



Pharmacological evaluation of euphorbia hirta l. Leaves for the management of diabetes mellitus

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ABSTRACT

This research utilized in vivo models to investigate the anti-diabetic properties of an extract from *Euphorbia hirta* leaves in rats that were induced with diabetes using streptozotocin. (Wistar albino rodents). Ethanol was collected, identified, and extracted from fresh leaves of *Euphorbia hirta* using the Soxhlet method. As per OECD guideline 423, the extract was deemed safe following an acute toxicity test that delivered doses as high as 2000 mg/kg body weight. No negative effects were observed. Animals received streptozotocin (50 mg/kg body weight) to create a diabetic state and were administered extracts of *Euphorbia hirta* (200 mg/kg and 400 mg/kg, respectively, for 21 days) to induce diabetes. Rats in the extracted group had greater weights than the diabetic control animals and exhibited significant enhancements in their fasting blood glucose levels. Several renal function markers, such as blood urea and serum creatinine, along with liver enzyme levels (SGOT and SGPT), demonstrated significant enhancement. Results from the histology of the pancreatic tissues demonstrated that the islets of Langerhans were more organised, and patients treated with extracts demonstrated partial β -cell regeneration, which was more effective at higher dosages. The results of the current experiment show that *Euphorbia hirta* has considerable antidiabetic, hypolipidemic, hepatoprotective, and nephroprotective properties and can be used to manage diabetes mellitus. **Keywords:** *Euphorbia hirta*, Diabetes mellitus, Streptozotocin, Antidiabetic activity, Histopathology, Wistar rats.

1. INTRODUCTION

Diabetes mellitus is one of the most prevalent endocrinological disorders around the world. Diabetes is marked by high concentrations of blood sugar owing to abnormalities in insulin secretion and function [1]. The chronic condition of high sugar levels results in serious complications, such as cardiovascular disorders, kidney disease, nervous system disorders, eye conditions, and poor wound healing. In accordance with current statistics on health globally, the occurrence of diabetes is rising at an alarming rate owing to various risk factors [2].

Traditional anti-diabetic medicines like sulfonylurea, biguanide, and insulin treatment have proved successful for blood glucose management, but long-term usage can cause some unwanted consequences like hypoglycemia, gastro-intestinal issues, liver toxicity, and obesity [3]. For this reason, there is a strong demand for safer alternatives with higher efficacy.

Plants used medicinally for treating diabetes and other metabolic diseases have been in use since ancient times [4]. Out of many such medicinal plants, one plant that has caught much attention due to its wide array of pharmacological properties is *Euphorbia hirta* L., which

belongs to the Euphorbiaceae family [5]. *Euphorbia hirta* L. is also referred to as the asthma weed. This herb is widely distributed in tropical and subtropical areas [6].

The phytochemical screening conducted on *Euphorbia hirta* has indicated the existence of flavonoids, tannins, alkaloids, terpenoids, saponins, phenolics, and glycosides, which are known to have antioxidant and antihyperglycemic activity [7]. Past studies conducted on the plant have shown that *E. hirta* might help to manage glucose metabolism and minimize oxidative stress. Nonetheless, in-depth in vivo analysis of its effects on managing diabetes is yet to be conducted [8].

This study was thus planned for the pharmacological evaluation of ethanolic leaf extract of *Euphorbia hirta* in diabetic rats induced with streptozotocin, using biochemical and histopathological parameters [9].

2. REVIEW OF LITERATURE

Rawal, P. et al. (2023) [10] examined the in vitro anti-diabetic properties of an ethanolic *Euphorbia hirta* extract. Their research showed that the extract significantly reduced glucose levels and enhanced insulin sensitization. The results were thought to have been produced by the presence of different phytochemicals in the extract.

Sharma, A. D. et al. (2024) [11] studied the chemical composition and biological activity of milky latex from wild *Euphorbia hirta*. The research found that the plant had remarkable antioxidant, antidiabetic, and antibacterial activity in an in vitro study. It was concluded that the plants have different bioactive constituents that are responsible for radical scavenging and glucose regulation.

Silalahi, M. (2021) [12] discussed the medical applications and biological activity of *Euphorbia hirta*. This review mentioned the extensive use of *Euphorbia hirta* in herbal medicine for curing respiratory ailments, digestive problems, infectious diseases, and metabolic imbalances. Furthermore, the review emphasized the occurrence of biologically active phytochemicals exhibiting antioxidant and antidiabetic activities.

Tarfa, A. N. et al. (2024) [13] carried out the phytochemical analysis of the ethanolic extract of *Ziziphus spina-christi* and *Euphorbia hirta* and performed an evaluation of the analgesic properties in Wistar albino mice. The analysis revealed that *Euphorbia hirta* contained various phytochemicals like flavonoids, alkaloids, tannins, and phenols which were linked with several pharmacological properties.

Thokchom, S. et al. (2023) [14] explored the medicinal value of *Euphorbia hirta* and highlighted the varied pharmacological effects that include antidiabetic, antioxidant, anti-inflammatory, antimicrobial, and hepatoprotective actions. This study discussed the medicinal value of this plant and implied that it may have possible applications in the treatment of metabolic diseases.

Uddin, M. S. et al. (2019) [15] offered an assessment of the pharmacological characteristics of *Euphorbia hirta*. The authors indicated that the plant exhibited various biological effects, such as antioxidant, antidiabetic, anti-inflammatory, antimicrobial, and wound-healing properties. Additionally, the review examined the role of phytochemicals present in the plant in contributing to its therapeutic effects

3. AIM AND OBJECTIVES

3.1 Aim

To evaluate the effectiveness of ethanolic extract from *Euphorbia hirta* leaves as a diabetes treatment in streptozotocin-induced diabetic Wistar albino rats through biochemical and histopathological examination

3.2 Objectives

1. To determine the antidiabetic potential of ethanolic leaf extract of *Euphorbia hirta* in diabetic Wistar albino rats induced with streptozotocin.
2. To evaluate the impact of *Euphorbia hirta* extract on fasting blood sugar levels, body weight, lipid profile, and liver and kidney function metrics in diabetic rats
3. To examine histological alterations in the pancreas after administering *Euphorbia hirta* extract and evaluate its effectiveness against that of conventional antidiabetic medications.

4. MATERIALS AND METHODS

The methodologies used in the experiment were preparation of ethanolic leaf extracts of *Euphorbia hirta* and evaluation of the antidiabetic effect of the plant on the diabetic Wistar rats induced with streptozotocin. The methodologies employed also include toxicology study, treatment groups, and statistical analysis.

4.1 Collection and Preparation of Plant Extract

After collecting, identifying, cleaning, and air-drying fresh leaves of *Euphorbia hirta*, they were milled into a powder. Using ethanol as the extracting solvent, the plant powder was extracted using the Soxhlet process. A semisolid extract was prepared by filtering and concentrating the resultant extract using rotary evaporation; this was then refrigerated at 4°C for use in further studies.

4.2 Experimental Animals

A group of healthy adult Wistar albino rats, each weighing between 150 and 200 grams, were selected for the experiment. The animals were kept in a controlled setting with 12 hours of light followed by 12 hours of darkness, and the temperature and humidity were also regulated.

4.3 Acute Toxicity Study

According to the guidelines set by the OECD 423, an oral acute toxicity test was carried out. Soon after the animals received the plant extract, they were watched for signs of poisoning and death. Mortality did not occur even when the dose was as high as 2000 mg per kilogram of body weight.

4.4 Induction of Experimental Diabetes

Streptozotocin was injected into the abdominal cavity using a citrate buffer with a pH of 4.5, and the dose given was 50 milligrams per kilogram of body weight, which led to the development of diabetes. Animals were chosen for the experiment three days after receiving the injection if their blood sugar levels measured after fasting were above 250 mg per dl.

4.5 Experimental Design

There was a total of sixty-five rats divided into five groups. Different groups were studied, including those without diabetes, those with diabetes, those treated with conventional drugs,

those given extract at doses of 200 mg/kg, and those given 400 mg/kg. The oral administration lasted for a total of twenty-one days without interruption.

4.6 Biochemical Evaluation

Blood sugar and weight measurements were taken throughout the period of this experiment. After the completion of the experiment, blood samples were drawn to measure the serum lipid profile, liver function test (SGOT & SGPT), and kidney function test (creatinine & blood urea).

4.7 Histopathological and Statistical Analysis

The pancreatic tissue was collected, fixed in formalin, processed, stained, and sections were taken through staining with hematoxylin and eosin. A statistically significant result was defined as a p-value less than 0.05, and the findings were analysed using ANOVA and displayed as Mean \pm SD.

5. RESULTS

The histopathology results revealed that there was severe pancreatic β -cell injury in the diabetic control rats; however, the experimental groups receiving *Euphorbia hirta* extracts showed an improvement in islet morphology with partial regeneration of the β -cells. Moreover, the effect was more prominent with the high-dose treatment group.

5.1 Acute Toxicity Study

The leaf extract from *Euphorbia hirta* was tested for acute oral toxicity following the procedures described in the OECD manual 423. During the 14-day trial, no signs of toxicity or deaths were observed in the test animals when they were given a dose of 2000 mg per kilogram of body weight. We chose 200 mg/kg and 400 mg/kg body weight for the antidiabetic study because the extract was found to be safe for more research into its drug potential.

5.2 Effect of *Euphorbia hirta* Extract on Fasting Blood Glucose Levels

After 21 days of treatment with streptozotocin, rats with diabetes were studied to see how an ethanolic leaf extract of *Euphorbia hirta* affected their fasting blood glucose levels. The group of diabetic control had elevated glucose levels, while the glucose level started to drop in the group of diabetic animals treated with the extract. The group which received a dosage of 400 mg/kg had more reductions than that receiving 200 mg/kg. Standard drug had the highest reduction in glucose level.

Table 1: Effect of *Euphorbia hirta* Extract on Fasting Blood Glucose Levels (mg/dL)

Groups	Day 0	Day 7	Day 14	Day 21
Normal Control	92	94	91	90
Diabetic Control	285	298	305	312
Standard Drug	280	220	165	118
Extract (200 mg/kg)	282	248	210	168
Extract (400 mg/kg)	284	230	185	136

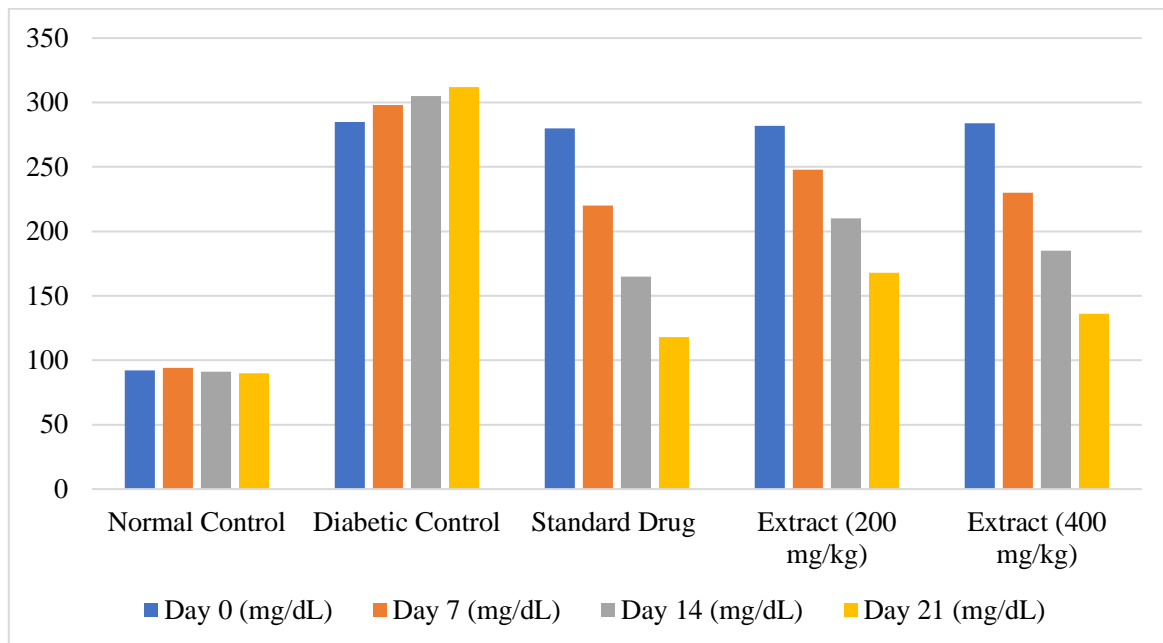


Figure 1: Graphical Representation of Effect of *Euphorbia hirta* Extract on Fasting Blood Glucose Levels

These findings reveal that the extract of *Euphorbia hirta* has a considerable antidiabetic potential. The lowering of the fasting blood glucose level implies enhanced glucose control and antihyperglycemic properties of the herbal extract. The high dose was more effective, reflecting dose-related action on diabetes mellitus.

5.3 Effect of *Euphorbia hirta* Extract on Body Weight

The effect of ethanol extract of the leaves of *Euphorbia hirta* on body weight in the case of diabetic rats induced with streptozotocin was observed in the experiment. It was observed that the control diabetic group exhibited significant loss of body weight from 184 g to 160 g. However, the extract-treated groups were found to exhibit improved body weight. Among them, the 200 mg/kg extract-treated group demonstrated final body weight of 176 g, while the 400 mg/kg extract-treated group demonstrated increased final body weight of 183 g.

Table 2: Effect of *Euphorbia hirta* Extract on Body Weight

Groups	Initial Body Weight (g)	Final Body Weight (g)
Normal Control	182	190
Diabetic Control	184	160
Standard Drug	183	186
Extract (200 mg/kg)	181	176
Extract (400 mg/kg)	182	183

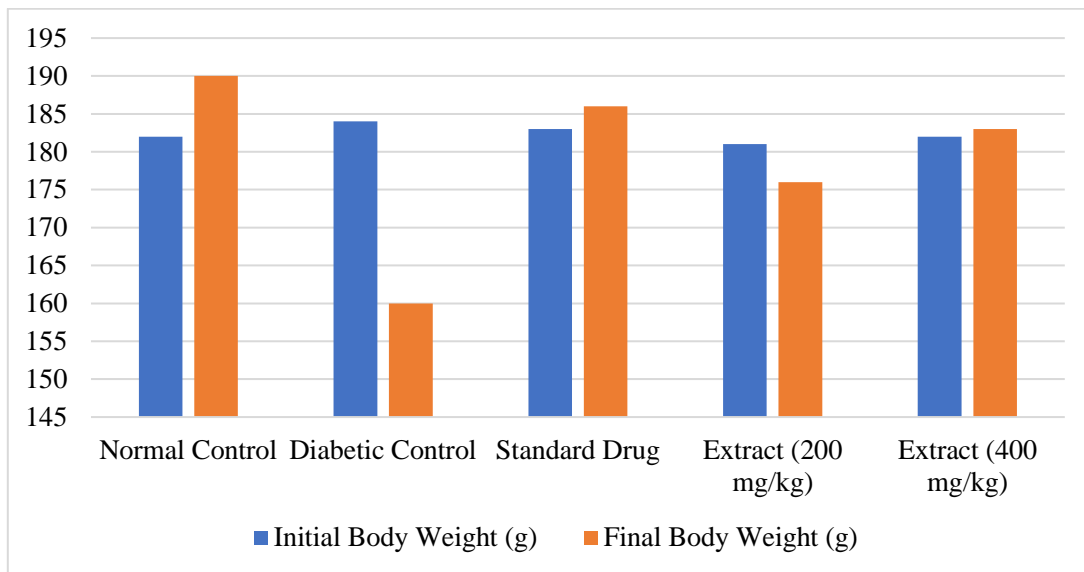


Figure 2: Graphical Representation of Effect of *Euphorbia hirta* Extract on Body Weight. These findings show that the extract of *Euphorbia hirta* can aid in the prevention of body weight reduction caused by diabetes mellitus. The increase in body weight in the extract-treated groups demonstrates more efficient glucose metabolism. There is a dose-dependent effect, meaning that the higher dose (400 mg/kg) was more effective.

5.4 Effect of *Euphorbia hirta* Extract on Serum Lipid Profile

The extract from the leaves of *Euphorbia hirta*, made with alcohol, was used in an experiment on rats that had diabetes. The purpose of the study was to check how this extract influences the levels of lipids in the blood of these rats. In diabetic rats, the levels of total cholesterol, triglycerides, and low-density lipoprotein (LDL) were all higher compared to the control group, which had normal levels of high-density lipoprotein (HDL). To the benefit of diabetic rats, an ethanolic leaf extract from *Euphorbia hirta* considerably altered lipid profile values. Treatment with 400 mg/kg of extract was associated with greater improvements in HDL levels and decreased levels of cholesterol, triglycerides, and LDL compared to treatment with 200 mg/kg.

Table 3: Effect of *Euphorbia hirta* Extract on Lipid Profile

Parameters	Diabetic Control	Standard Drug	Extract 200 mg/kg	Extract 400 mg/kg
Total Cholesterol (mg/dL)	220	145	172	152
Triglycerides (mg/dL)	190	120	145	130
HDL Cholesterol (mg/dL)	28	45	38	42
LDL Cholesterol (mg/dL)	160	90	118	102

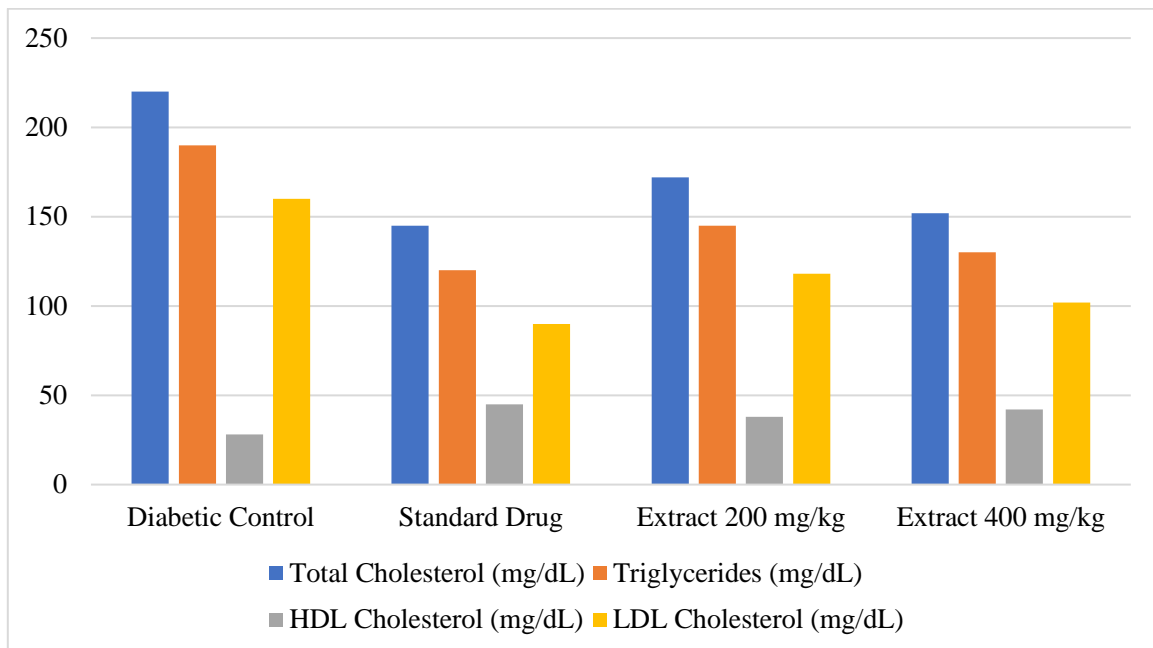


Figure 3: Graphical Representation of Effect of *Euphorbia hirta* Extract on Lipid Profile
The study shows that the extract from *Euphorbia hirta* has a clear effect in reducing cholesterol levels in rats with diabetes. Results showing a rise in HDL cholesterol and a marked reduction in total and triglyceride cholesterol suggest it may be useful in preventing lipid problems in animals with diabetes.

5.5 Effect of *Euphorbia hirta* Extract on Liver and Kidney Function Parameters

The study looked at how an extract made from the leaves of *Euphorbia hirta* using alcohol affects the liver and kidney function in rats that were made diabetic with streptozotocin. In the group where people had diabetes and were not getting treatment, the levels of serum creatinine, blood urea, SGOT, and SGPT were all higher. The treatment with *Euphorbia hirta* extract led to improvements that were both dose-dependent and statistically significant. There was a significant difference between the two groups that received the extracts at doses of 200 and 400 mg per kilogram. The standard drug group showed results that were almost normal.

Table 4: Effect of *Euphorbia hirta* Extract on Liver and Kidney Function Parameters

Parameters	Diabetic Control	Standard Drug	Extract 200 mg/kg	Extract 400 mg/kg
SGOT (U/L)	98	56	72	61
SGPT (U/L)	92	50	68	58
Serum Creatinine (mg/dL)	1.8	0.9	1.2	1.0
Blood Urea (mg/dL)	62	34	46	38

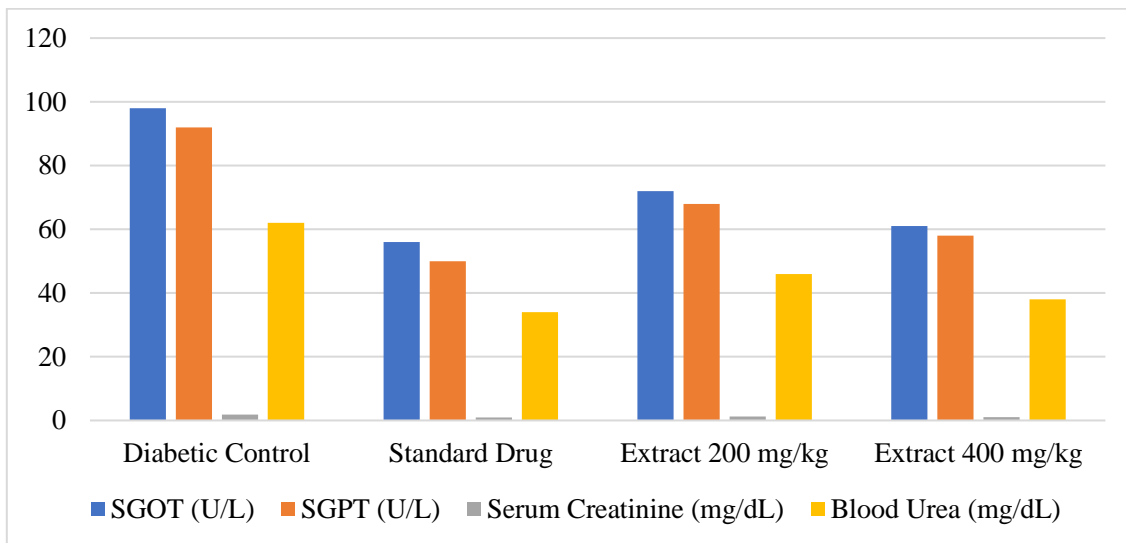


Figure 4: Graphical Representation of Effect of *Euphorbia hirta* Extract on Liver and Kidney Function Parameters

These findings suggest that there is some protective effect of the *Euphorbia hirta* extract on the liver and kidneys of diabetics. Improvement in terms of SGOT, SGPT, creatinine, and blood urea values implies better functioning of the organs concerned. Furthermore, the higher dosage level showed more protection, which means that its effectiveness is in proportion to the dose.

5.6 Histopathological Findings

Histopathological study of pancreatic tissue in normal control rats revealed normal islet morphology with healthy β -cells. In diabetic control rats, there was significant deterioration in islet morphology with necrotic changes in β -cells, decreased cellularity, and islet atrophy caused by diabetes.

Pancreatic sections in treatment groups with *Euphorbia hirta* leaf extract displayed an improved architecture of islets and partial regeneration of β -cells with less cellular damage. Pancreatic tissue in the high dose group (400 mg/kg) recovered more effectively than the low dose group. Pancreatic sections in the standard drug group displayed almost normal histology, validating the antidiabetic efficacy of *Euphorbia hirta* leaf extract.

6. DISCUSSION

The study conducted on live animals showed that the ethanol extract from the leaves of *Euphorbia hirta* has strong anti-diabetic effects in rats that were made diabetic using streptozotocin. Diabetes mellitus was successfully induced in the control group of rats through the development of high fasting blood glucose levels, low body weight, an abnormal lipid profile, and damaged liver and kidney function. When more of the *Euphorbia hirta* extract was given to diabetic rats, specifically at a higher dose of 400 mg per kilogram of body weight, it significantly lowered their blood sugar levels and helped them gain more weight. However, giving a smaller dose of 200 mg per kilogram had a much smaller effect on their blood sugar and weight. The presence of plant-based compounds like tannins, flavonoids, and phenolic substances might be the reason why the extract helps reduce high blood sugar levels.

Furthermore, hypolipidemic, hepatoprotective, and nephroprotective activities were evidenced through normalization of serum lipids and lowering of the increased values of SGOT, SGPT, serum creatinine, and blood urea concentration in diabetic rats. Moreover, histopathology results revealed that *Euphorbia hirta* had a protective role, as shown through the restoration of pancreatic islet structure and regeneration of β -cells in the treated rats. Histologically, the high-dose group had better recovery than the low-dose group. From the scientific data gathered, it can be said that *Euphorbia hirta* has medicinal value as an anti-diabetic agent.

7. CONCLUSION

This study shows that the ethanolic extract from the leaves of *Euphorbia hirta* has a strong ability to help reduce diabetes in rats that were made diabetic with streptozotocin. In diabetic rats, the *E. hirta* extract showed antidiabetic effects by reducing fasting blood sugar levels, helping to increase body weight, improving the levels of fats in the blood, and repairing the function of the liver and kidneys. Furthermore, histological results indicated that the pancreatic islet structures were normalised and β -cell regeneration occurred, particularly at high dosages (400 mg/kg), lending further credence to the extract's protective powers. The results of the study have scientifically validated the traditional usage of *Euphorbia hirta* in diabetes mellitus management and suggested that it has the potential of becoming an alternative antidiabetic, hypolipidemic, hepatoprotective, and nephroprotective remedy.

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**International of Advanced Research and Multidisciplinary
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An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 7.2 Website: <https://ijarnt.com> ISSN No.: 3048-9458

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