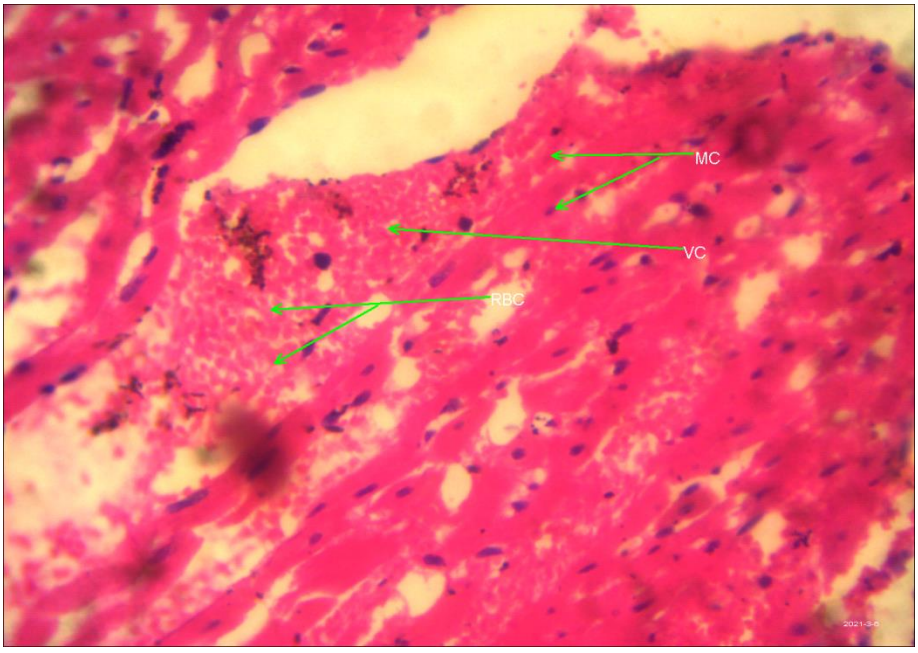

Figure 4: (Bridelia ferruginea 400mg/kg+ Diclofenac group 4) shows vascular congestion with improved appearance.

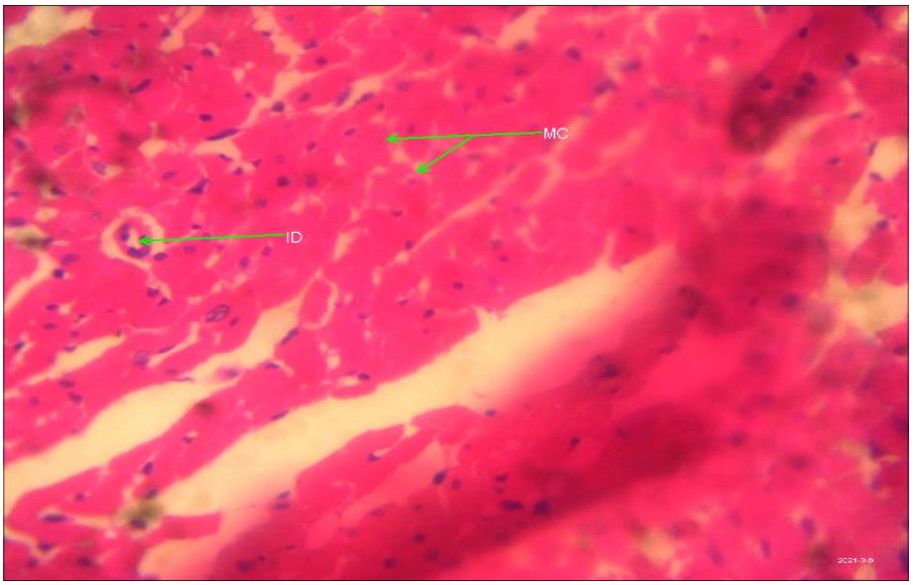

Figure 5: (cardiac section of diclofenac + vitamin E 200mg/kg group 5). shows disarrangement of cardiac cell,vacular congestion but with nuclear appearance.

Discussion

Diclofenac is a pharmacological agent belonging to the class of nonsteroidal anti-inflammatory drugs (NSAIDs). It is widely employed for its analgesic and antipyretic properties in the management of pain and fever. According to Hawkins & Hanks (2000), the utilisation of this treatment modality is frequently observed in the management of several chronic conditions, such as rheumatoid arthritis, ankylosing spondylitis, and osteoarthritis. Diclofenac functions by inhibiting prostaglandin synthesis derived from arachidonic acid, exhibiting similar effectiveness in inhibiting both cyclooxygenase-1 (Cox-I) and cyclooxygenase-2 (Cox-II) enzymes. According to Gan (2010), The accessibility of Diclofenac as a non-prescription medication has the potential to contribute to its misuse, resulting in adverse consequences for the liver, kidneys, and gastrointestinal system. The inappropriate use of Diclofenac has been associated with adverse effects on the gastrointestinal system, liver toxicity, kidney toxicity (Ahmed et al., 2017), and neurotoxicity (Owumi and Dim, 2017). Oxidative stress and mitochondrial damage are identified as the principal factors contributing to diclofenac toxicity. According to Masubuchi et al. (2002).Plants have long been used to treat a variety of human ailments. To avoid, mitigate, or restore abnormalities to normal. Plant parts like the leaf, stem, bark, and root have been used. Most pharmacological compounds, such as opium, aspirin, digitalis, and quinine, have a long history of use as herbal remedies. Modern medicine employs active chemicals derived from higher plants, and more than 80% of these active components have a strong relationship between their current therapeutic application and their historical use. (Sarkar *et al*., 2015). *Bridelia ferruginea* is a popular herbal treatment in Western Africa, and the bark is widely available in local markets. The leaves and bark are both used, and the therapeutic properties are thought to be mostly owing to tannins and saponins. These chemicals—superoxide dismutase (SOD), catalase, malondialdehyde (MDA), total cholesterol, triglycerides, HDL, LDL, and lactate dehydrogenase (LDH)—show how well the heart is protecting itself and how much tissue damage there is.

SOD, catalase, and LDH are vital antioxidant defence system enzymes. The current study revealed that diclofenac treatment resulted in a significant drop in superoxide dismutase (SOD) and catalase activities in the positive control group 2 compared to the normal control, probably due to oxidative stress. This significant increase in the SOD, catalase, and LDH levels is concentration-dependent when animals in group 3 are compared to group 4. SOD and catalase levels were also increased in animals in group 5, which were pretreated with vitamin E at a concentration of 200 mg/kg compared to the positive control group 2. Diclofenac also increased the activity of LDH compared to the normal control group. However, there was a significant decrease in groups 3 and 4 and also in animals pretreated with vitamin E (group 5) compared to the positive control (group 2), as reported in Table 3.2.

Malondialdehyde (MDA) is a well-known lipid peroxidation indicator (Gaweet al., 2004). The current investigation found that the level of MDA in the positive control (group 2) was substantially higher than in the normal control. This big rise in MDA suggests that there is more lipid peroxidation because of oxidative stress. Diclofenac may have caused this stress because the heart cells in group 2 animals were breaking down. This finding is consistent with Yanpalleware et al.'s (2003) earlier research. However, pretreatment with *Bridelia ferruginea* methanol extract at 200 mg/kg and 400 mg/kg dosages resulted in a significant decrease in MDA when compared to the positive control (group 2). This may imply that the administration of a methanol leaf extract of Bridelia ferruginea significantly inhibited the oxidative stress induced by diclofenac. When compared to the positive control (group 2), treatment with Vitamin E at a dose of 200 mg/kg resulted in a substantial drop in MDA levels.

The present study shows that administration of Diclofenac caused a significant increase in total cholesterol, low-density lipoprotein (LDL), and triglycerides in animals in the positive control (group 2) but caused a significant decrease in the levels of high-density lipoprotein (HDL) in the positive control (group 2). However, pretreatment with *Bridelia ferruginea* at concentrations of 200 mg/kg and 400 mg/kg significantly caused a decrease in total cholesterol, low-density lipoprotein (LDL), and triglycerides compared to the positive control (group 2). However, they caused a significant increase in the levels of high-density lipoprotein (HDL), which was in a concentration-dependent manner compared to the positive control (group 2) animals. Treatment with vitamin E at a concentration of 200 mg/kg also caused a significant decrease in total cholesterol, low-density lipoprotein (LDL), and triglycerides compared to the positive control (group 2). However, it caused a significant increase in the high-density lipoprotein (HDL) levels compared to the positive control (group 2). This is probably due to the cytotoxic effects of NSAIDs (Diclofenac), which have been extensively reported in previous studies (Trelle *et al*., 2011).

This observation implies that *Bridelia ferruginea* may exhibit anti-lipidemic characteristics or anti-inflammatory action in relation to lipid-related disorders. In previous research, a correlation between inflammation and atherosclerosis has been established (Gonzalez-Gay et al., 2005). Previous studies have also shown that people with untreated rheumatoid arthritis and chronic systemic inflammation may have changed lipoprotein patterns, which makes them more likely to develop atherosclerosis (Choi & Seeger, 2005). In people with rheumatoid arthritis, the study by Dursunoglu et al. (2005) found a consistent and long-lasting trend of decreased HDL cholesterol levels. Research has furthermore demonstrated that medications with the ability to decrease overall cholesterol, LDL-cholesterol, and triglycerides while increasing HDL-cholesterol levels may offer substantial defence against inflammatory-related ailments, particularly cardiovascular diseases (Dursunoglu et al., 2005). As previously mentioned, *Bridelia ferruginea* has a high concentration of phenolic chemicals. According to Lupoli et al. (2020), these chemicals exhibit the ability to enhance the stabilisation of cholesterol within the human body.

The current investigation examines the histological findings of albino rats, specifically focusing on the histopathology of the heart tissues. Figure 2, representing the positive control group 2, demonstrates a disrupted arrangement of cardiac cells, suggesting cellular harm to the heart tissues caused by oxidative stress induced by diclofenac. This is in contrast to the histopathological observations in figure 1, representing the normal control group 1, which exhibits a typical morphology of the heart. The cardiac histology of group 3, as depicted in Figure 3, demonstrates slight deformation but is well-differentiated following the administration of a 200 mg/kg concentration of the methanol extract of *Bridelia ferruginea.* The histopathology report for Figure 4 (Group 4) and Figure 5 (Group 5), treated with a dosage of 400 mg/kg of methanol extract derived from *Bridelia ferruginea,* reveals the organisation of cardiac cells exhibiting vascular congestion and enhanced nuclear morphology. This finding suggests a decrease in cellular damage when compared to the results presented in Figure 2 for group 2.

In conclusion, it may be inferred that the aforementioned points support the notion that...

The findings of this study demonstrated that the methanol leaf extract of *Bridelia ferruginea* exhibited hypocholesterolemic characteristics and antioxidant effects while also mitigating the adverse effects of diclofenac-induced toxicity by reducing lactate dehydrogenase activities. The concentration-dependent cardioprotective effect of the methanol extract derived from *Bridelia ferruginea* was observed. However, additional research should be undertaken in order to gain a comprehensive understanding of the mechanism of action underlying hypocholesterolemic effects as well as to explore its potential applications in the creation of pharmaceutical drugs.

Compliance with ethical standards

Acknowledgments

The authors are grateful to the Technical laboratory staff of the Department of Biochemistry Niger Delta University, Amassoma.

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 stud

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