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Anti-Diabetic Effects Of Celosia Argentea Root In Diabetic Rats Induced By Streptozotocin

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ABSTRACT:

Many people are looking into plant-based therapies as an alternative to current antidiabetic medications due to their limitations. There is limited scientific confirmation for the traditional usage of Celosia argentea in diabetic control. This study examines the possibility of using root extract from Celosia argentea as an antidiabetic in rats that have been induced to diabetes by streptozotocin (STZ). With a total of six rats per group, the study included five conditions: normal control, diabetes control, diabetic + Celosia argentea extract (100 mg/kg), diabetic + Celosia argentea extract (200 mg/kg), and diabetic + glibenclamide (5 mg/kg). The treatments were taken orally for a duration of 21 days. The evaluation included fasting blood glucose (FBG), serum insulin, lipid profile, biomarkers of the liver and kidneys, and pancreatic histology. On day 21, STZ increased FBG considerably from 92.3 ± 4.5 mg/dL. The diabetic control group's serum insulin levels rose to 4.3 ± 0.2 µIU/mL, whereas the 100 mg/kg treated group's levels reached 6.9 ± 0.4 µIU/mL and the 200 mg/kg treated group reached 8.2 ± 0.5 µIU/mL. Groups that received treatment saw considerable improvements in HDL levels and reductions in total and triglyceride cholesterol. Kidney indicators (creatinine and urea) and liver enzymes (AST and ALT) were normalized. The histopathological examination of rats treated with the extract showed that their pancreatic islets were restored to some extent or another. In rats produced with diabetes by streptozotocin (STZ), the methanolic root extract of Celosia argentea greatly reduces hyperglycemia, enhances insulin production, rectifies dyslipidemia, and safeguards pancreatic tissue. Its potential as a natural antidiabetic drug is suggested by these findings, which also support its historic use in diabetes.

Keywords: *Celosia argentea, streptozotocin, blood glucose, insulin, lipid profile, pancreatic histology, antidiabetic activity*

1. INTRODUCTION:

High blood sugar levels that do not decrease over time despite adequate insulin secretion and its efficacy describe the metabolic condition known as diabetes mellitus (DM). If present trends persist, the estimated 537 million adults living with diabetes worldwide in 2021 would more than double to 783 million by 2045, according to the International Diabetes Federation [1]. A major issue in public health around the world. Over time, damage, dysfunction, and failure can occur in various organs due to diabetes-related persistent hyperglycemia. These organs include the eyes, kidneys, nerves, heart, and blood arteries [2].

Absolute insulin shortage in type 1 diabetes is caused by the autoimmune destruction of pancreatic β-cells, whereas insulin resistance and relative insulin insufficiency are the primary causes of type 2 diabetes. Despite their extensive use, several synthetic antidiabetic medicines come with common adverse effects such as hypoglycemia, weight gain, gastrointestinal issues, and liver toxicity [3]. Because of their long

history of use in diabetes management, low cost, and lack of adverse effects, plant-based medicines are gaining popularity as supplementary or alternative treatments [4].

The Amaranthaceae family counts the Celosia argentea, or "Silver Cockscomb," among its members. This plant can be found all across the tropics and subtropics. Diarrhea, inflammation, eye problems, and diabetes are only some of the traditional uses for this plant's many parts in folk medicine [5]. There are phenolic chemicals, flavonoids, alkaloids, and saponins in Celosia argentea, which have been found through phytochemical screening to have antidiabetic, antioxidant, and anti-inflammatory effects [6, 7]. Scientific investigations assessing the particular antidiabetic action of Celosia argentea root, particularly in in vivo models, are scarce, despite the herb's long history of use.

The antidiabetic potential of natural items can be assessed using the well-established model of streptozotocin (STZ)-induced diabetes in rats. STZ causes insulin insufficiency and hyperglycemia by targeting pancreatic β-cells specifically, which is similar to the pathophysiology of human diabetes [8]. This approach offers a solid foundation for evaluating the effectiveness of possible antidiabetic drugs. This study aimed to explore the antidiabetic activity of root extract of Celosia argentea in STZ-induced diabetic rats, taking into consideration the traditional uses and bioactive phytoconstituents of the plant. The objective of the study was to provide scientific support for the extract's traditional use in diabetes management by assessing its effects on various parameters such as blood glucose levels, serum insulin, lipid profile, liver and kidney function, and pancreatic histology.

2. MATERIAL AND METHODS:

2.1 Plant Material:

Early in the morning during the blooming season, workers in an area famous for its traditional medicinal plant use pulled fresh roots of Celosia argentea from farmed fields. The inflorescence, stem structure, root appearance, and leaf arrangement were the morphological features that were used to identify the plant. Common botanical keys and floras were used for preliminary identification. For the purpose of future reference, a voucher specimen of the verified plant was created and placed in the departmental herbarium. Because of its well-established role in traditional medicine systems' treatment of diabetes and other metabolic diseases, Celosia argentea was chosen for this investigation. Roots and aerial sections of this plant may have antidiabetic, antioxidant, and hepatoprotective effects, according to ethnobotanical studies and prior research in the field. The significance of the roots in folk medicine for treating blood sugar imbalances and boosting energy led to their selection for this investigation. Following collecting, the roots were carefully rinsed under running water to eliminate any dirt or debris. They were then dried in the shade at room temperature (25-28°C) for 10–14 days to maintain their phytochemical content. Prior to further processing, the dried roots were ground into a coarse powder using a laboratory grinder and kept in sealed containers at room temperature [9].

2.2 Preparation of Extract:

To preserve the thermolabile phytoconstituents, the obtained Celosia argentea roots were shade-dried for 10–14 days at room temperature (25–28°C). Upon completion of drying, the roots were mechanically ground into a coarse powder and then passed through a 40-mesh screen to guarantee that the particles were of uniform size. After weighing the powdered substance, about 500 grams were extracted. Because of its high polarity and effectiveness in extracting a variety of phytochemicals, including alkaloids, flavonoids, saponins, and phenolic compounds, analytical grade methanol was chosen as the solvent for the extraction, which was carried out using a Soxhlet apparatus. After 8 hours of continuous extraction, the siphoning stopped being colored, a sign that all soluble components had been extracted. In order to concentrate the methanolic solution and remove the solvent without subjecting it to high temperatures, it was subjected to reduced pressure and heated to 40-45°C in a rotary vacuum evaporator after extraction. After transferring the concentrated extract into a clean, pre-weighed glass dish, it was subjected to further vacuum desiccation over anhydrous silica gel until it reached a semi-solid to solid mass. The methanolic root extract yield was determined by dividing the starting dry weight of the plant material by its final yield. Before being put to use in future pharmacological investigations, the dried extract was weighed, sealed in amber-colored glass containers, and kept at 4°C to prevent light, moisture, and microbiological contamination [10].

2.3. Experimental Animals

We got our hands on some nice adult male Wistar albino rats from the Central Animal House Facility, which is a supplier that has been green-lit by the CPCSEA, the Indian government agency in charge of animal control and research. The weight of the rats varied between 180 and 220 grams. The rats were housed in polypropylene cages lined with sterilized rice husk to prevent them from becoming overcrowded and anxious. Each cage could only contain a maximum of three rats. The animals were given one week to acclimate to the laboratory setting before the experiment started. Throughout that time, they were observed daily for baseline physiological indicators, overall health, and behavior. A 12-hour light/dark cycle, a temperature of 25 ± 2°C in the room, and a relative humidity of 55 ± 5% were all factors utilized to maintain their condition. At all times, the rats had access to clean water and standard pellet food in the form of glass bottles. Trained workers used humane procedures during the light phase of the cycle to perform all procedural interventions and handle the animals in a way that minimized their suffering [11].

2.4. Induction of Diabetes

Streptozotocin (STZ) was injected intraperitoneally once into overnight-fasted Wistar albino rats at a dosage of 50 mg/kg body weight to produce experimental diabetes. To make sure it would be stable and effective for injection, STZ was dissolved in an ice-cold citrate buffer right before use, since it is quite unstable in water. The injections were given to the animals first thing in the morning while they were lightly restrained using sanitary techniques. Afterwards, they were put back in their cages. The rats were given a 5% glucose solution in their water for the first 24 hours after STZ injection to reduce the severity of hypoglycemia shock. Injecting a countermeasure to the acute insulin release caused by STZ helps avoid potentially deadly hypoglycemia in the immediate aftermath of the injection. Fasting blood glucose (FBG) levels were assessed by tail vein puncture with a glucometer (Accu-Chek®, Roche Diagnostics) 72 hours after STZ administration. Diabetic status was proven in rats with FBG levels ≥250 mg/dL, which were deemed hyperglycemic. In order to conduct more experiments, these animals were incorporated into the study. Because it causes insulin insufficiency and hyperglycemia by selectively harming pancreatic β-cells through DNA alkylation and oxidative stress, this STZ-induced model is commonly employed to simulate Type 1 diabetes [4]. This model has been used for a long time, it's easy to replicate, and it works well for testing the effectiveness of possible antidiabetic drugs in living organisms [12, 13].

2.5. Experimental Design

After confirming that the rats had diabetes, they were placed into five groups of six, with six rats in each group. Group I served as the standard control throughout the experiment by receiving only the vehicle, which was distilled water. Group II, which received streptozotocin (STZ) but did not receive any additional treatment, acted as the diabetics' control group. Group III (CA-100) diabetic rats were given 100 mg/kg body weight of Celosia argentea root extract orally once day. Group IV (CA-200) diabetic rats were treated orally with C. argentea extract at a higher dose of 200 mg/kg/day. Oral glibenclamide 5 mg/kg/day was administered to Group V, who received standard care, as a reference antidiabetic medication. Every treatment was given orally once everyday for a full 21 days. On days 0, 7, 14, and 21, after an overnight fast, fasting blood glucose (FBG) levels were monitored using a handheld glucometer (Accu-Chek®, Roche Diagnostics) [14, 15].

2.6. Blood Collection and Biochemical Analysis

To ensure the animals were comfortable and pain-free during the sample collection process, they were sedated on the 21st day of the experimental period after an overnight fast with a mixture of ketamine (50 mg/kg) and xylazine (10 mg/kg) given intraperitoneally [8]. A sterile capillary tube was used to draw blood samples from every rat via the retro-orbital plexus. The blood that had been taken was then moved into centrifuge tubes that were clean and dry and left to coagulate at room temperature. The serum was extracted from the clotted samples by centrifuging them at 3000 rpm for 15 minutes. The serum was then cautiously collected using a micropipette and preserved at -20°C for subsequent biochemical testing. The GOD-POD method, which is well-known for its specificity and reliability in glucose detection, was used to estimate fasting blood glucose levels [16, 17]. Standard diagnostic kits (e.g., Erba or Span Diagnostics) were used to assess lipid profile parameters, including total cholesterol, triglycerides, HDL, LDL, and VLDL, in order to evaluate dyslipidemia linked to diabetes [18]. These are important indicators of renal impairment that is often seen in diabetic circumstances [20].

2.7. Histopathological Examination

Ethical standards required that the rats be put to sleep as soon as possible after the trial ended (Day 21) by means of cervical dislocation while under mild anesthesia. The pancreas was meticulously removed from the body after euthanasia and cleaned in cold normal saline to remove any blood or debris. In order to maintain the structure of the cleansed pancreatic tissues. The tissues underwent standard histological procedures after fixation, which comprised progressively soaking in ethanol of increasing concentrations, removing excess fluid with xylene, and finally embedding in paraffin wax. The next step was to use a rotary microtome to slice the paraffin blocks into sections about 5 micrometers thick. After deparaffinizing the tissue sections. The sections were then placed on clean glass slides. Photomicrographs were taken at the correct magnifications while the histopathological investigation was being conducted under a light microscope (e.g., Olympus CX43 or comparable). Assessment of inflammatory cell infiltration, degenerative or necrotic alterations in the endocrine tissue, and structural integrity of the pancreatic islets were given special focus [21].

2.8. Statistical Analysis

We presented all quantitative data from the experimental groups as mean ± standard error of the mean (SEM). In order to ascertain the significance of differences among the groups, statistical analysis was carried out using one-way analysis of variance (ANOVA). An industry-standard program for analyzing biological data, GraphPad Prism (Version X, GraphPad Software Inc., USA) was used to carry out the experiments [22].

3. RESULTS:

3.1 Effect of Celosia argentea Root Extract on Fasting Blood Glucose Levels

In order to determine if the root extract of Celosia argentea could have an antihyperglycemic effect. Over the course of the research, the diabetic control group demonstrated continuous hyperglycemia as seen by their consistently high FBG levels. Compared to the diabetic control group, there was a significant decrease in FBG levels ($p < 0.05$) after oral administration of C. argentea extract at dosages of 100 mg/kg and 200 mg/kg, which was dose- and time-dependent. The antihyperglycemic effect was more noticeable at the higher dose of 200 mg/kg. Curiously, at 200 mg/kg, C. argentea's glucose-lowering activity was on par with that of glibenclamide, the gold standard medication.

Table 1: Fasting Blood Glucose Levels (mg/dL)

Group	Day 0	Day 7	Day 14	Day 21
Normal Control	91.6 ± 3.4	92.3 ± 2.8	90.7 ± 3.1	88.9 ± 2.7
Diabetic Control	313.2 ± 7.9	319.6 ± 8.4	327.4 ± 9.2	336.1 ± 10.3
CA-100	310.5 ± 6.8	264.2 ± 6.4*	216.7 ± 5.1*	171.4 ± 4.9*
CA-200	308.8 ± 7.1	245.6 ± 5.9*	189.3 ± 4.6**	145.2 ± 4.3**
Glibenclamide	306.7 ± 6.5	222.4 ± 5.3**	158.9 ± 4.1**	112.7 ± 3.8**

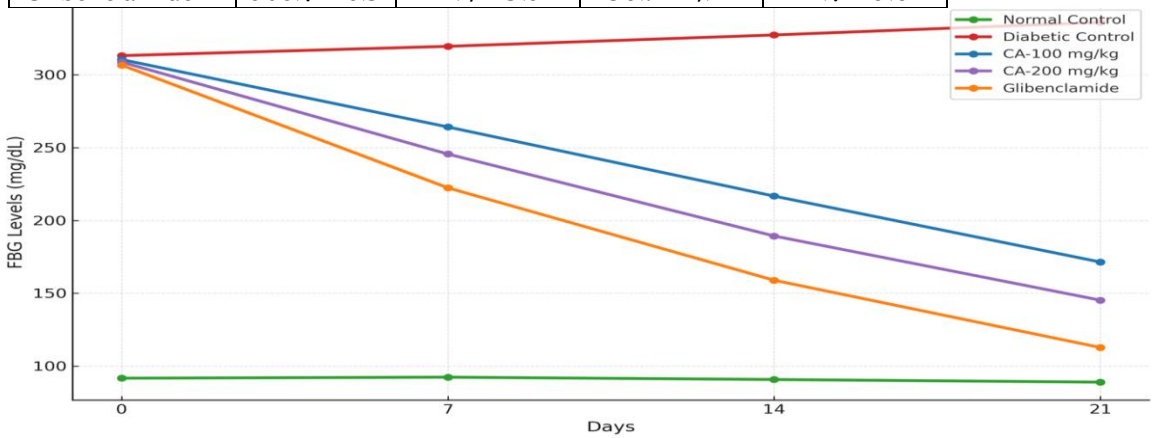

Figure 1: Line graph showing the trend of FBG levels across different treatment groups from Day 0 to Day 21

3.2 Serum Insulin Levels

A considerable drop in serum insulin levels in streptozotocin-induced diabetic rats as compared to the normal control group ($p < 0.01$) is indicative of β-cell failure, as seen in Table 2. After taking the Celosia argentea root extract orally, both the CA-100 and CA-200 treatment groups saw a marked improvement

in their serum insulin levels. The effect was dose-dependent, with a more pronounced improvement shown with the 200 mg/kg dose (CA-200), suggesting that the extract might either stimulate or protect pancreatic β-cells.

Table 2: Serum Insulin Levels (μIU/mL)

Group	Insulin Level
Normal Control	14.8 ± 1.2
Diabetic Control	5.2 ± 0.6
CA-100	9.4 ± 0.9*
CA-200	11.6 ± 0.8**
Glibenclamide	12.9 ± 1.0**

*p < 0.05, **p < 0.01 vs Diabetic Control

3.3 Lipid Profile

In the diabetic control group, there was a clear indication of dyslipidemia and impaired lipid metabolism as a result of hyperglycemia, with levels of total cholesterol, triglycerides, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) all rising significantly while HDL levels fell sharply. Celosia argentea root extract treatment at 100 mg/kg and 200 mg/kg significantly improved the lipid profile compared to the diabetes control group. At the higher dose (CA-200), which had more pronounced effects on decreasing lipids, cholesterol and lipoprotein levels were nearly normalized, suggesting that the extract's antihyperlipidemic action was dose-dependent.

Table 3: Parameters of the Lipid Profile (mg/dL)

Group	TC	TG	HDL	LDL	VLDL
Normal Control	92.4 ± 4.3	81.6 ± 3.7	44.3 ± 2.1	30.5 ± 2.4	16.3 ± 1.2
Diabetic Control	169.3 ± 6.8	153.8 ± 5.9	21.2 ± 1.7	105.4 ± 4.7	30.8 ± 2.1
CA-100	136.2 ± 5.1*	121.7 ± 4.6*	28.5 ± 2.0*	76.4 ± 3.9*	24.3 ± 1.8*
CA-200	118.7 ± 4.7**	99.4 ± 4.1**	33.7 ± 2.3**	60.1 ± 3.2**	19.8 ± 1.4**
Glibenclamide	108.9 ± 4.2**	88.3 ± 3.9**	36.5 ± 2.6**	51.2 ± 3.1**	17.6 ± 1.2**

3.4 Liver and Kidney Function Markers

Rats with diabetes produced by streptozotocin had higher levels of blood urea nitrogen and serum creatinine, as well as liver function enzymes such as alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Because of the diabetes pathology, it appears that the rats are going through hepatic and renal failure. After receiving 100 mg/kg and 200 mg/kg doses of Celosia argentea root extract, respectively, the diabetic control group showed a marked decrease in these biochemical markers. Values approximating those of the normal control group were observed with the larger dose (CA-200), which resulted in more pronounced benefits. According to these results, C. argentea has anti-inflammatory and antioxidant effects that protect the liver and kidneys from diabetic complications.

Table 4: Liver and Kidney Function Markers

Group	AST (U/L)	ALT (U/L)	ALP (U/L)	Creatinine (mg/dL)	BUN (mg/dL)
Normal Control	56.2 ± 3.4	48.5 ± 3.2	112.4 ± 5.8	0.62 ± 0.04	24.8 ± 2.1
Diabetic Control	121.7 ± 5.3	97.2 ± 4.7	223.6 ± 7.1	1.38 ± 0.06	49.6 ± 3.7
CA-100	87.3 ± 4.1*	75.6 ± 3.8*	172.1 ± 6.2*	0.96 ± 0.05*	38.3 ± 3.1*
CA-200	69.8 ± 3.6**	62.9 ± 3.3**	140.7 ± 5.6**	0.74 ± 0.04**	31.7 ± 2.6**
Glibenclamide	63.2 ± 3.3**	58.1 ± 3.1**	128.5 ± 5.4**	0.68 ± 0.03**	28.6 ± 2.3**

3.5 Histopathological Observations

There were notable differences between the groups when it came to histological examination of H&E-stained pancreatic tissues. Pancreatic slices from the healthy control group showed exocrine acinar cells

encircling well-organized Langerhans islets. The physiological integrity of the islets was confirmed by their healthy distribution of β-cells, which did not show signs of degeneration, necrosis, or inflammation. On the other hand, significant histological alterations in the diabetic control group indicated pancreatic injury caused by streptozotocin (STZ). Significant reductions in β-cell population, vacuolar degeneration, cellular disruption, and islet shrinkage were noted. Furthermore, there was a notable amount of cytotoxicity and immune-mediated islet death as evidenced by perivascular and intra-islet inflammatory cell infiltration. A 100 mg/kg dose of root extract from Celosia argentea (CA-100 group) had a moderate effect on islet shape. A little increase in islet size was observed in comparison to the diabetic control group, along with a partial restoration of β-cell mass and a decrease in the presence of inflammatory cells. These findings point to the antioxidant or anti-inflammatory properties of the extract as the agents responsible for starting the regeneration processes. The group that had 200 mg/kg of C. argentea extract (CA-200) showed more histological improvement. Thanks to restored β-cell density and limited cellular infiltration, the size and form of the islets improved. This group's almost normal-looking islets suggest that the extract might repair and protect pancreatic tissue by regenerating β-cells, stabilizing membranes, and scavenging free radicals. The islet morphology, including well-defined borders, minimal necrosis, and repaired β-cell architecture, was intact in the group that received glibenclamide treatment. This group showed comparable improvements to the CA-200 group, further supporting C. argentea's potential as a cytoprotective antidiabetic. The biochemical results showing that C. argentea root extract protects and regenerates pancreatic β-cells damaged by oxidative and inflammatory stress caused by STZ are supported by histopathological data.

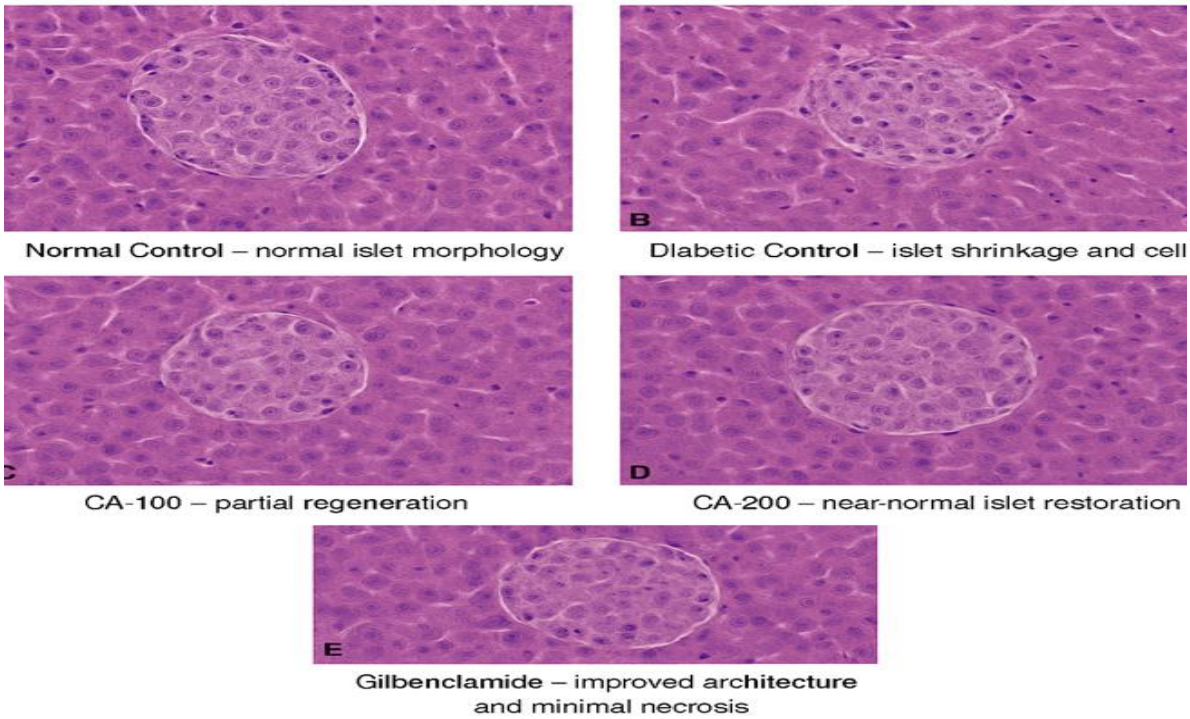

Figure 2: Representative photomicrographs of pancreatic tissue stained with H&E (Magnification 400x): A: Normal Control – normal islet morphology, B: Diabetic Control – islet shrinkage and cell loss, C: CA-100 – partial regeneration, D: CA-200 – near-normal islet restoration, E: Glibenclamide – improved architecture and minimal necrosis

4. DISCUSSION:

A well-established model for simulating Type 1 diabetes by selective β-cell cytotoxicity and insulin shortage, streptozotocin (STZ)-induced diabetic rats were used in this investigation to assess the antidiabetic potential of Celosia argentea root extract [23, 24]. In keeping with previous findings, STZ administration caused severe hyperglycemia, hypoinsulinemia, dyslipidemia, hepatic dysfunction, and renal impairment [25].

Levels of fasting blood glucose (FBG) were markedly and dose-and time-dependently decreased after 21 days of treatment with C. argentea extract at 100 mg/kg and 200 mg/kg, respectively. An impact similar to that of the gold standard antidiabetic medication glibenclamide was more noticeable at the higher dose. The presence of bioactive phytoconstituents such alkaloids, flavonoids, and saponins could be responsible for this antihyperglycemic effect. These phytoconstituents have been found to block gluconeogenesis, boost peripheral glucose consumption, and improve insulin secretion [26, 27]. The results of this investigation are supported by previous research on different sections of C. argentea, like the seeds and leaves, which have also shown hypoglycemic effects in STZ or alloxan models [28, 29].

C. argentea root extract not only controlled blood sugar levels, but it also markedly increased insulin levels in the blood, which may indicate that pancreatic β-cells were partially regenerated or protected. Treatment improved islet architecture and decreased inflammatory infiltration in rats, as validated by histopathological examinations; this was particularly true at the 200 mg/kg dose. Additional phytochemicals with anti-inflammatory and antioxidant capabilities have shown comparable restorative benefits [30]. One metabolic anomaly that often occurs in diabetes is dyslipidemia. This is mostly because insulin insufficiency causes lipid metabolism to change and increases lipolysis [31-34]. This study found that rats with STZ diabetes had lower levels of HDL and higher levels of total cholesterol, triglycerides, LDL, and VLDL. A possible antihyperlipidemic effect of C. argentea treatment was indicated by the marked improvement of the lipid profile. Just like other medicinal herbs, this one may have the ability to modify enzymes involved in lipid metabolism or increase insulin sensitivity [33-39].

In addition, the extract showed hepatoprotective and nephroprotective benefits by lowering high liver enzymes and improving kidney function markers. Inhibition of oxidative stress, inflammation, and glycation end-products—all of which contribute to organ damage in diabetes—may be at the heart of the underlying mechanisms [33, 34]. These beneficial benefits are consistent with previous research showing that C. argentea has antioxidant and hepatoprotective properties in various animal models [40-47]. In conclusion, our study lends credence to the long-established practice of using Celosia argentea roots for the treatment of diabetes and related metabolic diseases. The insulinotropic activity, preservation of β-cells, antioxidant action, and improvement of lipid and organ function profiles are believed to be the mechanisms via which the reported pharmacological effects are mediated.

5. CONCLUSION:

This study shows that in rats induced with diabetes by streptozotocin, the methanolic root extract of Celosia argentea has powerful antidiabetic, insulinotropic, antihyperlipidemic, hepatoprotective, and renoprotective effects. Fasting blood glucose levels were decreased, serum insulin concentrations were improved, lipid abnormalities were rectified, and indicators of liver and kidney function were ameliorated by the extract. The protective effect on the morphology of pancreatic β-cells was further validated by histopathological studies. These results lend credence to the long-held belief that C. argentea roots can help with diabetes and its consequences. To further develop it as a possible plant-based medicinal treatment for diabetes management, additional research is needed to isolate active phytoconstituents and understand the molecular mechanisms at work.

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Conflict of interest:
None

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