



Research Paper

The effect of ethanol leaf extract of *Dryopteris dilatata* on biochemical parameters on the liver, histological architecture of STZ-induced diabetic Wistar rats.

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Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. This study investigated the hepatoprotective and antihyperglycemic effects of ethanol leaf extract of *Dryopteris dilatata* in streptozotocin (STZ)-induced diabetic Wistar rats. Thirty-six rats were divided into six groups and treated orally for 20 days with extract doses of 200, 400, and 800 mg/kg, metformin (50 mg/kg), or vehicle. Biochemical parameters, oxidative stress markers, and histological changes were evaluated. Results showed that the extract significantly reduced blood glucose, restored liver enzyme activities, enhanced antioxidant enzyme levels, and improved hepatic histoarchitecture in a dose-dependent manner. The findings demonstrate that *D. dilatata* possesses antihyperglycemic, antioxidant, anti-inflammatory, and hepatoprotective activities, supporting its ethnomedicinal use in diabetes management.

Keywords: *Dryopteris dilatata*, Diabetes mellitus, Antioxidant, Hepatoprotection, Streptozotocin, Phytomedicine, Inflammation

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I. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. It has become a global public health challenge, with the International Diabetes Federation (IDF) estimating that approximately 537 million adults are currently affected worldwide, and this figure is projected to rise to 783 million by 2045 (Alp *et al.* 2023). The burden of diabetes is particularly high in developing countries, including Nigeria, where limited healthcare access and delayed diagnosis contribute to disease complications and mortality (Kabir *et al.*, 2022).

Prolonged hyperglycemia in diabetes is associated with oxidative stress, inflammation, and metabolic disturbances that can lead to hepatic injury and dysfunction. The liver plays a central role in glucose and lipid metabolism; hence, hepatic impairment contributes significantly to diabetes-related complications such as non-alcoholic fatty liver disease (NAFLD) and hepatic fibrosis (Zhang & Li, 2023). Elevated liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), are commonly observed in diabetic individuals and serve as biomarkers of hepatocellular injury (Noroozi *et al.*, 2022).

Current pharmacological management of diabetes involves the use of synthetic agents such as metformin, sulfonylureas, and insulin therapy. While effective, these drugs may cause adverse effects, high cost, and limited accessibility, especially in low-income settings (Florez *et al.*, 2022). Consequently, attention has shifted toward medicinal plants as potential sources of safer, affordable, and efficacious antidiabetic and hepatoprotective agents (Naimi *et al.*, 2022).

Dryopteris dilatata, commonly known as the broad buckler fern, is a perennial plant belonging to the family Dryopteridaceae. Traditionally, it is used in parts of Nigeria for pain relief, wound healing, and the treatment of various ailments including diabetes and inflammation (Ikpa *et al.*, 2022). Phytochemical investigations have revealed that *D. dilatata* contains flavonoids, alkaloids, saponins, tannins, phenolic compounds, and terpenoids, which contribute to its antioxidant and anti-inflammatory properties (Akpotu *et al.*, 2023). Recent reports have shown its potential antihyperglycemic and organ-protective effects in experimental

animals, although most studies have focused on renal or pancreatic functions rather than hepatic outcomes (Ajiriohene et al., 2021; Akpotu et al., 2022).

Therefore, this study aimed to investigate the effects of ethanol leaf extract of *Dryopteris dilatata* on biochemical parameters and histological architecture of the liver in streptozotocin-induced diabetic Wistar rats. The findings are expected to provide scientific evidence supporting the ethnomedicinal use of this plant in managing diabetes-associated liver dysfunction.

II. Background theory

2.1 Diabetes mellitus

Diabetes mellitus (DM) encompasses a range of metabolic disorders characterized primarily by chronic high blood sugar levels, resulting from either impaired insulin secretion, diminished insulin effectiveness, or often a combination of both (Antar et al, 2023). A major source of the morbidity of diabetes is chronic end-organ damage that arises from prolonged hyperglycaemia and includes retinopathy, neuropathy, nephropathy, and cardiovascular disease (Jesraniet *et al*, 2023). These chronic complications can be alleviated in many patients by sustained control of the blood glucose and treatment of comorbidities such as hypertension and dyslipidemia (Jesrani *et al*, 2023). The symptoms of diabetes include; frequent urination, Extreme hunger, increased thirst, unintended weight loss, Irritability and other mood changes, Fatigue and weakness, Blurred vision. (Vlachou *et al*, 2022)

There are two primary types of diabetes: type 1 DM (T1DM) results from a complete lack of insulin secretion, often due to autoimmune destruction of pancreatic β -cells or idiopathic causes. In contrast, type 2 DM (T2DM), accounting for 90% to 95% of diabetic cases, is referred to as non-insulin-dependent diabetes. It involves insulin resistance and inadequate compensation through insulin secretion. Individuals with T2DM may exhibit normal or elevated insulin levels, but this secretion falls short of effectively countering insulin resistance (Huynh *et al*, 2023). Several risk factors contribute to T2DM. genetic factors play a significant role, evident in higher concordance rates among relatives (Huynh *et al*, 2023). Acquired factors like obesity, sedentary lifestyles, physical inactivity, high-glycemic and low-fiber diets, vitamin deficiencies, smoking and alcohol consumption act synergistically to induce T2DM. T2DM is associated with numerous complications.

2.2 Types of diabetes mellitus

Type 1 diabetes is an autoimmune disease that develops when the body's immune system unintentionally attacks healthy cells in the pancreas (Nekoua *et al*, 2022). When enough of these cells are gone, the body becomes unable to produce insulin, which raises blood glucose levels. In contrast to type 2 diabetes, type 1 diabetes can advance very rapidly. Symptoms may start off lightly and swiftly get worse over the course of weeks or months (Syed, 2022).

Type 1 diabetes accounts for 5% to 10% of diabetes and results from autoimmune-mediated destruction of the β cells of the islet, leading to total or near-total insulin deficiency (Cano-Cano *et al*, 2022).

Type 1 diabetes can occur at any age, with up to 40% of individuals developing type 1 diabetes after the age of 30 (Syed, 2022). Individuals with type 1 diabetes and their families have an increased prevalence autoimmune disease such as autoimmune adrenal insufficiency, Graves' disease, pernicious anemia, vitiligo, and celiac sprue (Nekoua *et al*. 2022). Although they are still unaware of the precise cause of type 1 diabetes in some people, scientists think that genetics may play a part in the disease's development. Although it can happen to anyone at any age, it seems to be diagnosed most frequently in children and young adults (Bassi *et a.*, 2022).

The most common kind of diabetes is type 2. In type 2 diabetes, the pancreas still produces insulin, but the body becomes resistant to it (Ke *et al*. 2022). This indicates that as time goes on, the insulin gradually loses its potency, causing glucose to accumulate in your body. Symptoms of type 2 diabetes often develop gradually over several years. In addition to genetics, other risk factors for type 2 diabetes include age, diet, and lifestyle (Sanz-Canovas *et al*. 2022). Obesity or a lack of physical activity increases a person's chance of developing type 2 diabetes (Klein et al, 2022). Type 2 diabetes symptoms typically appear gradually and are frequently asymptomatic. The etiology of type 2 diabetes has a strong genetic component. It is a heritable condition, and persons with a diabetic parent or sibling have a relative 4-fold increased risk of disease, increasing to 6-fold if both parents have type 2 diabetes (DeForest and Majithia, 2022).

2.3 Pharmacological treatment

This involves various new treatment choices. Doctors primarily prescribe these medications to people with type 2 diabetes, and they've completely changed the treatment landscape. These medications can help lower difficult-to-treat high blood sugar levels and may reduce the need for insulin in some people. They may also provide additional protection against diabetes complications. The drugs available for the treatment of diabetes include; Metformin a biguanide that works by decreasing glucose production in the liver, by increasing the insulin sensitivity of body tissues, and by increasing GDF15 secretion, which reduces appetite and caloric intake. Most

people who take metformin tolerate the drug well. However, about 30% of people experience gastrointestinal side effects, such as diarrhea, nausea, and vomiting. The efficacy and benefits of metformin treatment in type 2 diabetes have been confirmed by large-scale studies and recognized by many consensus statements (Florez *et al.* 2022).

Another class of drug is the Sulphonylureas (Glibenclamide, Gliclazide, Glipizide) are drugs that exert their hypoglycemic effects by stimulating insulin secretion from the pancreatic beta-cell. Their primary mechanism of action is to close ATP-sensitive K-channels in the beta-cell plasma membrane, and so initiate a chain of events which results in insulin release. Hence, they are potent drugs that carry the risk of low sugars if used inappropriately. side-effects are gastrointestinal upset, headache and hypersensitivity reactions. The safety of sulphonylurea therapy in pregnancy is unestablished (Florez *et al.* 2022). Dipeptidyl-Peptidase-4 inhibitor (DPP4 inhibitor)(Sitagliptin, Vildagliptin, Linagliptin, Saxagliptin) is a class of diabetic drug that inhibit an enzyme called DPP4 which in turn increases the concentration of hormones called Incretins. It increases incretin levels which inhibit glucagon release, which in turn increases insulin secretion, decreases gastric emptying, and decreases blood glucose levels (Florez *et al.* 2022). Alpha Glucosidase Inhibitors (Acarbose, Voglibose) are drugs that decrease carbohydrate break down and absorption from the gut and help in bringing down postprandial sugars to some extent. They are taken along with food (Florez *et al.* 2022).

Thiazolidinediones (Pioglitazone) is another class of diabetic drug that increases Insulin sensitivity. They are synthetic ligands for peroxisome proliferator-activated receptors (PPARs). They alter the transcription of genes influencing carbohydrate and lipid metabolism, resulting in changed amounts of protein synthesis and, therefore, metabolic changes. (May cause weight gain, fluid retention, weakness of bones and is not advisable in patients with impaired cardiac or renal function.) (Florez *et al.* 2022). Sodium/Glucose Cotransporter 2 (Canagliflozin, Dapagliflozin, Empagliflozin) are relatively new drugs and they function through a novel mechanism of reducing renal tubular glucose reabsorption, producing a reduction in blood glucose without stimulating insulin release. Other benefits may include favorable effects on blood pressure and weight (Florez *et al.* 2022).

Another class of drug is the Glucagon-Like Peptide-1 (Glp 1) Analogues (Liraglutide, Exenatide) which are a class of diabetic drugs that enhance Insulin secretion by the pancreas and also suppress appetite. Available as injections. May help in weight loss in obese patients (Florez *et al.* 2022). Insulin (Injection) are the most potent drug for Diabetes. Drives blood glucose into the cells. Hypoglycemia, i.e., low sugars are the only complication if used inappropriately. It can be used in conditions like renal, cardiac, hepatic impairments, sepsis and pregnancy where most oral drugs cannot be used (Domingo-Lopez *et al.* 2022).

2.4 Liver function test

Liver Function Tests (LFTs) are a group of blood tests used to assess the health and function of the liver. LFTs measure various enzymes, proteins, and substances in the blood that are indicative of liver function and potential liver damage (Noroozi *et al.* 2022). LFTs typically include the following components: Alanine Aminotransferase (ALT) is an enzyme found primarily in the liver. Elevated levels of ALT in the blood can indicate liver cell damage, such as in conditions like hepatitis or liver cirrhosis (Noroozi *et al.* 2022). Aspartate Aminotransferase (AST) is an enzyme found in various tissues, including the liver, heart, muscles, and kidneys. Elevated AST levels can also suggest liver cell damage, but it is less specific to the liver compared to ALT (Noroozi *et al.* 2022). Alkaline Phosphatase (ALP) is an enzyme found in the liver, bile ducts, bones, and intestines. Elevated ALP levels may indicate liver or bile duct obstruction, as well as certain bone disorders (Noroozi *et al.* 2022).

Gamma-Glutamyl Transferase (GGT) is an enzyme found in the liver and other organs, such as the kidneys and pancreas. Elevated GGT levels are associated with liver and bile duct disorders, particularly alcohol-related liver disease (Noroozi *et al.* 2022). Total Bilirubin is a waste product formed from the breakdown of hemoglobin in red blood cells. Elevated bilirubin levels can indicate liver dysfunction or impaired bile flow (Noroozi *et al.* 2022). Albumin is a protein produced by the liver that helps maintain blood volume and pressure. Low albumin levels may suggest liver damage or impaired liver function (Noroozi *et al.* 2022). Total protein measures the overall number of proteins in the blood, including albumin and other proteins. Abnormal levels can indicate liver disease or other medical conditions (Noroozi *et al.* 2022).

2.5 Dryopteris dilatata (D.d)

Dryopteris dilatata is one of these plants that is highly valued. The Dryopteridaceae family includes the medicinal plant known as D.d (Broad buckler fern). It grows to 120 cm tall and 90cm wide, with dark green tripinnate fronds, with the ribs covered in brown scales, (Runk *et al.*, 2012). *Dryopteris dilatata* is known as *Ato Asii* in Ogbogolo ethnic group of people in Ahoada West Local Government Area, Rivers State, Nigeria. The People use the plant for several purposes including, to attract earthworms, as pain reliever, due to pains resulting

from hard work or beatings, as sponge to bath, as head support for carrying heavy load and other loads and palm wine tappers uses it to cover their gourds.

In Bonny Local Government Area, Rivers State, Nigeria the *Dryopteris dilatata* plant is known as *Ogirishi* and they see it as a spiritual leaf, they also use it to identify some cultures going on by placing it on their windows during cultural seasons. It is known as Okpomie in Olomoro in Isoko South Local Government Area, Delta State, Nigeria. People from Olomoro in the Isoko South Local Government Area of Delta State prepare mixtures of this plant when diabetic, and their circumstances seem to improve. D.d is distributed across the tropical region of Nigeria. The roots and leaves are both utilised medicinally. It is also frequently employed as a worm and anti-dandruff expeller (Ikpa *et al.* 2022).

Dryopteris dilatata root contains "filicin," a worm expulsion agent that incapacitates tapeworms and other internal parasites. It is one of the most well-known tapeworm treatments and should be combined with a non-oily purgative, such as magnesium sulfate, to help the body expel the worms. Castor oil is an oily purge that can be dangerous since it stimulates fern root absorption. (Ikpa *et al.* 2022).

2.6 PHYTOCHEMICAL PROPERTIES

Dryopteris dilatata (broad buckler-fern) has been found to contain various phytochemical compounds that contribute to its medicinal and biological properties. Some of the notable phytochemicals reported in *Dryopteris dilatata* include: Flavonoids which are a group of polyphenolic compounds found in many plants, including *Dryopteris dilatata* (Akpotu *et al.* 2023). These compounds have antioxidant properties and are known for their potential to neutralize harmful free radicals in the body, thereby protecting cells from oxidative damage. Phenolic compounds are another group of antioxidants found in *Dryopteris dilatata*. They play a role in scavenging free radicals and reducing oxidative stress, which is associated with various health benefits.

Dryopteris dilatata contains tannins, which are a type of polyphenolic compound. Tannins have astringent properties and may have antimicrobial effects, making them potentially useful for wound healing and other medicinal applications (Akpotu *et al.* 2023). Terpenoids are a diverse group of compounds with various biological activities. Some terpenoids found in *Dryopteris dilatata* may have anti-inflammatory, antimicrobial, and other pharmacological properties, Saponins are glycosides that have surfactant properties and may have immunomodulatory effects. They are known for their potential to support the immune system and possess other biological activities, and Alkaloids which are nitrogen-containing compounds that can have diverse effects on the body, including analgesic and antipyretic properties. (Akpotu *et al.* 2023)

2.7 STREPTOZOTOCIN (STZ)

Often utilized as a diabetes-inducing drug in scientific studies, STZ is a naturally occurring chemical molecule. It is an antibiotic created by the *Streptomyces achromogenes* bacterium that has been discovered to have cytotoxic effects on pancreatic beta cells, which results in the death of these cells and the onset of diabetes mellitus. The prevalence of type 2 diabetes mellitus, a major cause of considerable morbidity and mortality, is rising to alarming levels worldwide. Therefore, there is a pressing need to find molecules that could either prevent or reverse the symptoms of type 2 diabetes. This goal can be served by the widely used model of streptozotocin (STZ)-induced type 2 DM (Gundala, 2018). DNA is alkylated by STZ when it reaches the beta cell through the GLUT2 glucose transporter. Activation is brought on by DNA damage. Although DNA damage induces the activation of poly-ADP-ribosylation, this process is more important for the diabetogenic properties of STZ than the DNA damage itself, as poly-ADP-ribosylation depletes cells of NAD⁺ and ATP. (Gandara *et al.* 2018).

III. Materials and Methods

3.1 Site selection

The study was carried out in the Animal House of the Department of Pharmacology, PAMO University of Medical Sciences, Port Harcourt, Rivers State, Nigeria. All experimental procedures followed international standards for the care and use of laboratory animals.

3.2 sample Collection, Identification, and Extraction

Fresh leaves of *Dryopteris dilatata* were collected from Ahoada West Local Government Area, Rivers State, Nigeria. The plant was authenticated by Dr. Harrison Erhenhi at the Forestry Research Institute of Nigeria (FRIN), Ibadan, and a voucher specimen was deposited under the herbarium number FHI 1100338.

The leaves were washed, air-dried at room temperature for two weeks, and ground into a fine powder using a mechanical grinder. About 500 g of the powdered material was macerated in 1.5 L of 70% ethanol for 72 hours with intermittent shaking. The mixture was filtered using Whatman No. 2 filter paper, and the filtrate was concentrated under reduced pressure using a rotary evaporator at 45°C. The concentrated extract was stored in a sealed container at 4°C until use. The percentage yield of the extract was calculated and recorded.

3.3 Experimental Animals

Thirty-six (36) healthy adult Wistar rats of both sexes, weighing between 110 and 160 g, were obtained from the central animal facility of PAMO University of Medical Sciences. The animals were housed in standard cages under controlled environmental conditions (12-hour light/dark cycle, $25 \pm 2^\circ\text{C}$, and 50–60% relative humidity) and were allowed free access to standard rat pellets and water ad libitum. The animals were acclimatised for seven days before the commencement of the experiment.

All procedures were reviewed and approved by the Institutional Animal Ethics Committee of PAMO University of Medical Sciences (Approval No. PUMS/PHM/ETH/2025/002), in compliance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 2011).

3.4 Induction of Experimental Diabetes

After overnight fasting, experimental diabetes was induced by a single intraperitoneal injection of freshly prepared streptozotocin (STZ) at a dose of 60 mg/kg body weight dissolved in cold 0.1 M sodium citrate buffer (pH 4.5). After 72 hours, fasting blood glucose levels were determined using a glucometer (Accu-Chek Active, Roche Diagnostics, Germany). Rats with fasting blood glucose levels ≥ 200 mg/dL were considered diabetic and selected for the study.

3.5 Experimental Design

The rats were randomly divided into six (6) groups of six animals each ($n = 6$). All animals were provided with standard feed and water ad libitum throughout the study. Treatments were administered orally once daily for 20 consecutive days.

Group Treatment Description

Group 1 Normal control — fed standard diet and water ad libitum

Group 2 Diabetic control — STZ only; fed standard diet and water ad libitum

Group 3 Diabetic + Metformin (50 mg/kg); fed standard diet and water ad libitum

Group 4 Diabetic + *D. dilatata* extract (200 mg/kg); fed standard diet and water ad libitum

Group 5 Diabetic + *D. dilatata* extract (400 mg/kg); fed standard diet and water ad libitum

Group 6 Diabetic + *D. dilatata* extract (800 mg/kg); fed standard diet and water ad libitum

3.6 Collection of Blood and Tissue Samples

At the end of the treatment period, the animals were anaesthetized with ketamine (0.38 mg/kg, i.p.) and sacrificed by cardiac puncture. Blood samples were collected into heparinized tubes and centrifuged at 3,000 rpm for 10 minutes to obtain plasma. The liver was excised, rinsed in ice-cold saline, blotted dry, and weighed. Portions of the liver were homogenized in 0.1 M phosphate buffer (pH 7.4) and centrifuged at 10,000 rpm for 10 minutes to obtain supernatants for biochemical assays. Other sections of the liver were fixed in 10% neutral buffered formalin for histopathological examination.

3.7 Biochemical Analysis

Liver function enzymes—alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP)—were estimated using Randox diagnostic kits according to the manufacturer's instructions. Oxidative stress markers such as malondialdehyde (MDA), reduced glutathione (GSH), nitric oxide (NO), superoxide dismutase (SOD), and catalase (CAT) were analyzed using established spectrophotometric methods. Pro-inflammatory cytokines, tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6), were quantified using enzyme-linked immunosorbent assay (ELISA) kits (Elabscience, UK).

3.8 Histopathological Examination

Liver tissues were processed and embedded in paraffin wax, sectioned at 5 μm thickness, and stained with hematoxylin and eosin (H&E). The slides were examined under a light microscope for hepatic structural alterations, including hepatocellular degeneration, necrosis, sinusoidal dilation, and inflammatory infiltration.

3.9 Statistical Analysis

Data were expressed as mean $\pm$ standard error of the mean (SEM). Statistical comparisons among groups were performed using one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test. A probability value of $p < 0.05$ was considered statistically significant. Data visualization and analysis were performed using GraphPad Prism software (version 5.01; GraphPad Software Inc., San Diego, CA, USA).

IV. Results and Discussion

4.1 Effects of ethanol ... on ...

4.1.1 Effects of ethanol extract of *D. dilatata* on body weight of experimental Wistar rats

On administering metformin group (D + Met 50mg/kg) on the experimental rats, there was statistically significant difference in body weight, than when compared with normal control. The expression of body weight after

induction of diabetic experimental rats revealed no statistically significant difference in body weight.

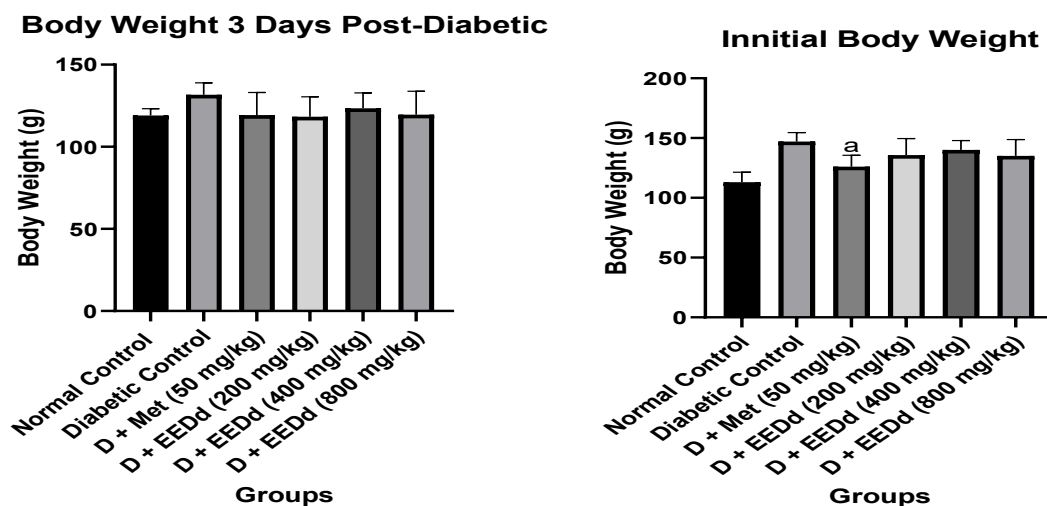


Fig.1: Effects of ethanol extract of *D. dilatata* on body weight of experimental Wistar rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

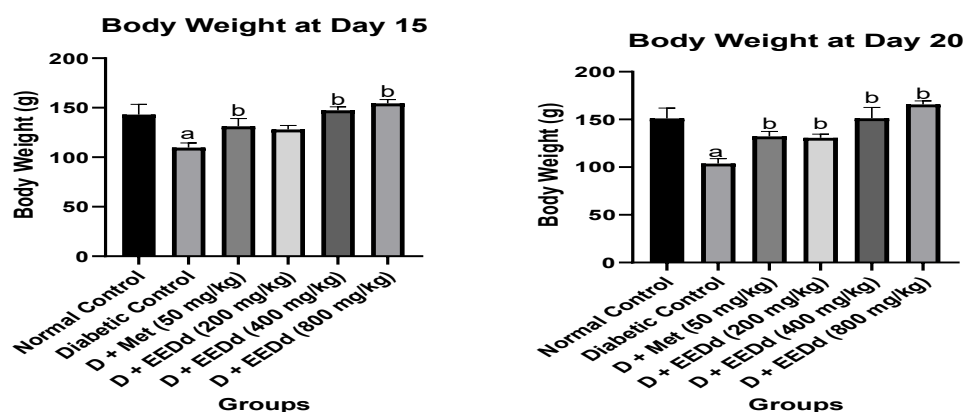


Fig. 2: Effects of ethanol extract of *D. dilatata* on body weight of experimental diabetic rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.2 Effects of ethanol extract of *D. dilatata* on body weight experimental diabetic rats

The results of the expression of body weight at day 15 of treatment of diabetic experimental rats revealed statistically significant difference in body weight when diabetic control was compared with normal control group,

and metformin group (D + MET 50mg/kg) and *Dryopteris dilatata* (D + EEDd 400mg/kg, 800mg/kg) respectively, was compared with the diabetic control group. The results of the expression of body weight after induction of diabetic experimental rats at day 20 of treatment Revealed statistically significant difference in body weight when diabetic control was compared with normal control group, and metformin group (D + MET 50mg/kg) and *Dryopteris dilatata* (D + EEDd 200mg/kg, 400mg/kg, 800mg/kg) respectively, was compared with the diabetic control group.

4.1.3 Effects of ethanol extract of *D. dilatata* on glucose level of experimental wistar rats

Effect of ethanol extract of *Dryopteris dilatata* (D.d) on initial glucose level of experimental rats as shown in **A** revealed no statistically significant difference between the normal control, diabetic control group, metformin group (D + MET 50mg/kg) and *Dryopteris dilatata* (D + EEDd 200mg/kg, 400mg/kg, 800mg/kg) respectively. Effect of ethanol extract of *Dryopteris dilatata* (D.d) on glucose level after induction of experimental rats as shown in **B** revealed statistically significant difference between the diabetic control group, when compared with normal control group

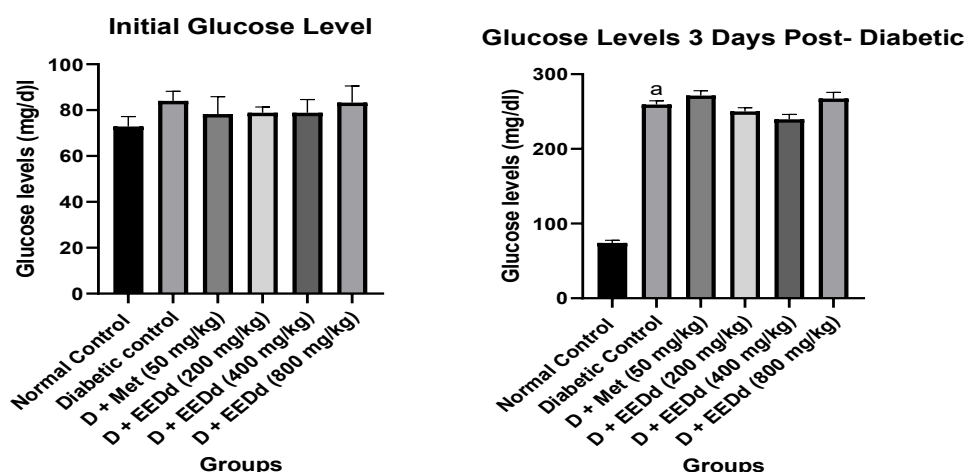


Fig.3: Effects of ethanol extract of *D. dilatata* on glucose level of experimental wistar rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap < 0.05 was significant when compared with the normal control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.4 Effects of ethanol extract of *D. dilatata* on glucose level of diabetic rats

Effect of ethanol extract of *Dryopteris dilatata* (D.d) on glucose level at day 15 of treatment of experimental rats revealed statistically significant difference in glucose level when the normal control group was compared with diabetic control group, and when the diabetic control group was compared with metformin group (D + Met 50mg/kg), and *Dryopteris dilatata* (D + EEDd 200mg/kg, 400mg/kg, 800mg/kg) respectively, while the effect of ethanol extract of *Dryopteris dilatata* (D.d) on glucose level at day 20 of treatment of experimental rats revealed statistically significant difference in glucose level when the normal control group was compared with diabetic control group, and when the diabetic control group was compared with metformin group (D + Met 50mg/kg), and *Dryopteris dilatata* (D+EEDd 200mg/kg, 400mg/kg, 800mg/kg) respectively.

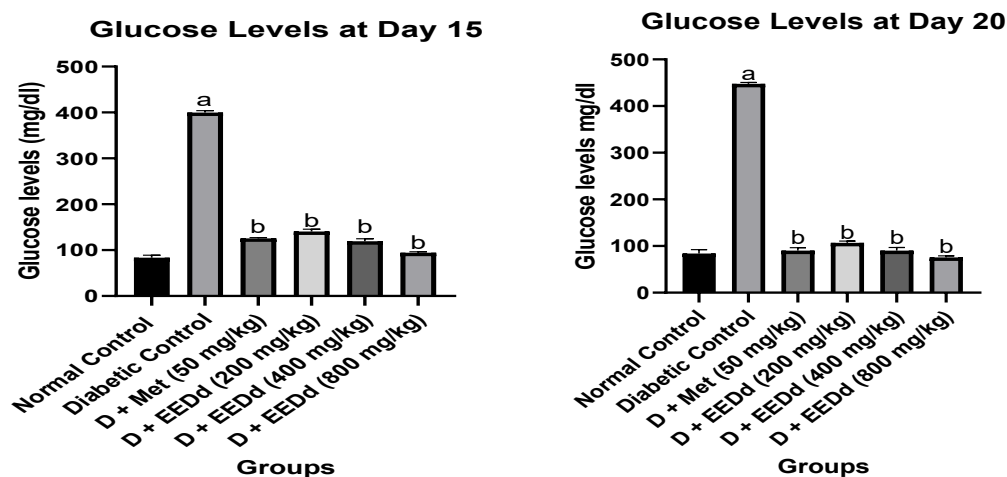


Fig.4: Effects of ethanol extract of *D. dilatata* on glucose level of diabetic rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.5 Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Liver Enzyme Levels on STZ Induced Diabetic Wistar Rats

The results of the expression of ethanol extract of Dd on diabetic experimental rats as shown in Figure 4.5 Revealed statistically significant difference in alkaline phosphate, alanine transferase and aspartate transferase when normal control was compared with diabetic control, while the treated groups metformin 50 mg/kg (D + Met 50mg/kg) and D + EEDd (200, 400, and 800 mg/kg) recorded reduced levels of ALP, ALT and AST respectively.

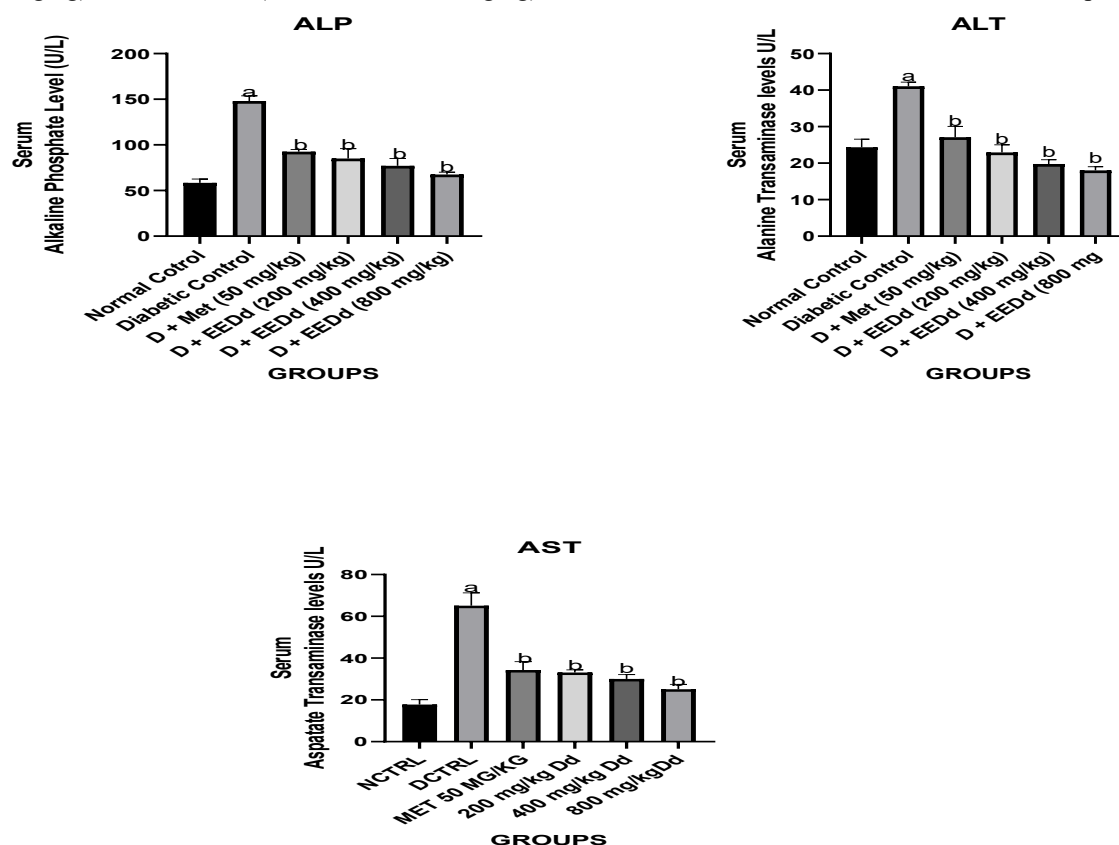


Fig.5: Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Liver Enzyme Levels on STZ Induced Diabetic Wistar Rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.6 Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Levels of oxidative stress markers in Liver on STZ Induced Diabetic Wister Rats

The expression of ethanol extract of Dd on diabetic experimental rats as shown in Fig. 4.6 revealed statistically significant difference in liver nitrite level and levels of liver Malondialdehyde (MDA) when normal control was compared with diabetic control while the treated groups metformin 50 mg/kg (D + Met 50mg/kg) and D + EEDd (200, 400, and 800 mg/kg) revealed statistically significant difference when compared with diabetic control group,

and recorded reduced levels of nitrite respectively.

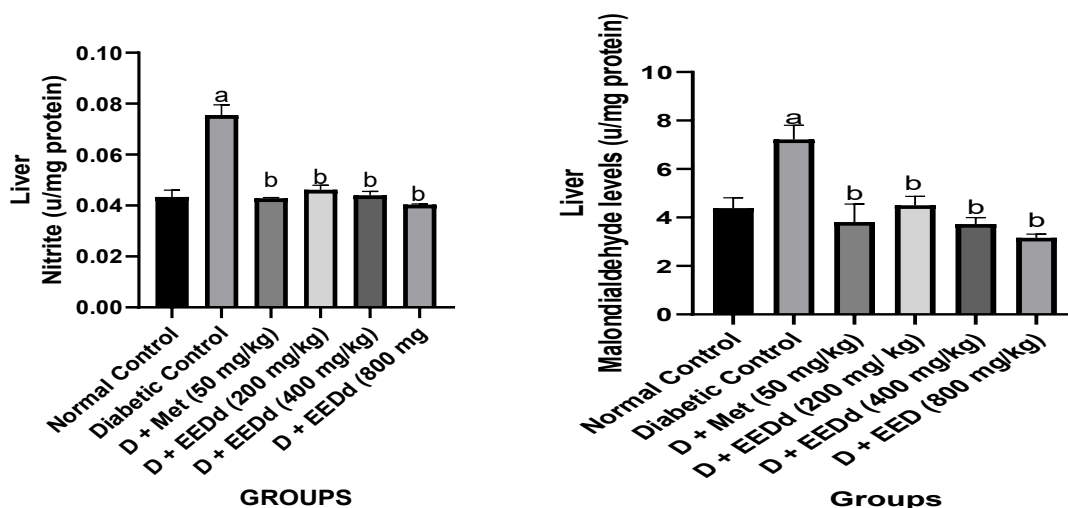


Fig.6: Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Levels of oxidative stress markers in Liver on STZ Induced Diabetic Wister Rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.7 Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Anti-oxidant markers Levels on STZ Induced Diabetic Wister Rats

Fig. 7 shows the levels of liver glutathione (GSH) and liver superoxide Dismutase (SOD) expression in Normal control, Diabetic control and treatment groups. Diabetic control group revealed a statistically significant difference when compared with normal control group. While the treated groups metformin 50 mg/kg (D + Met 50mg/kg) and D + EEDd (200, 400, and 800 mg/kg) revealed statistically significant difference when compared with diabetic control group, revealing an increase in GSH levels.

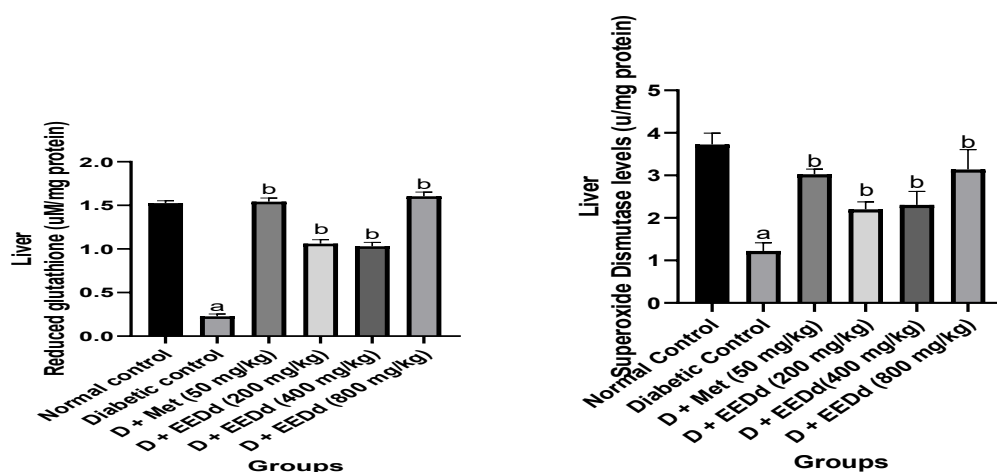


Fig.7: Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Anti-oxidant markers Levels on STZ Induced Diabetic Wister Rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.1.8 Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Pro-inflammatory Marker Levels on STZ Induced Diabetic Wister Rats

Figure 4.8 shows the levels of Tumor Necrosis Factor- alpha (TNF- alpha) and Interleukins-6 (IL-6) levels expression in Normal control, Diabetic control and treatment groups. Diabetic control group revealed a statistically significant difference when compared with normal control group. While the treated groups metformin 50 mg/kg (D + Met 50mg/kg) and D + EEDd (200, 400, and 800 mg/kg) revealed statistically significant difference when compared with diabetic control group, recording reduced levels of TNF- alpha respectively.

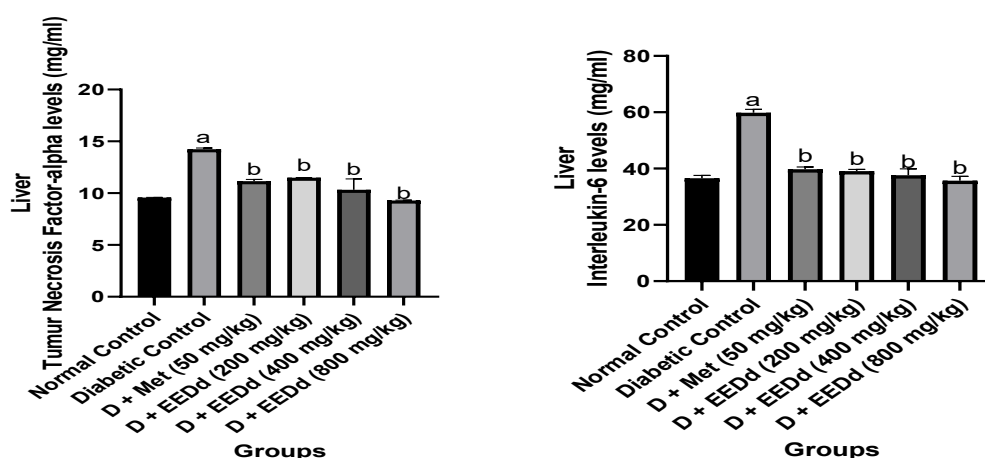


Fig.8: Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Pro-inflammatory Marker Levels on STZ Induced Diabetic Wister Rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap< 0.05 was significant when compared with the normal control while ^bp< 0.05 when compared with the

diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

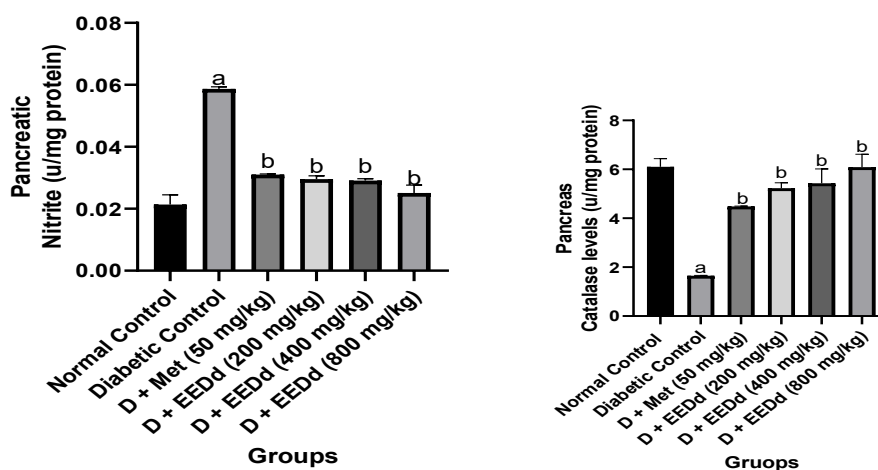


Fig.9: Effect of Ethanol Extract of *Dryopteris dilatata* (Dd) on Pancreatic Nitrite and Catalase Levels on STZ Induced Diabetic Wistar Rats

All values are expressed as Mean $\pm$ standard error of mean; analysis of variance was then performed to evaluate differences between the groups using a one-way analysis of variance (ANOVA). Subsequently, post Hoc Fisher's test (Dunnet) was done to identify the source of any statistically significant difference (p value), (n=5), ^ap < 0.05 was significant when compared with the normal control while ^bp < 0.05 when compared with the diabetes control. D = streptozotocin induction, EEDd = ethanol extract of *Dryopteris dilatata*, Met = Metformin.

4.2 HISTOLOGY OF THE LIVER

Normal Control

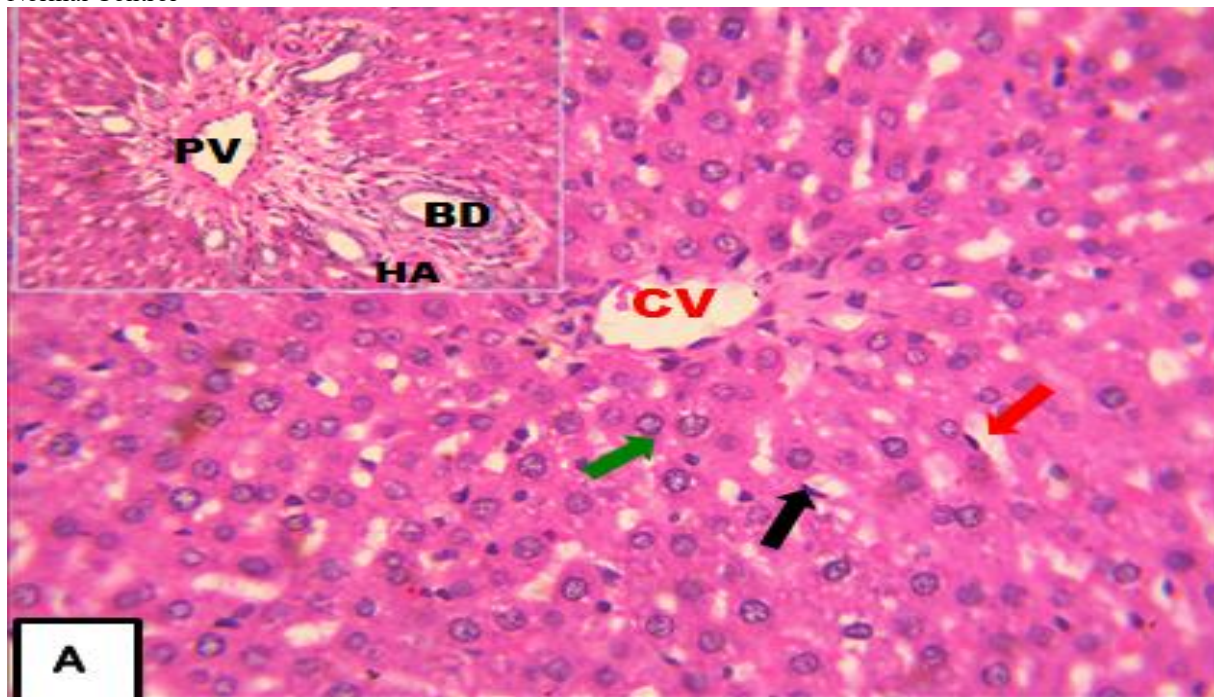


Plate 4.2.1 Photomicrograph of a hepatic lobule of rats; inset is portal area: A. Control group shows normal histology with central vein (CV), hepatocytes (green arrow), sinusoids (red arrow) and Kupffer cells (black arrow). The portal area demonstrates the portal vein (PV), hepatic artery (HA) and bile duct (BD). Magnification: portal area(x100),central vein and hepatocyte(x400)

Diabetic Control

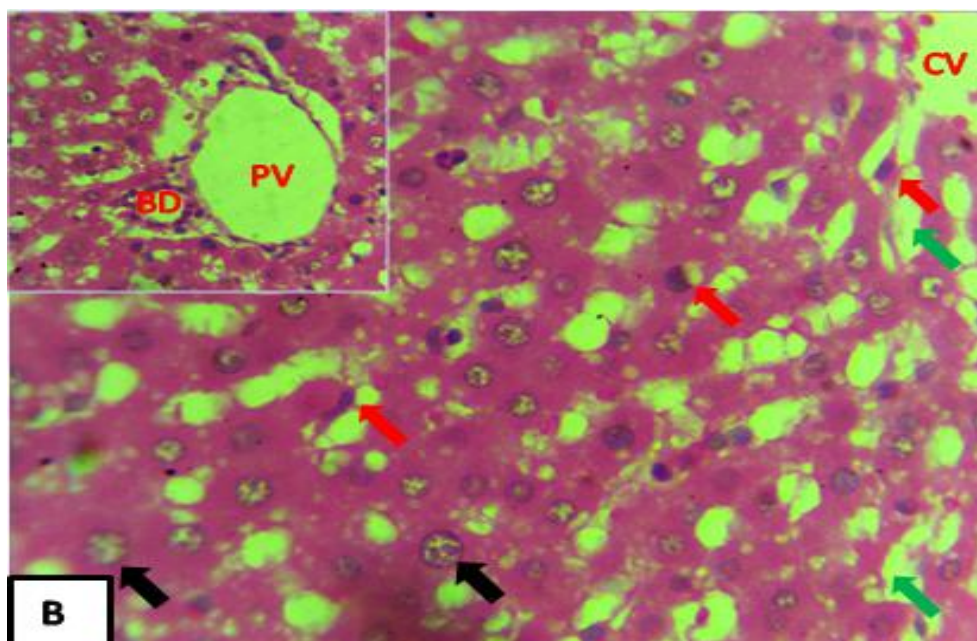


Plate 4.2.2 Photomicrograph of a hepatic lobule; inset is portal area: B. Diabetic group shows disrupted central vein (CV), necrosis of hepatocytes (red arrow), swollen hepatocytes (black arrow) and dilated sinusoids (green arrow). The portal area shows atrophy of portal vein (PV) with no recognizable hepatic artery. Magnification: portal area(x100), central vein and hepatocyte(x400)

D + Met (50 mg/kg)

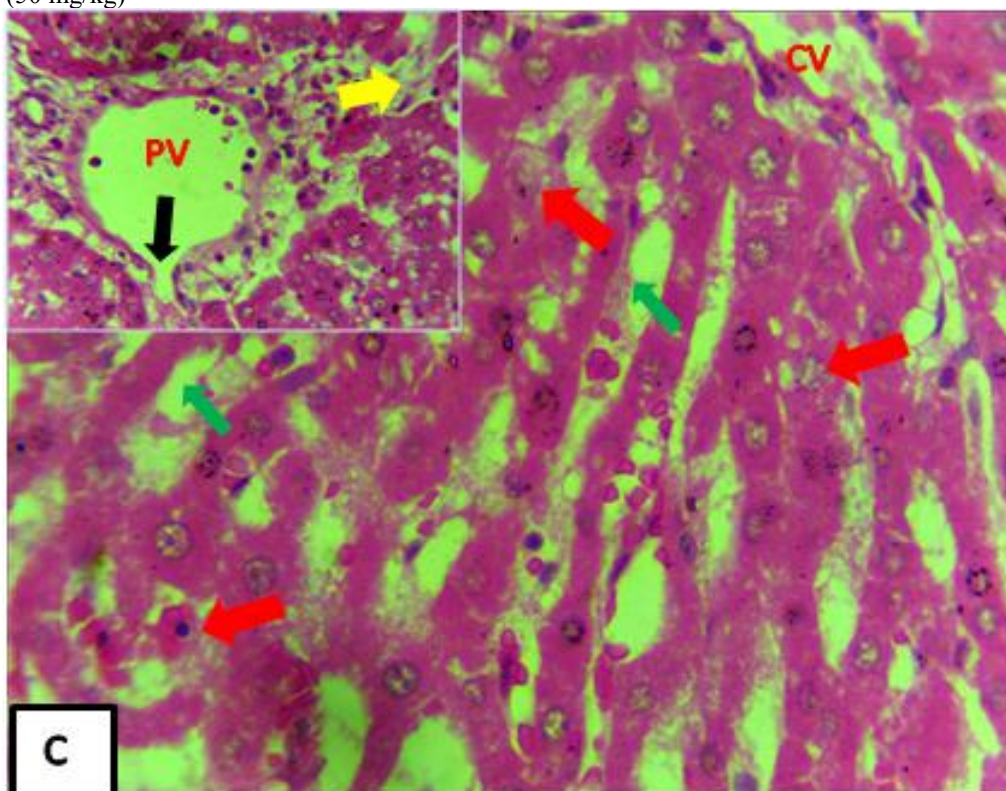


Plate 4.2.3 Photomicrograph of a hepatic lobule; inset is portal area: C. Diabetic + Metformin (50mg/kg body weight) group shows disrupted central vein (CV) with pericentral fibrosis, atrophy/necrosis of hepatic plates/hepatocytes (red arrow), and dilated sinusoids (green arrow). The portal area shows disruption of both limiting membrane (yellow arrow) and portal vein (PV). Magnification: portal area(x100), central vein and hepatocyte(x400)

D + EEDd (200 mg/kg)

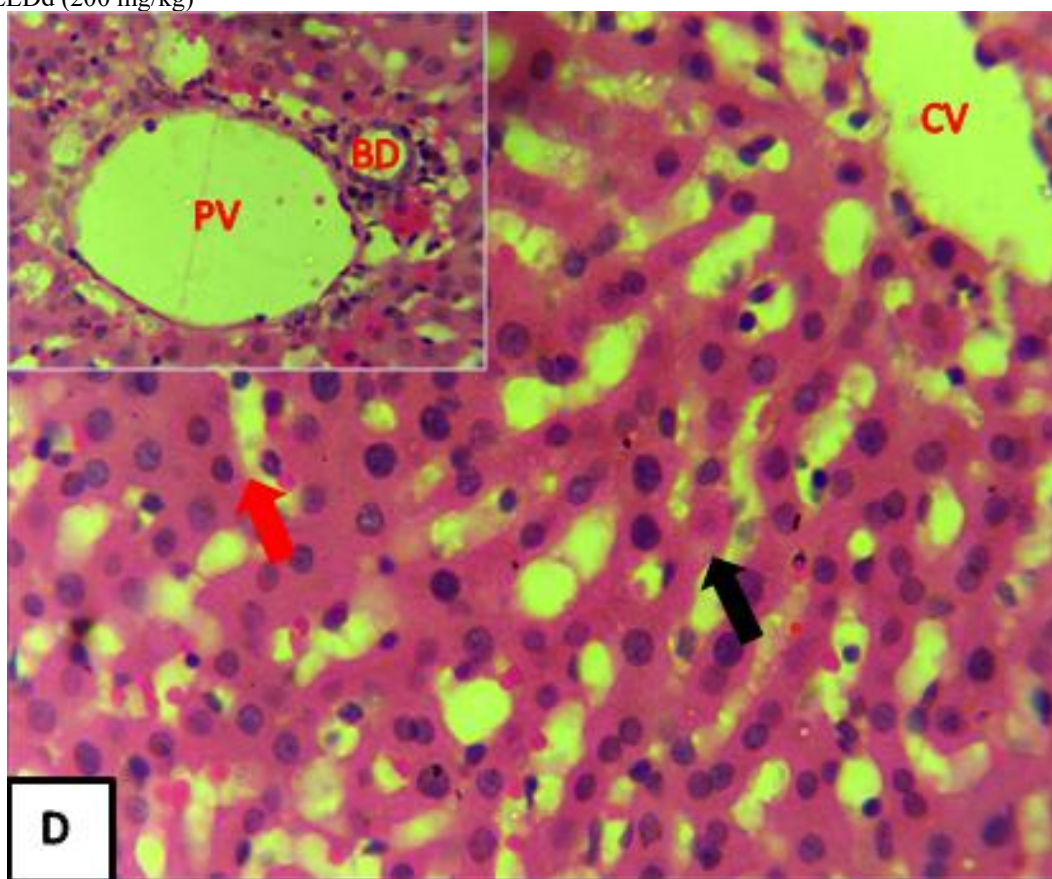


Plate 4.2.4 Photomicrograph of a hepatic lobule; inset is portal area: D. Diabetic + Ethanolic leaf extract *Dryopteris dilatata* (200mg/kg body weight) group shows normal histology with rows of hepatic plates (black arrow); however, there is mild focal disruption of plates (red arrow). The portal area shows normal triad with no recognizable hepatic artery. Magnification: portal area(x100), central vein and hepatocyte(x400). Magnification: portal area(x100), central vein and hepatocyte(x400)

4.3 HISTOLOGY OF THE PANCREAS

Pancreas (Normal Control)

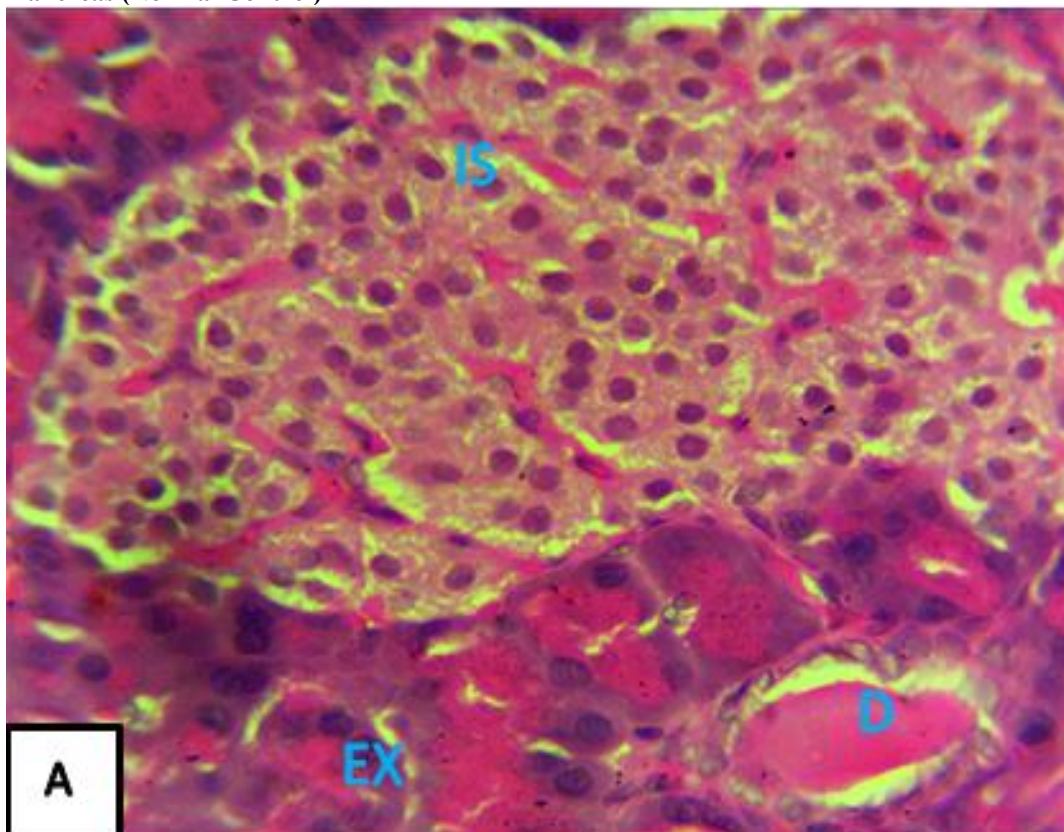


Plate 1: Photomicrograph of the pancreas: A. Control group shows normal pancreatic acinar cells (EX) and islet of Langerhans (IS) having endocrine cells of different subtypes; an intralobular duct (D) is also shown. Magnification: x400

Diabetic Control

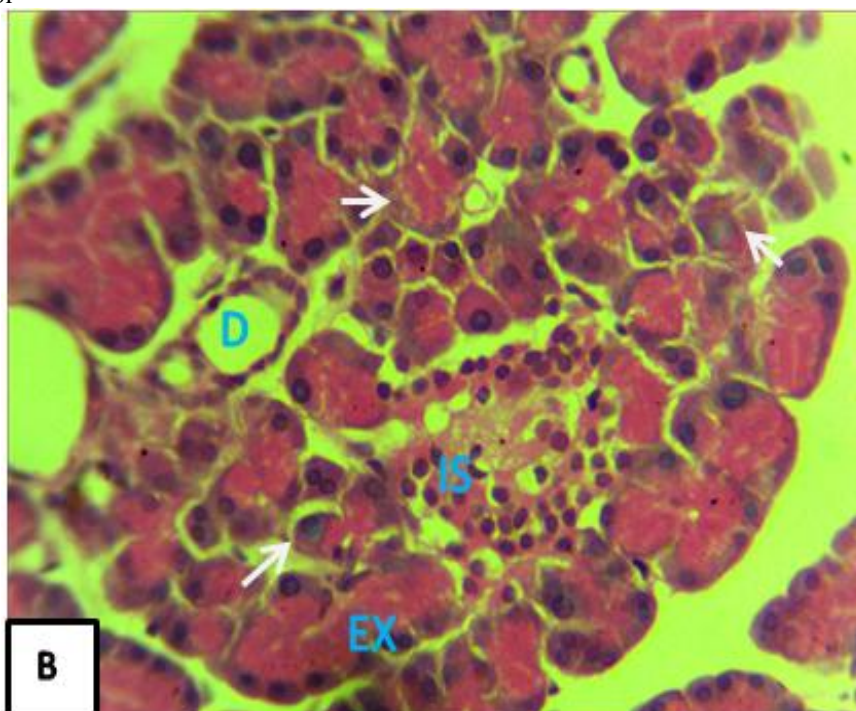
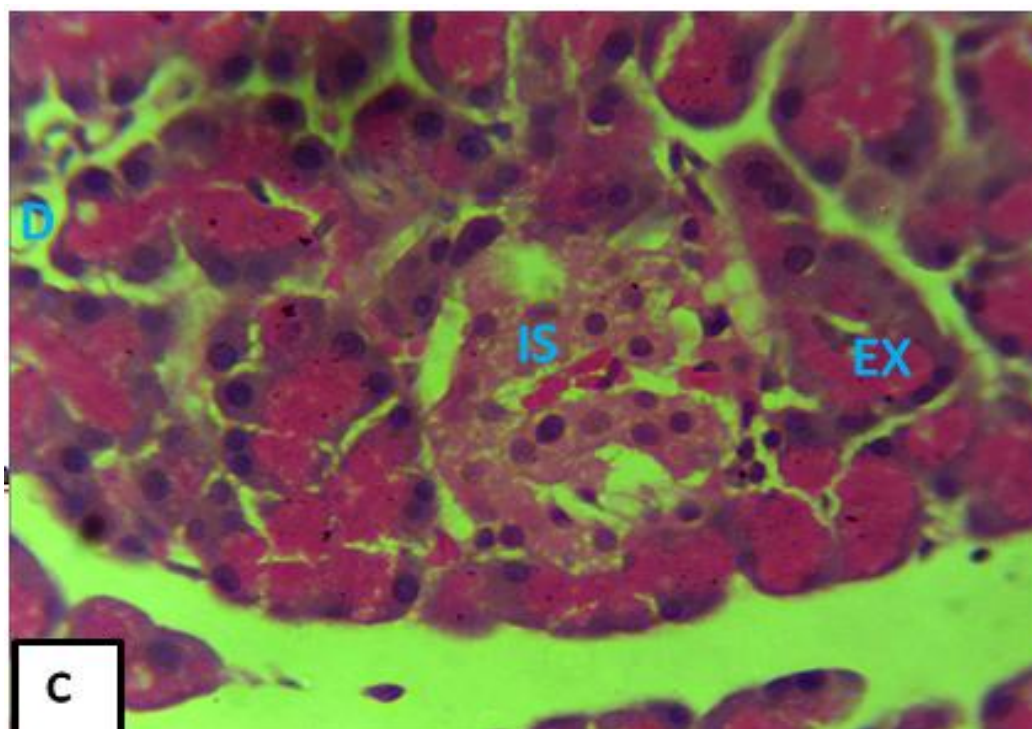


Plate 2: Photomicrograph of the pancreas: B. Diabetic group shows atrophy of pancreatic acini (EX), islet of Langerhans (IS) and duct (D). Note the shrunken islet and degenerating centrally placed β -cells within (IS) and degenerating acini (white arrow). Magnification: x400

D + Met



(50mg/kg)

Plate 3 Photomicrograph of the pancreas: C. Diabetic + Metformin (50mg/kg body weight) group shows atrophy of islet (IS), pancreatic acini (EX) and duct (D). Note the recovering centrally placed β -cells within (IS). Magnification: x400

D + EEDd (200 mg/kg)

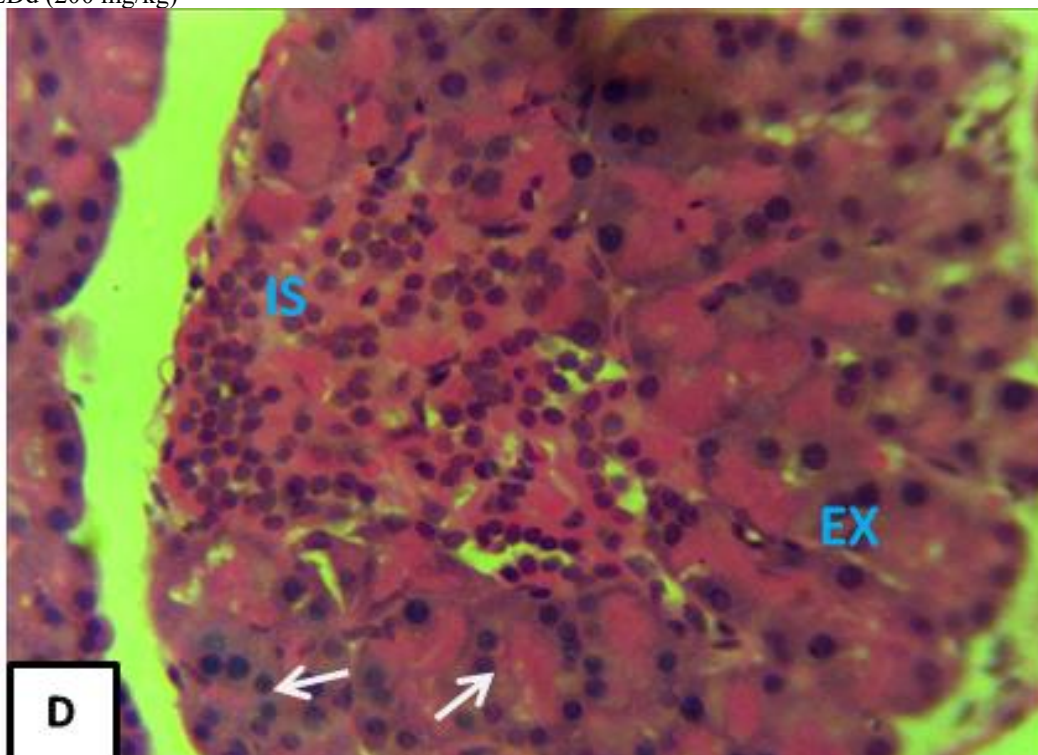


Plate 4 Photomicrograph of the pancreas: D. Diabetic + Ethanolic leaf extract *Dryopteris dilatata* (200 mg/kg body weight) group shows disorganized islet of Langerhans (IS) and normal pancreatic acini (EX). Note the hyperplasia of both endocrine cells within (IS) and acinar cells in (EX). Magnification: x400

V. Discussion

The present study evaluated the hepatoprotective and antihyperglycemic effects of ethanol leaf extract of *Dryopteris dilatata* in STZ-induced diabetic rats. The findings revealed that ELEDD significantly reversed diabetes-associated biochemical and histological alterations in a dose-dependent manner.

The reduction in blood glucose levels following ELEDD administration suggests improved glucose metabolism, either through enhanced insulin secretion or increased peripheral glucose uptake. Flavonoids and saponins in *Dryopteris dilatata* are known to exert insulin-mimetic effects and stimulate glucose transport, as reported by Ajirioghene et al. (2021) and Akpotu et al. (2022). The concurrent increase in body weight further supports improved metabolic recovery.

Liver enzyme elevation (ALT, AST, and ALP) in diabetic control rats indicated hepatocellular damage caused by hyperglycemia and oxidative stress. ELEDD significantly reduced these enzymes, demonstrating membrane-stabilizing and hepatoprotective activity. This aligns with findings by Manilla et al. (2023) and Naimi et al. (2022), who observed similar improvements with polyphenol-rich plant extracts in diabetic models.

Hyperglycemia enhances reactive oxygen species (ROS) generation, leading to lipid peroxidation and antioxidant depletion. The significant decrease in MDA and NO, alongside the increase in SOD, CAT, and GSH after ELEDD treatment, indicates strong antioxidant capacity. The extract likely neutralized free radicals and prevented oxidative damage, similar to the effects described by Anusiem et al. (2022) and Akpotu et al. (2023).

Pro-inflammatory cytokines such as TNF- α and IL-6 play a pivotal role in the pathogenesis of diabetes and its complications. ELEDD significantly lowered these cytokines, suggesting anti-inflammatory action. This could be attributed to the inhibition of NF- κ B signaling and modulation of inflammatory mediators, as reported by Nekoua et al. (2022).

Histopathological examination further confirmed the biochemical findings. The preservation of hepatocyte integrity and reduction of necrosis in ELEDD-treated rats demonstrate the extract's ability to restore hepatic structure. Asiwe et al. (2023) similarly reported hepatocellular recovery in diabetic rats treated with *Dryopteris* extracts, attributing it to the synergistic effect of flavonoids, terpenoids, and phenolic compounds.

Overall, the study demonstrates that *Dryopteris dilatata* exerts potent antihyperglycemic, antioxidant, anti-inflammatory, and hepatoprotective effects. The improvement in hepatic enzyme levels, antioxidant parameters, and histoarchitecture validates its traditional use in managing diabetes and liver dysfunction.

VI. Conclusion

The findings of this study demonstrate that the ethanol leaf extract of *Dryopteris dilatata* possesses potent antihyperglycemic, antioxidant, anti-inflammatory, and hepatoprotective properties in streptozotocin-induced diabetic Wistar rats. The extract significantly reduced fasting blood glucose, restored liver enzyme activities, enhanced endogenous antioxidant status, and improved hepatic histoarchitecture in a dose-dependent manner. These results suggest that *D. dilatata* mitigates hepatic damage through the suppression of oxidative stress and inflammation associated with diabetes.

Therefore, the study scientifically validates the ethnomedicinal use of *Dryopteris dilatata* in the management of diabetes mellitus and its related hepatic complications.

VII. Recommendation

Further studies are recommended to:

1. Isolate and characterize the bioactive constituents responsible for the observed pharmacological effects of *Dryopteris dilatata*.
2. Conduct mechanistic and molecular studies to elucidate the specific pathways through which the extract exerts its antidiabetic and hepatoprotective effects.
3. Evaluate the safety, toxicity, and pharmacokinetic profiles of the extract to establish its suitability for therapeutic application.

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CONFLICT OF INTEREST

The author declares no conflict of interest regarding the publication of this research work.

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