



Achyranthes Aspera Root Extract Attenuates the Damage Caused by High Fat Diet and Streptozotocin-Induced Diabetes in Wistar Rats

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Abstract: *Achyranthes aspera* is an herb found in the Indian subcontinent and has been used for decades because of its traditional anti-diabetic and anti-obesity properties. Since studies are not reported on *Achyranthes aspera* protection in high-fat diet and diabetes-induced animal models, our aim was to investigate the protective effect of root extract of *Achyranthes aspera* on the combined effect of high-fat diet and streptozotocin-induced biochemical changes in Wistar rats. To achieve this aim, the objectives of the study were to estimate the body weight, serum glucose, insulin, Glycated hemoglobin (HbA1c), Homeostatic Model Assessment of Insulin Resistance (HOMA- IR), serum lipid profile, and liver glycogen among the Wistar rats which were divided into 6 groups having 6 rats in each group. Group 1 - control rats Group 2 - diabetic group rats, Group 3 – HFD diabetic rats and the rats from groups 4 to 6 were given a high-fat diet+ Streptozotocin 40 mg/kg + a low dose of root extract of *Achyranthes aspera* (250 mg/kg), high dose of root extract of *Achyranthes aspera* (500 mg/kg), metformin (250 mg/kg), respectively treated for 35 days. Body weight followed by serum glucose, insulin, HbA1c, HOMA- IR, serum lipid profile, and liver glycogen were evaluated. HFD + Diabetic group showed an elevated level of lipid profile and alterations in serum glucose, HbA1c, HOMA- IR, Insulin and liver glycogen. Administration of Metformin and hydro alcoholic root extract of *Achyranthes aspera* 500 mg/kg to HFD + diabetic group protected the biochemical alterations and serum insulin, glucose levels, HbA1c, HOMA- IR, liver glycogen. In comparison with HFD group, there was 1.76, 2.02, and, 1.3-fold decrease in Glucose levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively. In comparison with HFD group, there was a 1.38, 1.15 and, 1.59-fold increase in Insulin levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively. The HbA1c levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 7.36±0.22, 10.18±0.74, 8.94±0.33, 8.10±0.22, 8.94±0.22 and 7.0±0.41 respectively. The HOMA-IR levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 2.08±0.12, 3.99±0.85, 1.70±0.53, 1.61±0.28, 2.46±0.74 and 2.01±0.20 respectively. The study findings reveal the protective role of *Achyranthes aspera* on high-fat diet and a diabetic induced biochemical changes.

Key words: *Achyranthes aspera*, HEAA, Lipid profile, HbA1c, HOMA- IR, Diabetes mellitus, Rats

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1. INTRODUCTION

Diabetes is rapidly becoming a serious global health issue, with the number of diabetics expected to reach 380 million by 2025. Diabetes mellitus is on the rise around the world, with substantial social, health, and economic consequences. Diabetes inhibits a person's capacity to regulate blood glucose levels, resulting in a variety of minor and serious complications. The development of diabetes can be caused by two factors: Advanced age and obesity¹. Genetic factors, nutritional conditions, and a sedentary lifestyle are risk factors. One of the main risk factors for the onset of atherosclerotic heart disease in diabetic individuals is hyperlipidemia. Chronic hyperglycemia caused by diabetes is connected to organ damage, dysfunction, and failure, including the eyes, kidneys, nerves, heart, and blood vessels. The severity of the underlying metabolic process and therapy determines the degree of hyperglycemia. Over the last three decades, a significant increase in obesity and type 2 diabetes prevalence has been accounted for globally. The cause of diabetes is linked to a network of genetic and epigenetic predispositions which interact with sociocultural features³. A well-designed global diabetes study, such as ICMR-INDIAB study provides an indication of diabetes across the country. This study proved diabetes prevalence and also pre-diabetes and metabolic syndrome⁴. Epidemiological studies have revealed the role of impaired microcirculation in individuals with diabetes and the Aetiopathogenesis of cardiovascular disease over the last few decades. The above research has enhanced the available evidence in support of systemic microvascular activity monitoring and encouraged the start of investigations by redefining the existing understanding of the vascular disease, particularly in diabetics⁵. Type 2 diabetes is a diverse range of diseases marked by insulin resistance and decreased insulin production. Type 2 diabetes in animals is also diverse and complex, like a human disease. Animal models are important in developing potential treatments for diabetes mellitus in humans⁶. In particular, Glucagon-like peptide 1 (GLP1) agonists (incretins) are favorable, except for semaglutide, which has been associated with an increased risk of diabetic retinopathy⁷. Ayurveda is a traditional branch of Indian medicine that focuses on using plants and plant-based products. The medicinal components found in plants are used in this conventional type of medicine to alleviate illness. Many believe those plant products are less harmful and have fewer adverse effects than manufactured ones. Among the recent research projects, is the anti-diabetic properties of *Achyranthes aspera* (AA). AA is an herb found in the Indian subcontinent and has been used for decades because of its traditional properties. It also has been used in Ayurveda for vomiting, piles, dysentery, diabetes, obesity, blood disease, and other chronic diseases. Ayurvedic practitioners have always used the whole plant of *Achyranthes aspera* to manage diabetes⁸. A. A has been considered for anti-diabetic and anti-obesity properties. There's no literature reported on *Achyranthes aspera* protection in HFD and diabetes-induced animal models, which we investigated in the present study. Therefore, the present study aims to evaluate the therapeutic potential of ethanolic extract of *Achyranthes aspera* root extract in male Wistar rats induced with high-fat diet and STZ through biochemical investigations.

2. MATERIALS AND METHODS

2.1. Plant collection and Authentication

The *Achyranthes aspera* root parts were collected from the

field. The Botanical identification and authentication were performed by qualified botanists and a specimen was deposited in the herbarium (Voucher No: 57403).

2.2. Extraction

1litre of ethanol (95% v/v) was used to immerse 100 g of root parts of the *Achyranthes aspera* for one month. The contents were filtered using a muslin cloth., Concentrated using a rotary evaporator followed by lyophilization. The dried material was stored at 4 °C. (yield percentage)

2.3. Animals

The studies were carried out as per the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines and after approval of the Institutional Animal Ethics Committee inhSaveetha Medical College's Centre for Laboratory and Animal Research (CLAR) (SU/CLAR/RD/002/2021). For this study, three-month-old male albino Wistar rats weighing between 150 and 200 g were procured from the institutional animal house. The animals were acclimatized to animal house facilities for one week and sustained under standard conditions (temperature 25 ± 2 °C, 12-h light: 12-h dark cycle) during the experimental period.

2.4. Experimental Groups

Streptozotocin was given intraperitoneally at a dose of 40 mg/kg for 5 weeks as diabetes-induced hyperglycemia, and Vanaspati + coconut oil (3:2) at a dose of 0.5mL/kg.bw for 28days as high-fat diet-induced hyperlipidemia. A low dose of *Achyranthes aspera* root hydroalcoholic extract was orally given at a dose of 250 mg/kg for five weeks, and a high dose (500 mg/kg) of *Achyranthes aspera* root extract was likewise orally administered for five weeks. The therapeutic doses were given after Streptozotocin and a high-fat diet was administered. In this experiment, thirty-six male Wistar albino rats were employed. Six groups of animals were used (6 rats each). The rats in Group 1 were used as a control group; instead of a high-fat diet, 0.5 mL/kg of normal saline was administered orally. The rats in Group 2 were provided with a single dose of Streptozotocin 40 mg/kg, intraperitoneally. The rats in Group 3 were given a high-fat diet and a single dose of Streptozotocin 40 mg/kg intraperitoneally to induce diabetes and the rats from groups 4 to 6 were given a high-fat diet+ Streptozotocin 40 mg/kg + a low dose of root extract of *Achyranthes aspera* (250 mg/kg), high dose of root extract of *Achyranthes aspera* (500 mg/kg), metformin (250 mg/kg), respectively.

2.5. Sample preparation

On the 36th day, the animals were anaesthetized with isoflurane (24hr after the last administration). Blood was collected in vacutainer tubes without anticoagulant from retroorbital puncture. It was allowed to coagulate for 20 minutes before being centrifuged at 3000 rpm at 4°C to separate the serum. For subsequent usage, the serum was collected and stored at -80°C.

2.6. *Achyranthes aspera* - Root hydro alcoholic extract

The *Achyranthes aspera* root parts were collected from the field. The Botanical identification and authentication were

performed by a qualified botanists Examination of body weight: The body weight of rats from each group was measured in the initial stage for 28 days. Weight was measured using standard digital weight balance to get accuracy.

2.7. Biochemical analysis

Total cholesterol (TC), Triglycerides (TG), and high-density lipoproteins (HDL) were estimated by semi-autoanalyzer (ROBONIK) using a diagnostic reagent kit (Aspen Laboratories, Delhi). Cholesterol concentration⁹, Triglyceride content¹⁰, and HDL values¹¹ expressed as mg/dl plasma. Very low-density lipoproteins (VLDL) = Triglycerides (mg/dl) 5. A biochemical test (Crest Biosystems) was used to quantify glycated hemoglobin, whereas an ELISA kit was used

to detect serum insulin. (Image courtesy of Enzo Diagnostics.) An ELISA (BIORAD) at 450 nm was used to measure the quantity of serum insulin. An alkali technique was used to assess liver glycogen levels (Stetten&Katzen, 1961). The insulin resistance was measured by HOMA-IR by the following formula: $HOMA-IR = \frac{\text{Fasting plasma glucose (mg/dl)} \times \text{Fasting plasma insulin } (\mu\text{IU/ml})}{405}$

2.8. Statistical analysis

The results were presented as Mean \pm SEM for six animals in each group for each parameter. The statistical comparison was made by using SPSS software. A significant variation was observed, and mean values were related using one-way ANOVA. A p-value less than 0.05 were meant statistically significant.

3. RESULTS AND DISCUSSION

Table 1: Effect of HEAA extract on serum Glucose, Insulin, Liver Glycogen Level

S. No	Parameters	control	STZ	HFD+STZ	HFD+STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
1.	Glucose	86.0 \pm 7.9	291.1 \pm 46.7	523.1 \pm 38.9	152.7 \pm 12.4	258.5 \pm 14.1	115.7 \pm 20.4	P=0.0004
2.	Insulin	29.0 \pm 0.9	17.4 \pm 2.9	17.6 \pm 1.7	524.4 \pm 1.7	20.4 \pm 2.0	28.0 \pm 1.6	P=0.0002
3.	Liver Glycogen	37.3 \pm 0.6	26.1 \pm 1.4	29.7 \pm 2.1	36.7 \pm 2.2	20.32 \pm 2.5	38.6 \pm 1.4	P=0.0004

HEAA: Hydroethanolic extract of *Achyranthesaspera*, HFD: High fat diet, STZ:streptozotocin

The Glucose levels (mean \pm SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 86.0 \pm 7.9, 291.1 \pm 46.7, 523.1 \pm 38.9, 152.7 \pm 12.4, 258.5 \pm 14.1 and 115.7 \pm 20.4 mg/dl respectively. The glucose levels of HFD group increased by 6.08 fold as compared with control, and these changes are beyond the reference range of rat species. However, in HFD+HEAA treated groups, the increase in the glucose level was less than the HFD group. In comparison with HFD group, there was 1.76, 2.02, and 1.3-fold decrease in Glucose levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively. The Insulin levels (mean \pm SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 29.0 \pm 0.9, 17.4 \pm 2.9, 17.6 \pm 1.7, 524.4 \pm 1.7, 20.4 \pm 2.0, and 28.0 \pm 1.6 μ U/ml respectively. The insulin levels of HFD group decreased by 1.64 fold as compared with control, and these changes are

beyond the reference range of rat species. However, in HFD+HEAA treated groups, the increase in the insulin level was more than the HFD group. In comparison with HFD group, there was 1.38, 1.15 and 1.59-fold increase in Insulin levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively. The Glycogen levels (mean \pm SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 37.3 \pm 0.6, 26.1 \pm 1.4, 29.7 \pm 2.1, 36.7 \pm 2.2, 20.32 \pm 2.5, and 38.6 \pm 1.4 mg/100g respectively. The Glycogen levels of HFD group decreased by 1.25 fold as compared with the control, and these changes are beyond the reference range of rat species. However, in HFD+HEAA treated groups, the increase in the glycogen level was more than the HFD group. In comparison with HFD group, there was 1.23, 1.08 and 1.29-fold increase in Glycogen levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively.

Table 2: Changes in levels of Glycosylated Hemoglobin and changes in Body weight of normal and experimental animals.

S. No	Parameters	control	STZ	HFD+STZ	HFD+ STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
1	Body weight (g)Initial	192.00	201.72 \pm 12.12	212.34 \pm 10.21	192.452 \pm 10.14	198.72 \pm 15.12	204.24 \pm 10.12	P=0.0003
2	Body weight (g)Final	215.21	182.42 \pm 8.12	202.12 \pm 12.42	212.412 \pm 11.45	207.23 \pm 14.23	208.32 \pm 12.28	P=0.0004
3	Glycosylated hemoglobin (%)	7.36 \pm 0.22	10.18 \pm 0.74	8.94 \pm 0.33	8.10 \pm 0.22	8.94 \pm 0.22	7.0 \pm 0.41	P=0.0007

The HbA1C levels (mean \pm SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 7.36 \pm 0.22, 10.18 \pm 0.74, 8.94 \pm 0.33, 8.10 \pm 0.22, 8.94 \pm 0.22 and 7.0 \pm 0.41 respectively. The HbA1C levels of the HFD group increased by 1.21 fold as compared with the control, and these changes are beyond the reference range of rat species. In comparison with the HFD group, there was 1.1, 1 and

1.27-fold decrease in HbA1C levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively. The body weight of diabetic rats significantly decreased when compared with the control group. Supplementation of hydroalcoholic root extracts of *Achyranthesaspera* showed a significant improvement in the body weight of diabetic rats.

Table3: Effect of HEAA extract on HOMA- IR levels

S. No	Parameters	Control	STZ	HFD+STZ	HFD+ STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
I.	HOMA- IR	2.08±0.12	3.99±0.85	17.05±3.53	1.61±0.28	2.46±0.74	2.01±0.20	P=0.0008

HEAA: Hydroalcoholic extract of *Achyranthesaspera*, HFD: High fat diet, STZ: streptozotocin, HbA1C: Glycosylated haemoglobin, HOMA-IR: Homeostasis modal assessment estimated insulin resistance

The HOMA-IR levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 2.08±0.12, 3.99±0.85, 17.05±3.53, 1.61±0.28, 2.46±0.74 and 2.01±0.20 respectively. The HOMA- IR levels of the HFD group increased by 8.19 fold as compared with the control, and

these changes are beyond the reference range of rat species. In comparison with the HFD group, there was 10.5, 6.93 and 8.48-fold decrease in HOMA-IR levels in HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 groups respectively.

Table 4: Effect of HEAA extract on Cholesterol

S. No	Parameters	Control	STZ	HFD+STZ	HFD+ STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
I.	Cholesterol	66.20±5.65	245.80±59.8	147.00±14.9	95.6±16.98	165.74±38.11	72.00±18.54	P=0.0004

The Cholesterol levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 66.20±5.65, 245.80±59.8, 147.00±14.9, 95.6±16.98, 165.74±38.11 and 72.00±18.54 mg/dl respectively. The Cholesterol levels of HFD group increased by 4.08fold as compared with the control, and these changes are beyond the reference range of rat species. However, in

HFD+HEAA treated groups, the increase in the Cholesterol level is less than the HFD group. In comparison with HFD group, there were 1.53 ,2.04-fold decrease in Cholesterol levels in HFD+STZ+ Metformin, and HFD+STZ+HEAA500 groups respectively. However, in HFD+STZ+HEAA250 treated group, the increase in the cholesterol level 1.12 fold more than in the HFD group.

Table 5: Effect of HEAA extract on Triglycerides

S. No	Parameters	Control	STZ	HFD+STZ	HFD+STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
I.	Triglycerides	70.46±8.23	275.82±72.87	132.00±25.33	112.20±22.53	208.94±64.91	75.31±24.41	P=0.008

The Triglycerides levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 70.46±8.23, 275.82±72.87, 132.00±25.33, 112.20±22.53, 208.94±64.91 and 75.31±24.41 mg/dl respectively. The Triglyceride levels of the HFD group increased by 1.88 fold as compared with control, and these changes are beyond the reference range of rat species.

However, in HFD+HEAA treated groups, the increase in the Triglycerides level is less than the HFD group. In comparison with HFD group, there was 1.08 ,1.76-fold decrease in Triglyceride levels in HFD+STZ+ Metformin, and HFD+STZ+HEAA500 groups respectively. However, in HFD+STZ+HEAA250 treated group, the increase in the Triglyceride level 1.57 fold more than the HFD group.

Table 6: Effect of HEAA extract on LDL

S. No	Parameters	Control	STZ	HFD+STZ	HFD+ STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
I.	LDL	110.80±6.50	89.22±13.05	124.28±6.36	104.40±14.96	93.38±24.24	86.36±13.26	P=0.330

The LDL levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 110.80±6.50, 89.22±13.05, 124.28±6.36, 104.40±14.96, 93.38±24.24 and 86.36±13.26 mg/dl respectively. The LDL levels of the HFD group increased by 1.88 fold as compared with the control, and these changes are beyond the reference range of rat

species. However, in HFD+HEAA treated groups, the increase in the LDL level less than the HFD group. In comparison with HFD group, there was 1.19 ,1.44-fold decrease in LDL levels in HFD+STZ+ Metformin, and HFD+STZ+HEAA500 groups respectively. However, in HFD+STZ+HEAA250 treated group, the increase in the LDL level 1.33 fold less than the HFD group.

Table 7: Effect of HEAA extract on HDL

S. No	Parameters	Control	STZ	HFD+STZ	HFD+ STZ +Metformin	HFD+STZ +HEAA250	HFD+STZ +HEAA500	Pvalue
I	HDL	46.02±1.06	33.12±3.95	38.67±2.58	35.61±1.47	36.12±1.67	41.51±2.40	P=0.012

The HDL levels (mean±SEM) of control, STZ, HFD+STZ, HFD+STZ+ Metformin, HFD+STZ+HEAA250, and HFD+STZ+HEAA500 were 46.02±1.06, 33.12±3.95, 38.67±2.58, 35.61±1.47, 36.12±1.67 and 41.51±2.40 mg/dl respectively. The HDL levels of the HFD group decreased by 1.21 fold as compared with the control, and these changes

are beyond the reference range of rat species. However, in HFD+HEAA treated groups, the increase in the HDL level is more than in the HFD group. In comparison with the HFD group, there was a 1.07-fold increase in HDL levels in the HFD+STZ+HEAA500 group. However, in HFD+STZ+ Metformin, and HFD+STZ+HEAA250 treated groups, the

increase in the HDL level was 1.08, 1.07 fold less than the HFD group. Metformin is an oral hypoglycemic drug. Metformin reduces chronic inflammation by lowering blood sugar levels, insulin resistance, and atherogenic dyslipidemia¹². Because of metformin's remarkable overall effectiveness profile, it would be contradictory to reject metformin to the vast majority of patients with long-term diabetes¹³. The anti-diabetic effect of the ethanolic leaves extract of *Achyranthes aspera* was studied in Streptozotocin-induced diabetic rats. 14 The most important findings of this study are that in streptozotocin-induced diabetics rats, at a dose of 500 mg/kg body weight for 15 days, an aqueous leaves extract of MK, PG, and CR had a favorable effect on blood glucose, body weight, glucose and ketone levels in urine, and pancreas tissue. (Catharanthus roseus, CR; Murrayakoenigii, MK; Psidium guajava, PG) The body weight was significantly lower in high doses of HEAA treatment rats. The weight reduction in HEAA-treated rats was similar to that of metformin-treated rats. The delayed body weight improvement was noted in the HEAA (250mg) dose group. Trigonelline might have an anti-diabetic effect in this study, as revealed by the results of the OGTT and liver glycogen content. In HFD-fed STZ-induced diabetic rats, Trigonelline has an insulin-sensitizing effect, as evidenced by HOMA-IR and plasma insulin levels. (Subramanian et al., 2014). The high dose of EAA (500 mg/kg) treated rats decreased glycogen content in the liver. In diabetic rats, *A. aspera* L. at a dose of 500mg/Kg resulted in a significant (P<0.05) decrease in blood sugar and glycosylated hemoglobin levels¹⁵. Animals treated with HEAA (500 mg/kg) show a significant reduction in blood sugar and HbA1C (Glycosylated hemoglobin). The effects of processing the *Achyranthes aspera* Linn plant into an herbal tea on blood glucose and blood lipids were studied in alloxan-induced diabetic rats. There was a considerable decrease in serum triglycerides, but no effect on HDL or LDL cholesterol¹⁶. When compared to high-fat diet control (HFDC) rats, saponin extract of *A. aspera* (SAA) considerably lowered serum TC, TG, VLDL-C, and LDL-C levels while significantly increasing serum HDL-C levels¹. The HEAA 500 mg/kg significantly reduced serum lipid profile and lipoprotein. In streptozotocin-induced diabetic rats, Ethyl acetate fraction of hydroalcoholic extract of *Achyranthes aspera* Linn. (HEAA) treatment causes a hypoglycemic effect by improving serum Insulin and GLUT2 levels, which enhances cell activity. Finally, the results of this investigation show that *Achyranthes aspera* may have a protective effect against STZ-induced hyperglycemia¹⁸. The animals treated with a high dose of HEAA (500 mg/kg) showed a reduced level of glucose values proving its anti-diabetic properties. The findings suggest that water-soluble polysaccharide from roots of *Coptis Chinensis* (CCPW-I) has comprehensive and effective anti-diabetic and antioxidant action in diabetic mice. As a result, we are hopeful that CCPW-I will be used as a primary consideration medicine in the treatment of diabetes in the coming years¹⁹. The lowest dose of cinnamon extract (200 mg/kg bw) was shown to be the most effective in decreasing FBG and cholesterol indices in rats in our experiment²⁰. The purification of the most active phytochemical against hyperglycemia can be done using the most effective plant, *Rhazya stricta* leaves, and primarily its

ethyl acetate fraction²¹. The findings of this study suggested that *Galega officinalis* could be useful in the treatment of diabetes and the reduction of FBS by improving insulin serum levels and preventing kidney tissue damage due to its antioxidant properties²². After solidoside administration, lipid peroxidation products such as MDA levels in the kidney and liver of diabetic mice were significantly lowered²³. The seeds, roots, and shoots of *Achyranthes aspera* are the most important components that are administered medicinally in traditional systems of medicine. Carbohydrates, protein, glycosides, alkaloids, tannins, saponins, flavonoids, lignin, and other chemical components have been among the most important²⁴. According to previous studies, *Achyranthes aspera* extracts, both aqueous and ethanol, show considerable wound healing and antioxidant activities²⁵. Methanolic extracts were shown to have better concentrations of phytoactive chemicals than chloroformic extracts in this analysis of phytochemical evaluation of flower, leaf, and root extracts of *Achyranthes aspera*²⁶. They suggest that if properly prepared, *A. aspera* seed saponins could be administered as significant hypolipidemic medications with antioxidant and hepatoprotective effects²⁷. The hyperlipidemic and hypercholesteremic symptoms were decreased when atherogenic feed was provided with *Achyranthes aspera*. *Achyranthes aspera* would seem to reduce hypercholesterolemia by promoting endogenous cholesterol transformation to bile acid and lowering exogenous absorption of cholesterol²⁸. The findings show that the alcohol extract of *Achyranthes aspera* possesses anti-inflammatory properties in both acute (inflammatory phase) and chronic (proliferative phase) inflammation²⁹.

4. CONCLUSION

The discovery of new diabetes medications has been greatly aided by developments in traditional medicine research. The current study found that a high-fat diet can exacerbate streptozotocin-induced diabetes alterations. However, treatment with an alcoholic extract of *Achyranthes aspera* roots significantly improved the disease status by adjusting several body weights and metabolic markers (serum glucose, insulin, HbA1C, HOMA-IR, serum lipid profile, and liver glycogen levels). In preclinical studies, *Achyranthes aspera* root shows potential in the treatment of diabetes and high-fat diet complications.

5. AUTHORS CONTRIBUTION STATEMENT

Dr. Gunapriya Raghunathan and Dr. Vijaya raghavan designed the conceptual framework of this research work. B. Shahajeer performed experiments and did the data collection. Dr. RVSNS. Ramachandrudu and B. Shahajeer analysed the data. Dr. Gunapriya Raghunath, Dr. R. Vijayaraghavan, and P. Priya wrote the manuscript with input from all authors. All authors read and approved the final version of the manuscript.

6. CONFLICT OF INTEREST

Conflict of interest declared none.

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