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EVALUATION OF THE ANTI-DIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF CLEOME VISCOSAIN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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ABSTRACT: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, impaired insulin function, oxidative stress, and disturbances in lipid metabolism. The present study was designed to evaluate the anti-diabetic activity of the ethanolic extract of Cleome viscosa in streptozotocin (STZ)-induced diabetic rats. The plant extract was subjected to preliminary phytochemical screening, which revealed the presence of flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, glycosides, and other bioactive constituents. Diabetes was induced in experimental rats by administration of streptozotocin, and the animals were treated with different doses of ethanolic extract of Cleome viscosa for the experimental period. The anti-diabetic activity was assessed by evaluating body weight changes, fasting blood glucose levels, and oral glucose tolerance test (OGTT). Serum biochemical parameters including total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), blood urea nitrogen (BUN), and glycated hemoglobin (HbA1c) were estimated. In addition, pancreatic oxidative stress markers such as superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and malondialdehyde (MDA) were evaluated. STZ administration significantly increased blood glucose levels, impaired glucose tolerance, reduced body weight, altered lipid profile, elevated BUN and HbA1c levels, decreased antioxidant enzyme activities, and increased MDA levels compared with normal control rats. Treatment with the ethanolic extract of Cleome viscosa significantly reversed these alterations in a dose-dependent manner. The higher dose of the extract exhibited marked antihyperglycemic activity, improved lipid metabolism, enhanced antioxidant defense mechanisms, and reduced oxidative damage, with effects comparable to the standard drug metformin.The findings suggest that the ethanolic extract of Cleome viscosa possesses significant anti-diabetic, hypolipidemic, antioxidant, and protective effects against STZ-induced diabetic complications. These activities may be attributed to the synergistic action of its phytoconstituents, particularly flavonoids and phenolic compounds. The present study supports the potential use of Cleome viscosa as a promising natural therapeutic agent for the management of diabetes mellitus and associated metabolic complications.

Keywords: Cleome viscosa, Streptozotocin, Diabetes mellitus, Antidiabetic activity, Oxidative stress, Lipid profile, Antioxidants, HbA1c.

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by alteration in the metabolism of carbohydrates, lipids and proteins. DM is probably one of the most terrible oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago1. It is well known that diabetes and hypertension are chief risk factors in the

development of nephropathy, retinopathy, and cardiomyopathy which progress to myocardial infarction.

MATERIALS AND METHODS

Collection and authentication of Plant material

The flowers of Cleome viscosa, was selected for investigation and were procured from the nearest area of Hyderabad Ranga Reddy District. The plant material was taxonomically identified and authenticated by Dr. Madhava Chetty, Head of Department, Botany, Sri Venkateshwara academia, Tirupathi, Andhra Pradesh.

Preparation of plant extract

The fresh flower was air dried in shade and extracted with 1:4 ratio ethanol extract, using a Soxhlet extractor for 8 hrs. at 55-600C. The supernatant was filtered through Whatman filter paper No.1 and concentrated under reduced pressure using vacuum at 44 ± 100C in a rotavapor (IKA ® RB 10 Rota Evaporator, India) The extract was stored at 220C in a seeded air tight container.

The percentage of extract yield was calculated by using the formula

$$\%\ of\ extract\ yield = \frac{weight\ in\ gm\ of\ extract\ obtained}{weight\ in\ gm\ of\ plant\ material\ taken} \times 100$$

Preliminary Phytochemical Studies

The hydroalcoholic extracts of the powdered drugs were subjected to various qualitative tests for the identification of plant constituents.

Dragendorff's Test: -To 2-3 ml of the extract, few drops of Dragendorff's reagent (Potassium bismuth iodide solution) was added. An orange-brown precipitate indicated the presence of alkaloids.

Mayer's Test: -To 2-3 ml of the extract, few drops of Mayer's reagent (Potassium mercuric iodide solution) was added. Whitish yellow or cream-colored precipitate indicated the presence of alkaloids.

Hager's Test: -To 2-3 ml of the extract, few drops of Hager's reagent (Saturated aqueous solution of picric acid) was added, yellow colored precipitate indicated the presence of alkaloids.

Wagner's Test: -To 2-3 ml of the extract, few drops of Wagner's reagent (Iodine in Potassium Iodide) was added, Formation of reddish-brown precipitate indicated the presence of alkaloids

Test for Carbohydrates

Molisch's Test: -To 2-3 ml of the extract, few drops of □-naphthol solution in alcohol were added, shaken and concentrated sulphuric acid was added through the side of the test tube. Violet color ring was formed at the junction of the two liquids reveals the presence of Carbohydrates.

Results:

Table 1: Body Weight Changes

Groups	Day 0 (g)	Day 7 (g)	Day 14 (g)	Day 21 (g)	Day 28 (g)
Normal Control	182.5 ± 4.2	186.8 ± 4.5	191.4 ± 4.8	195.7 ± 5.1	201.3 ± 5.4
Diabetic Control (STZ)	183.1 ± 4.6	175.6 ± 4.3	168.2 ± 4.0	160.7 ± 3.8	154.6 ± 3.5***
STZ + Cleome viscosa 200 mg/kg	182.8 ± 4.3	178.9 ± 4.2	176.5 ± 4.4	180.6 ± 4.6	185.2 ± 4.7**
STZ + Cleome viscosa 400 mg/kg	183.4 ± 4.5	180.7 ± 4.3	182.9 ± 4.5	188.6 ± 4.8	194.1 ± 5.0***
STZ + Metformin (150 mg/kg)	182.9 ± 4.4	183.8 ± 4.5	188.9 ± 4.7	194.3 ± 5.0	199.2 ± 5.3***

Body weight was recorded on Days 0, 7, 14, 21, and 28. Streptozotocin (STZ)-induced diabetic rats showed a significant reduction in body weight throughout the experimental period compared to the normal control group ($p < 0.001$), indicating severe metabolic disturbances associated with diabetes. Oral administration of the ethanolic extract of Cleome viscosa produced a dose-dependent improvement in body weight. Rats treated with the higher dose of the extract exhibited a significant increase in body weight compared to the diabetic control group ($p < 0.01$), suggesting improved glucose utilization and reduced protein catabolism. The standard drug-treated group (Metformin, 150 mg/kg, p.o.) demonstrated the greatest recovery in body weight, approaching normal values by the end of the study.

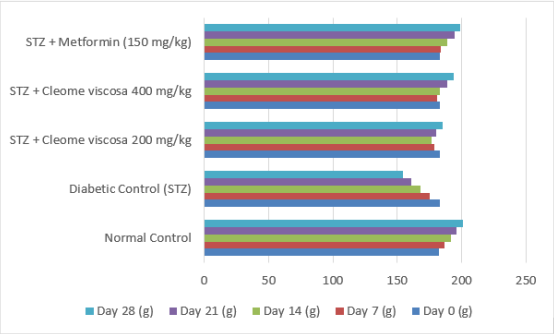

Table 2: Oral Glucose Tolerance Test (OGTT)

Group	0 min (mg/dL)	30 min (mg/dL)	60 min (mg/dL)	90 min (mg/dL)	120 min (mg/dL)
Normal Control	88.6 ± 3.2	132.4 ± 4.8	118.3 ± 4.5	102.6 ± 3.9	90.4 ± 3.3
Diabetic Control (STZ)	248.5 ± 8.4	334.8 ± 10.6	362.7 ± 11.8	341.5 ± 10.9	316.2 ± 9.8***
STZ + Cleome viscosa (200 mg/kg)	242.7 ± 7.9	305.6 ± 9.8	298.9 ± 9.2*	270.4 ± 8.5*	236.8 ± 7.6**
STZ + Cleome viscosa (400 mg/kg)	241.9 ± 8.1	286.3 ± 9.1	256.8 ± 8.3**	214.7 ± 7.0**	178.5 ± 6.2***
STZ + Metformin (150 mg/kg)	239.8 ± 7.8	252.6 ± 8.0	210.4 ± 6.8***	158.2 ± 5.4***	122.9 ± 4.1***

The Oral Glucose Tolerance Test (OGTT) demonstrated that streptozotocin (STZ)-induced diabetic rats exhibited significantly impaired glucose tolerance compared with the normal control group. Following oral glucose administration (2 g/kg), blood glucose levels in the diabetic control group increased markedly, reaching a peak at 60 minutes and remaining significantly elevated up to 120 minutes ($p < 0.001$). Treatment with the ethanolic extract of Cleome viscosa produced a dose-dependent improvement in glucose tolerance. Rats treated with 200 mg/kg of the extract showed a moderate reduction in blood glucose levels at 60, 90, and 120 minutes compared with the diabetic control group ($p < 0.05$), whereas the 400 mg/kg dose produced a more pronounced reduction ($p < 0.01$). The standard drug, Metformin (150 mg/kg), exhibited the greatest improvement in glucose tolerance, with blood glucose levels approaching those of the normal control group by the end of the observation period. These findings indicate that the ethanolic extract of Cleome viscosa enhances glucose utilization and effectively improves glucose tolerance in STZ-induced diabetic rats.

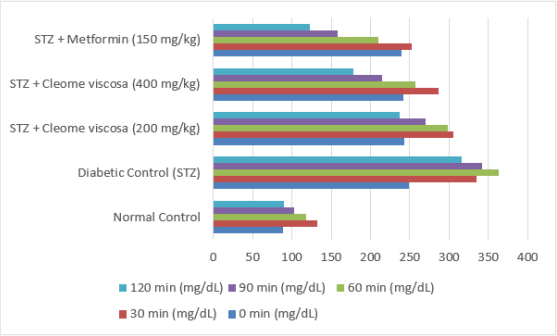

Table 3: Serum Lipid Profile

Groups	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
Normal Control	82.4 ± 3.1	76.8 ± 2.9	46.5 ± 1.8	20.5 ± 1.2	15.4 ± 0.6
Diabetic Control (STZ)	186.3 ± 5.8***	168.5 ± 5.2***	24.6 ± 1.1***	128.0 ± 4.3***	33.7 ± 1.0***
STZ + Cleome viscosa (200 mg/kg)	148.2 ± 4.9**	136.7 ± 4.6**	32.8 ± 1.4*	88.1 ± 3.2**	27.3 ± 0.9**
STZ + Cleome viscosa (400 mg/kg)	112.6 ± 3.8***	102.4 ± 3.5***	40.2 ± 1.6***	51.9 ± 2.1***	20.5 ± 0.7***
STZ + Metformin (150 mg/kg)	90.8 ± 3.2***	82.6 ± 3.0***	44.1 ± 1.7***	30.2 ± 1.4***	16.5 ± 0.6***

The serum lipid profile revealed that streptozotocin (STZ)-induced diabetic rats exhibited a significant increase in total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) levels, along with a marked decrease in high-density lipoprotein (HDL) levels compared with the normal control group ($p < 0.001$). Treatment with the ethanolic extract of Cleome viscosa significantly improved the lipid profile in a dose-dependent manner. Rats treated with the extract at 200 mg/kg showed a moderate reduction in TC, TG, LDL, and VLDL levels with a corresponding increase in HDL levels ($p < 0.05$). The 400 mg/kg dose produced a more pronounced hypolipidemic effect ($p < 0.01$–0.001), with lipid values approaching those of the standard drug-treated group. Metformin (150 mg/kg) produced the greatest improvement in serum lipid parameters, restoring them close to normal values. These findings indicate that the ethanolic extract of Cleome viscosa effectively ameliorates diabetes-induced dyslipidemia and improves lipid metabolism.

Table 4: Blood Urea Nitrogen (BUN) and Glycated Hemoglobin (HbA1c)

Groups	BUN (mg/dL)	HbA1c (%)
Normal Control	18.6 ± 0.8	4.8 ± 0.2
Diabetic Control (STZ)	43.8 ± 1.5***	10.9 ± 0.4***
STZ + Cleome viscosa (200 mg/kg)	33.4 ± 1.2**	8.2 ± 0.3**
STZ + Cleome viscosa (400 mg/kg)	24.5 ± 1.0***	6.1 ± 0.2***
STZ + Metformin (150 mg/kg)	20.3 ± 0.9***	5.2 ± 0.2***

The estimation of blood urea nitrogen (BUN) and glycated hemoglobin (HbA1c) demonstrated significant alterations in streptozotocin (STZ)-induced diabetic rats. The diabetic control

group exhibited a marked elevation in serum BUN and HbA1c levels compared with the normal control group ($p < 0.001$), indicating impaired renal function and poor long-term glycemic control. Treatment with the ethanolic extract of Cleome viscosa produced a dose-dependent reduction in both BUN and HbA1c levels. Rats treated with the extract at 200 mg/kg showed a moderate improvement ($p < 0.05–0.01$), whereas the 400 mg/kg dose significantly decreased BUN and HbA1c levels ($p < 0.001$) compared with the diabetic control group. The standard drug, Metformin (150 mg/kg), produced the maximum reduction in these parameters, with values approaching those of the normal control group. These findings suggest that the ethanolic extract of Cleome viscosa possesses significant anti-diabetic activity by improving long-term glycemic control and protecting against diabetes-associated renal dysfunction.

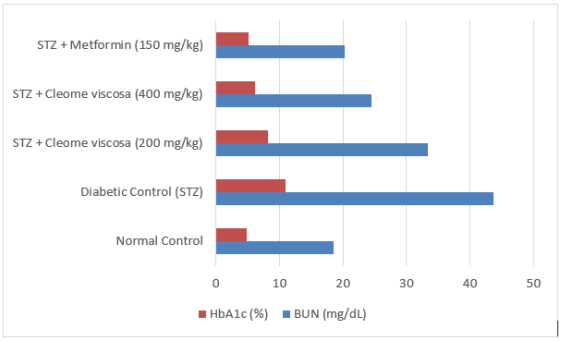

Table 5: Antioxidant Parameters

Groups	SOD (U/mg protein)	CAT (U/mg protein)	GSH (µmol/mg protein)	MDA (nmol/mg protein)
Normal Control	12.8 ± 0.4	58.6 ± 1.8	8.6 ± 0.3	1.8 ± 0.1
Diabetic Control (STZ)	5.3 ± 0.2***	28.4 ± 1.1***	3.2 ± 0.2***	5.9 ± 0.2***
STZ + Cleome viscosa (200 mg/kg)	8.1 ± 0.3**	41.8 ± 1.4**	5.6 ± 0.2**	3.8 ± 0.2**
STZ + Cleome viscosa (400 mg/kg)	10.9 ± 0.4***	52.3 ± 1.7***	7.4 ± 0.3***	2.4 ± 0.1***
STZ + Metformin (150 mg/kg)	12.2 ± 0.4***	56.4 ± 1.8***	8.2 ± 0.3***	2.0 ± 0.1***

The antioxidant status of pancreatic tissue was assessed by estimating superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and malondialdehyde (MDA) levels. Streptozotocin (STZ)-induced diabetic rats showed a significant decrease in the activities of endogenous antioxidant enzymes SOD, CAT, and GSH, accompanied by a marked increase in MDA levels compared with the normal control group ($p < 0.001$), indicating severe oxidative stress and lipid peroxidation in pancreatic tissue. Treatment with the ethanolic extract of Cleome viscosa significantly restored the antioxidant defense system in a dose-dependent manner.

DISCUSSION:

Diabetes mellitus is one of the most prevalent metabolic disorders worldwide and is characterized by chronic hyperglycemia resulting from impaired insulin secretion, defective insulin action, or both. Persistent hyperglycemia leads to disturbances in carbohydrate, lipid, and protein metabolism and is associated with the development of several complications, including nephropathy, neuropathy, retinopathy, cardiovascular disease, and pancreatic dysfunction. Streptozotocin (STZ) is widely used to induce experimental diabetes because of its selective toxicity toward pancreatic β-cells. STZ enters β-cells through the GLUT-2 transporter and causes DNA alkylation, activation of poly (ADP-ribose) polymerase (PARP), depletion of intracellular NAD^+ and ATP, excessive production of reactive oxygen species (ROS), and ultimately β-cell necrosis. The resulting insulin deficiency leads to sustained hyperglycemia, oxidative stress, and metabolic abnormalities. Therefore, the STZ-induced diabetic rat model closely resembles human diabetes and is considered suitable for evaluating the anti-diabetic potential of medicinal plants.In the present investigation, administration of STZ successfully induced diabetes in rats, as evidenced by significantly elevated fasting blood glucose levels. Treatment with the ethanolic extract of Cleome viscosa produced a marked and dose-dependent reduction in blood glucose concentration throughout the experimental period. The higher dose of the extract (400 mg/kg) demonstrated greater glucose-lowering activity and produced results comparable to those observed with the standard drug metformin. The antihyperglycemic activity of Cleome viscosa may be attributed to its rich phytochemical composition, including flavonoids, phenolic compounds, alkaloids, saponins, terpenoids, tannins, and glycosides. Flavonoids have been reported to stimulate insulin secretion from surviving pancreatic β-cells, enhance glucose uptake by peripheral tissues through increased GLUT-4 translocation, improve insulin receptor sensitivity, inhibit intestinal α-glucosidase and α-amylase enzymes, and reduce hepatic gluconeogenesis. Phenolic compounds possess potent antioxidant properties that protect pancreatic β-cells from

oxidative injury and preserve their insulin-secretory function. The combined action of these bioactive compounds may explain the significant reduction in hyperglycemia observed in the extract-treated groups.Body weight is an important physiological parameter in experimental diabetes because insulin deficiency causes increased breakdown of muscle proteins and adipose tissue to meet energy requirements. Consequently, diabetic animals exhibit progressive body weight loss due to enhanced protein catabolism, dehydration, reduced tissue protein synthesis, and impaired glucose utilization. In the present study, STZ-induced diabetic rats showed a significant decline in body weight throughout the experimental period. Administration of the ethanolic extract of Cleome viscosa significantly prevented body weight loss and gradually restored body weight toward normal values in a dose-dependent manner. This improvement may be associated with enhanced insulin action, improved glucose utilization by peripheral tissues, restoration of protein metabolism, increased glycogen synthesis, and reduction in muscle protein degradation. Preservation of body weight also indicates improved nutritional status and overall metabolic recovery following treatment with the plant extract.

CONCLUSION:

The present study demonstrated that the ethanolic extract of Cleome viscosa possesses significant anti-diabetic activity in streptozotocin (STZ)-induced diabetic rats. Administration of STZ produced characteristic diabetic changes, including elevated blood glucose levels, impaired glucose tolerance, reduction in body weight, dyslipidemia, increased HbA1c and BUN levels, and marked oxidative stress in pancreatic tissue. Treatment with the ethanolic extract of Cleome viscosa significantly attenuated these alterations in a dose-dependent manner. The extract effectively reduced fasting blood glucose levels and improved oral glucose tolerance, indicating enhanced glucose utilization and improved insulin sensitivity. The restoration of body weight in treated animals suggests improved metabolic regulation and prevention of diabetes-induced protein and lipid catabolism. Furthermore, the extract significantly improved serum lipid abnormalities by reducing total cholesterol, triglycerides, LDL, and VLDL levels while increasing HDL cholesterol levels, demonstrating its hypolipidemic potential.The significant reduction in HbA1c levels indicates improved long-term glycemic control, whereas decreased BUN levels suggest a protective effect against diabetes-associated renal dysfunction. The ethanolic extract also exhibited strong antioxidant activity by enhancing pancreatic antioxidant defenses, as evidenced by increased SOD, CAT, and GSH levels and reduced MDA concentration. This indicates that Cleome viscosa protects pancreatic tissue against oxidative damage and lipid peroxidation associated with diabetes. The observed pharmacological effects may be attributed to the presence of bioactive phytoconstituents such as flavonoids, phenolic compounds, alkaloids, terpenoids, tannins, and saponins, which possess antihyperglycemic, antioxidant, and lipid-regulating properties. The higher dose of the extract (400 mg/kg) showed greater therapeutic efficacy and produced effects comparable to the standard drug metformin.In conclusion, the ethanolic extract of Cleome viscosa exhibits promising anti-diabetic, hypolipidemic, antioxidant, and protective effects against STZ-induced metabolic disturbances. These findings support the traditional medicinal use of Cleome viscosa and suggest its potential as a natural therapeutic agent for the management of diabetes mellitus and its associated complications. Further studies involving isolation of active compounds, molecular mechanism evaluation, and clinical investigations are required to establish its therapeutic application.

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