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Research Article

# COMPREHENSIVE PHYTOCHEMICAL ANALYSIS AND THERAPEUTIC EVALUATION OF *ACALYPHA FRUTICOSA* LEAVES IN TYPE I DIABETIC RATS

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**ABSTRACT**

**Objectives:** The study evaluates the safety, phytochemical composition, and effectiveness of *Acalypha fruticosa* leaf extracts in managing Type I diabetes in rats.

**Methods:** The methodology involves collecting and verifying plant materials, preparing methanolic extracts, identifying phytochemicals, and determining morphological characteristics. Protective effects are assessed through monitoring body weight, feed, and water consumption, measuring plasma glucose and insulin levels, evaluating lipid peroxidative markers, assessing antioxidant activities, measuring inflammation-related cytokines, assessing liver health, and evaluating the impact on alpha-amylase glycogen levels. Histopathological study is also conducted to observe structural changes and protective effects. The aim is to provide a comprehensive evaluation of the efficacy and safety of *A. fruticosa* leaves extracts in managing Type I diabetes.

**Results:** Methanolic extract of *A. fruticosa* (MeAF) (*A. fruticosa*) was effective in preventing weight loss, with the higher dose (500 mg/kg) being particularly effective in maintaining body weight. MeAF 250 mg/kg moderately prevented weight loss and improved insulin levels, while MeAF 500 mg/kg significantly reduced blood glucose levels and improved various biomarkers in a dose-dependent manner. MeAF increased catalase activity and restored superoxide dismutase and glutathione levels, showing strong antioxidant potential similar to insulin. MeAF reduced inflammatory markers and showed moderate liver protection, with the higher dose being more effective in reducing alkaline phosphatase, serum glutamate pyruvate transaminase, and serum glutamic oxaloacetic transaminase levels. STZ-induced diabetic rats showed a significant elevation in serum α-amylase levels, whereas treatment with MeAF exhibited a dose-dependent reduction. Similarly, MeAF improved liver glycogen levels and restored plasma vitamin C, with 500 mg/kg producing effects comparable to those observed with insulin. MeAF preserved pancreatic structure with no significant damage to islets or acini at the higher dose, suggesting protective effects against diabetes-induced damage.

**Conclusion:** *A. fruticosa* (MeAF) has shown promising potential in managing diabetes and its complications. It improves glucose metabolism, reduces oxidative stress, and provides moderate protection to pancreatic and liver tissues in diabetic rats. MeAF could serve as a natural, complementary therapy, especially in areas with limited access to conventional treatments.

**Keywords:** *Acalypha fruticosa*, Diabetic prevalence, Type I diabetes mellitus, Antioxidant, Inflammation-related cytokines, Liver health, and Alpha-amylase glycogen.

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## INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by insulin deficiency or resistance, leading to disturbances in carbohydrate, protein, and lipid metabolism. It is the third leading cause of death worldwide, with an estimated 347 million people suffering from the disease, particularly in developing countries. The global prevalence is expected to increase by 50% in the next decade, with 5% of all deaths attributed to diabetes [1-3]. Poorly controlled diabetes can lead to severe complications such as retinopathy, neuropathy, nephropathy, and cardiomyopathy. Conventional therapies, including insulin and oral hypoglycemic agents, are effective but often associated with high costs, limited accessibility, and potential side effects. Moreover, increased production of reactive oxygen species in diabetic conditions contributes to oxidative stress, which plays a significant role in the progression of diabetic complications. Therefore, there is growing interest in identifying safer and more effective therapeutic alternatives, particularly from natural sources [4-8].

Medicinal plants have long been used in traditional systems of medicine, including Ayurveda, for the management of diabetes and related disorders. Among these, *Acalypha fruticosa* is a densely branched shrub widely distributed in East tropical Africa, India, Myanmar, and Sri Lanka. The leaves of this plant are commonly used as food and in traditional medicine. Phytochemical studies have revealed the presence of several bioactive compounds, including alkaloids, tannins, saponins, flavonoids, and cardiac glycosides. Conventionally, different parts of the plant have been used for the treatment of stomach disorders, dysentery, digestive ailments, skin infections, and inflammatory conditions, and have demonstrated antimicrobial and anti-inflammatory properties [9-12]. Herbal remedies such as bitter melon, fenugreek, turmeric, and neem are traditionally used to regulate blood glucose levels, improve insulin sensitivity, and reduce oxidative stress. These natural therapies are often considered safer for long-term use compared with synthetic drugs. In addition, Ayurvedic practices, including dietary regulation, lifestyle modification, yoga, meditation, and stress management, contribute to improved metabolic balance and may help prevent or

delay diabetic complications. In this context, medicinal plants such as *A. fruticosa* may represent promising natural therapeutic agents for the management of diabetes [13,14].

## METHODS

### Collection and authentication of plant material

The plant leaves of *A. fruticosa* collected from hills area of Thirunelveli district of Tamil Nadu, India and authenticated by Dr. V. Rama Rao, Research Officer and Dr. Sulochana Bhat Assistant Director In-charge, Central Ayurveda Research Institute, Bangalore with Authentication/ SMPU/CARI/BNG/2023-24-407.

### Extraction of *A. fruticosa* using soxhlet extractor and sample preparation

*Preparation of extracts*

The leaves of *A. fruticosa* were chopped into small pieces and dried in the shade for several days at room temperature until completely dry. The dried leaves were powdered and passed through the sieve (coarse 10/40). The powder was used for the preparation of methanolic extraction.

*Method of extraction*

About 100 g of powdered plant material was extracted with 1,000 mL methanol using a reflux condenser. The extraction was carried out in three reflux cycles of 2–3 h each. After each cycle, the extract was filtered, and the residue was re-extracted with fresh methanol, and the pooled extracts were concentrated under reduced pressure to reduce the solvent volume to half of the initial volume. Extract was filtered through Whatman filter paper No. 40 and evaporated to dryness to get a constant weight. The extract was concentrated on a rotary vacuum evaporator at 35–40°C to get semisolid residue, and the extract was stored in a screwcap vial at 2–8°C until further experimentation [15-19].

### Experimental animals

The anti-diabetic and antioxidant activities of the medicinal plant were carried out using Wistar albino rats (8–10 weeks old) weighing 150–200 g) was used for the experiment. They were acclimatized for 1 week before experiment. Animals were caged in a fully ventilated room, were maintained in 12:12 h light and dark cycle and were housed at temperature of 25±2°C. They had free access to a standard chow diet and water *ad libitum*. All the experiments conducted on the animals were in accordance with the standards set for the use of the laboratory animal use.

### Preliminary phytochemical(s) of the crude extract of leaves of *A. fruticosa*

Qualitative analysis of phytochemicals of plant extract was done as per the reported method [20,21].

*Dose selection*

Based on a previous acute toxicity study [22], which showed no mortality up to 5,000 mg/kg, doses of 250 and 500 mg/kg were selected for this efficacy study.

### Detailed study plan

*Induction of type I DM by streptozotocin in rats*

For the induction of diabetes, *Wistar* male rats (150–200 g and 5–6 weeks old) were used and administered a single dose of STZ 50 mg/kg, b.w., I.P., Reconstituted STZ in 0.1M sodium citrate, pH 4.5. A 5% glucose solution was administered to induced rats for 24 h to prevent sudden hypoglycemia. Induced rats with fasting blood sugar >180 mg/dL were selected for further experimentation [23].

*Experimental design*

Wistar Rats (40 numbers) (Male, approx. 150–20 mg/kg) were divided into the following groups, each of eight rats and were fed with the material as below (Table 1).

After the confirmation of hyperglycemia (>180–200 mg/dL), the standard drug, that is, Insulin 4IU, as well as plants extract methanolic extract of *A. fruticosa* (*MeAF*), was administered orally once daily for 30 days. Body weight and blood glucose levels of rats were measured before, that is, 0 day and 30$^{th}$ day of the treatment. Biochemical, Assay of oxidative stress and antioxidant enzymes and proinflammatory parameters – At the end of the experimental studies animals were anesthetized by the light dose of phenobarbital for the blood collection by the method of cardiac puncture and later it was sacrificed by high dose of phenobarbital sodium (on the 30$^{th}$ days of the experiment) and tissue sample (Pancreas and Liver) was isolated. Blood Samples were centrifuged at 2,500 rpm for 15 min and examined. The parameters:

*Behavior study*

Effects of extracts on body weight, Feed consumption, and Water consumption. Body Weight (Pre- and Post-treatment), Blood Glucose Level (Healthy, Diabetic, and Post-treatment), (Using Digital Glucometer, One touch select, LifeScan Scotland Ltd, UK).

*Changes in insulin level*

The levels of insulin in serum and pancreatic tissue were determined using a sandwich enzyme-linked immunosorbent assay (ELISA). The assay was performed according to the manufacturer's instructions given in the Elabscience Rat ELISA kit (EL-R3034) [24].

### Antioxidant enzyme studies [25-28]

*Lipid peroxidation (LPO)*

The levels of LPO markers, including thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides, and conjugated dienes, were estimated in pancreatic and liver tissues to assess oxidative stress. The assay was performed according to the manufacturer's instructions given in the Elabscience TBARS Colorimetric Assay kit (Cat. No., E-BC-K176-M-48).

*Enzymatic antioxidants*

Superoxide dismutase (SOD) activity is determined based on its ability to inhibit the reduction of nitroblue tetrazolium by superoxide radicals generated during the reaction, catalase (CAT) activity is measured based on its ability to catalyze the decomposition of hydrogen peroxide

**Table 1: Experimental design and grouping of animals**

| Sn | Model | Grouping | Number of animals |
|---|---|---|---|
| 01. | STZ induced type I diabetes mellitus in rat's | Group I: Normal Control Group – Saline 2 mL/kg, b.w., P.O. | 8 rats |
| | | Group II: Disease Control, Received a single dose of STZ 50 mg/kg, i.p. | 8 rats |
| | | Group III: Standard drug, Diabetic rats (Received STZ), After the confirmation of diabetic, treated by Insulin 4IU i.p. once daily for 30 days | 8 rats |
| | | Group IV: Test drug (Methanolic extract of *Acalypha fruticose,* 250 mg/kg, p.o./day), Diabetic rats (Received STZ), After the confirmation of diabetic, treated by test drug, MeAF once daily for 30 days | 8 rats |
| | | Group V: Test drug (Methanolic extract of *Acalypha fruticosa*, 500 mg/kg, p.o./day), Diabetic rats (Received STZ), After the confirmation of diabetic, treated by test drug, MeAF once daily for 30 days | 8 rats |

MeAF: Methanolic extract of *Acalypha fruticosa*

**Table 2: Body weight**

| Parameters/group | NC: Normal saline | DC: STZ 50 mg/kg | STD drug: Insulin 4IU | Test drug: MeAF 250 mg/kg | Test drug: MeAF 500 mg/kg |
|---|---|---|---|---|---|
| Initial body weight | 153.0±0.115 | 154.0±2.3 | 160.0±1.86 | 151.3±1.15 | 159.0±1.16 |
| Post-treatment body weight | 164.0±2.3 | 139.7±2.9$^{###}$ | 163.7±2.6*** | 156.3±1.85** | 165.0±1.53*** |

Values are expressed as mean±standard error of the mean, (n=8 rats in each group). ns, p>0.05 (non-significant between the initial body weight) and $^{###}$p<0.001 compared to normal control, ***p<0.001, **p<0.01 compared to disease control. MeAF: Methanolic extract of *Acalypha fruticosa*

**Table 3: Anti-oxidant enzyme study**

| Parameters/group | NC: Normal saline | DC: STZ 50 mg/kg | STD drug: Insulin 4IU | Test drug: MeAF 250 mg/kg | Test drug: MeAF 500 mg/kg |
|---|---|---|---|---|---|
| LPO, Pancreatic tissue supernatant | 1.017±0.006 | 2.937±0.3$^{###}$ | 1.243±0.076*** | 1.920±0.07** | 1.473±0.12***, $^{ns}$ |
| LPO, Liver tissue supernatant | 0.9800±0.04 | 2.737±0.3$^{###}$ | 1.207±0.05*** | 1.833±0.04* | 1.330±0.12***, $^{ns}$ |
| CAT, Pancreatic tissue supernatant | 10.58±0.55 | 5.227±0.01$^{##}$ | 18.81±0.25*** | 12.85±0.28*** | 16.06±1.71***, $^{ns}$ |
| CAT, Liver tissue supernatant | 11.21±0.64 | 6.797±0.23$^{#}$ | 17.60±0.65*** | 13.21±1.16** | 16.18±0.85***, $^{ns}$ |
| SOD, Pancreatic tissue supernatant | 21.94±1.27 | 5.410±0.43$^{###}$ | 40.93±2.6*** | 25.18±1.83*** | 38.08±1.76***, $^{ns}$ |
| SOD, Liver tissue supernatant | 18.04±0.84 | 8.377±0.58$^{##}$ | 28.53±1.41*** | 18.76±1.84** | 25.95±1.29***, $^{ns}$ |
| GSH, Pancreatic tissue supernatant | 36.27±0.47 | 16.89±1.72$^{###}$ | 40.58±0.39*** | 25.43±2.67* | 32.58±1.33***, * |
| GSH, Liver tissue supernatant | 31.25±1.52 | 14.50±1.22$^{###}$ | 35.04±3.74*** | 24.83±0.89* | 31.27±0.9***, $^{ns}$ |
| GST, Pancreatic tissue supernatant | 114.6±2.65 | 94.50±1.22$^{###}$ | 135.0±3.74*** | 124.8±0.85*** | 131.3±0.91***, $^{ns}$ |
| GST, Liver tissue supernatant | 129.3±2.6 | 96.00±1.52$^{###}$ | 142.7±1.45*** | 129.0±1.15*** | 133.3±2.73***, * |

Values are expressed as Mean±standard error of the mean, (n=8 rats in each group). $^{#}$p<0.05, $^{##}$p<0.01, and $^{###}$p<0.001 compared to normal (Healthy) control, ***p<0.001, **p<0.01, and *p<0.05 compared to disease (STZ) control versus treatment groups, $^{ns}$p>0.05 compared to std drug, Insulin versus MeAF 500 mg/kg. SOD: Superoxide dismutase, GSH: Glutathione, LPO: Lipid peroxidation, CAT: Catalase, GST: Glutathione-S-transferase, MeAF: Methanolic extract of *Acalypha fruticosa*

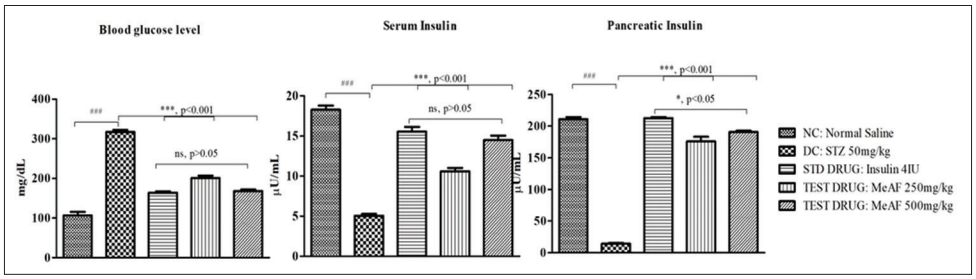


**Fig. 1: Blood glucose and insulin levels. Values are expressed as mean±standard error of the mean (n=8 rats in each group). $^{###}$p<0.001 compared to normal healthy control, ***p<0.001 compared to disease (STZ) control, $^{ns}$p>0.05, and *p<0.05 compared to Insulin versus methanolic extract of *Acalypha fruticosa* 500 mg/kg**

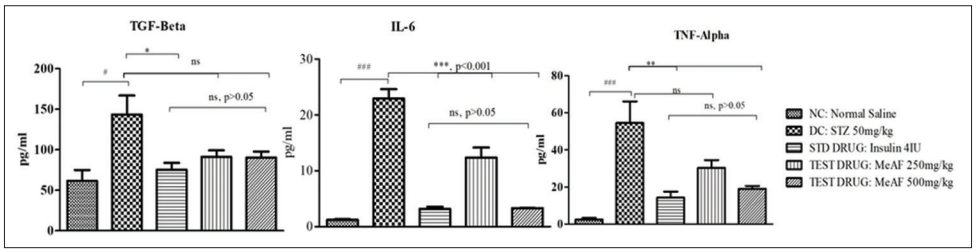


**Fig. 2: Transforming growth factor-beta, interleukin-6, and tumor necrosis factor-alpha plasma. Values are expressed as mean±standard error of the mean (n=8 rats in each group). $^{#}$p<0.05 and $^{###}$p<0.001 compared to normal control, **p<0.01, ***p<0.001, and *p<0.05 compared to disease (STZ) control. $^{ns}$p>0.05 compared to Insulin versus methanolic extract of *Acalypha fruticosa* 500 mg/kg**

($H_2O_2$) into water and molecular oxygen, and Glutathione-S-transferase (GST) activity is determined by measuring the conjugation of reduced glutathione (GSH) with a suitable substrate such as 1-chloro-2,4-dinitrobenzene were determined in pancreatic and liver tissue homogenates. The assay was performed according to the manufacturer's instructions given in the Elabscience Colorimetric Assay kit, for CAT (Cat. No., E-BC-K031-S-100), for SOD (Cat. No., E-EL-R1424), and for GST (Cat. No., E-BC-K800-M-96).

*Non-enzymatic antioxidants*

The levels of non-enzymatic antioxidants, including reduced GSH in pancreatic and liver tissues were determined using a commercially available Reduced Glutathione Colorimetric Assay Kit (Elabscience, Cat. no. E-BC-K030-M-48) following the manufacturer's protocol. The assay was based on the 5,5′-dithiobis-2-nitrobenzoic acid method, and the absorbance was measured at 405 nm. Plasma vitamin C levels were also determined as an indicator of non-enzymatic antioxidant status.

*Preparation of tissue homogenate for antioxidant assays*

Pancreatic and liver tissues were excised, washed with ice-cold normal saline to remove blood and other contaminants, and weighed. The tissues were then homogenized in cold normal saline using a tissue homogenizer under chilled conditions to preserve enzyme activity. The homogenates were centrifuged at low temperature to separate insoluble

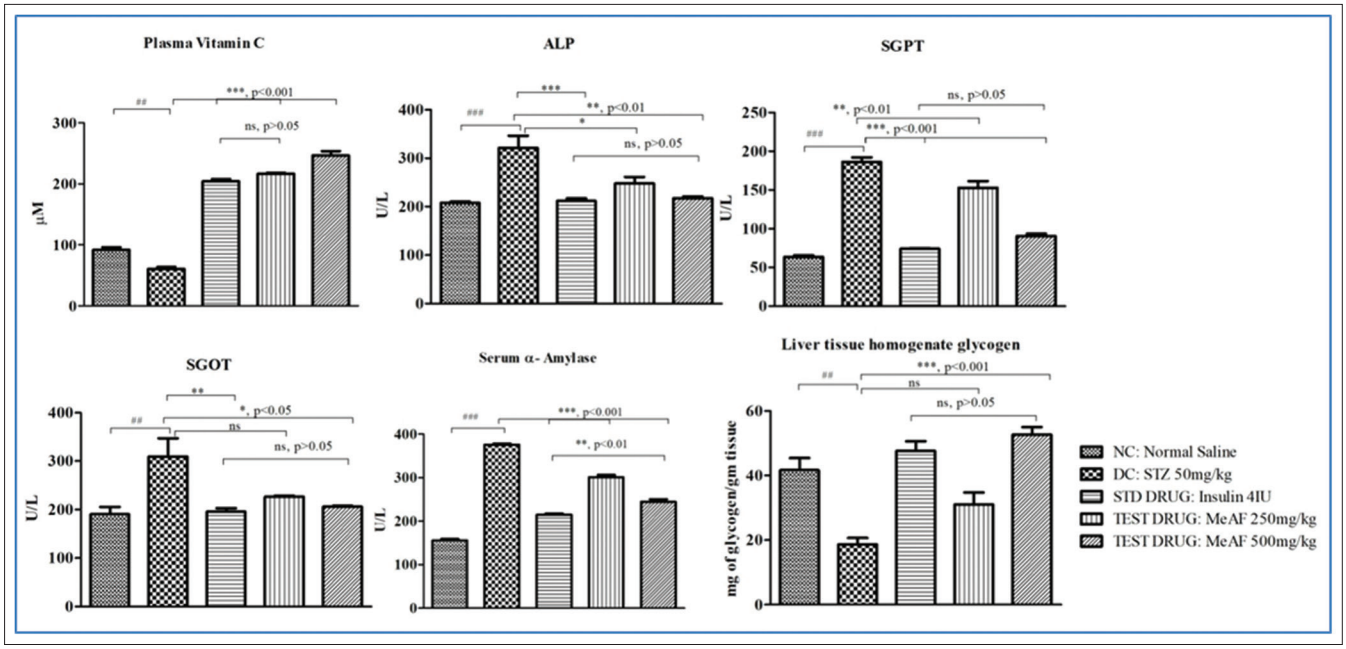


**Fig. 3: Biochemical markers. Values are expressed as mean±standard error of the mean (n=8 rats in each group). ##p<0.01, ###p<0.001 compared to normal healthy control versus disease (STZ) control, ***p<0.001, **p<0.01, *p<0.05 compared to disease (STZ) control versus Treatment groups**

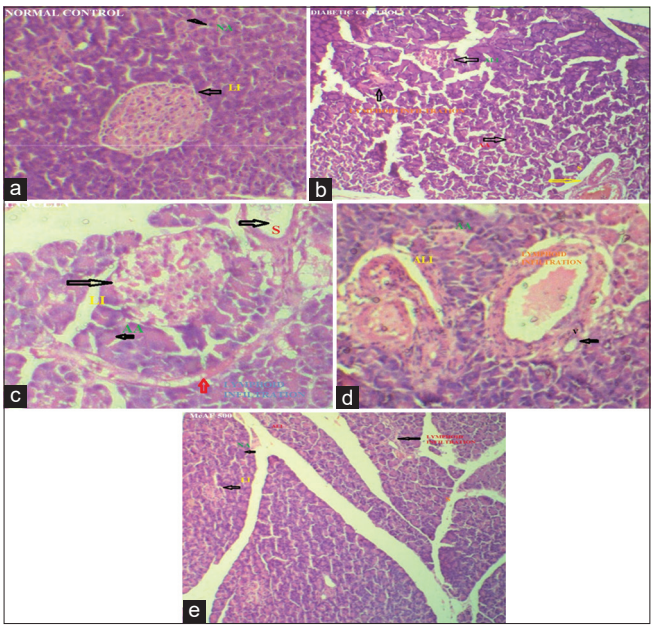


**Fig. 4: Histological assessments of the pancreatic tissue. (a) A histological section (TS, H&E stain, ×10 magnification) of the pancreas from a normal control rat. (b) A histological section (TS, H&E stain, ×10 magnification) of the pancreas from a diabetic control rat. (c) A histological section (TS, H&E stain, ×10 magnification) of the pancreas from a standard drug-treated rat. (d) A section (TS, H&E stain, ×10 magnification) of the pancreas from a rat treated with a test drug (MEAF – 250 mg/kg). (e) The pancreas from a rat treated with a higher dose of the test drug MEAF (500 mg/kg). The observations in this section (TS, H&E stain, ×10 magnification). H&E: Hematoxylin and eosin stain, MEAF: Methanolic extract of *Acalypha fruticosa***

cellular debris from the soluble fraction. The resulting supernatant containing soluble proteins and enzymes was collected and used for the estimation of enzymatic and non-enzymatic antioxidant parameters. All procedures were carried out under cold conditions to maintain enzyme stability and activity.

*Liver enzyme biomarker studies*

Serum biochemical parameters, including alkaline phosphatase (ALP), serum glutamate pyruvate transaminase/alanine transaminase (SGPT/ALT), serum glutamic oxaloacetic transaminase/aspartate aminotransferase (SGOT/AST), and α-amylase, were estimated using commercially available diagnostic kits obtained from Agappe Diagnostics Ltd., India, according to the manufacturer's instructions. ALP activity was determined by the DGKC kinetic method using diethanolamine buffer at 405 nm (ALP IFCC Method Reagent Kit; Cat. No. 12001001). SGPT (ALT) and SGOT (AST) activities were measured using the IFCC kinetic method at 340 nm (SGPT Enzymatic Reagent Kit; Cat. No. 12002001, and SGOT Enzymatic Reagent Kit; Cat. No. 12003001, respectively). α-Amylase activity was determined using the CNPG3 kinetic method at 404 nm (Alpha-Amylase CNPG3 Method Kit; Cat. No. 12009002). Liver glycogen content was determined using standard biochemical methods.

*Determination of proinflammatory mediators*

Transforming growth factor (TGF)-beta, interleukin-6 (IL-6) and tumor necrosis factor (TNF)-Alpha from plasma [29]. The Lowry et al. approach is used to normalize protein concentration in plasma using the Sandwich ELISA technique. This method involves plate coating, standard preparation, sample and standard addition, incubation, detection, washing, detection antibodies, secondary antibody addition, and substrate addition. The plate is coated with antibodies specific to the cytokine of interest, such as anti-TGF-beta, anti-IL-6, and anti-TNF-α antibodies. Unbound sites on the plate are blocked with a blocking buffer to prevent nonspecific binding of detection antibodies and other reagents. Standard curves are generated by preparing known concentrations of recombinant cytokine proteins (standards). Patient samples are diluted appropriately to fall within the linear range of the standard curve.

Incubation steps involve adding diluted standards and samples to the plate wells in duplicate or triplicate, incubating for a specified period at a controlled temperature. After incubation, the plate is washed to

remove unbound substances, and detection antibodies specific to the cytokines are added to the plate wells. Streptavidin-conjugated enzyme is added to bind to the biotinylated detection antibodies. A chromogenic substrate solution is added to each well, catalyzing a color change reaction. Data analysis involves colorimetric measurement, standard curve analysis, and considerations such as controls, quality control, and data interpretation. By performing sandwich ELISA assays for TGF-beta (Cat. No., E-EL-R0084), IL-6 (Cat. No., EK0064244-48T), and TNF-α (Cat no., PKSR030457-50), researchers can quantify these proinflammatory cytokines, which serve as important markers of disease severity and immune response in diabetic conditions.

Histopathological study [30] – Pancreas. The pancreas was isolated and divided into two portions; one portion was homogenized to be used for biochemistry studies, and the other portion was preserved in 10% formaldehyde for histological examination.

*Histology of pancreas tissue – hematoxylin and eosin stain staining*

The animals were euthanized using a high dose of Pentobarbital and then sacrificed, and the pancreas of each animal was isolated and was cut into small pieces, preserved and fixed in 10% formalin for 2 days, dehydrated with alcohol, embedded in paraffin, cut into 4–5 m thick sections, and stained with Hematoxylin-Eosin dye for photo microscopic observation. The microscopic features of the pancreas of rats were compared with the control group.

**Statistical analysis**

The results are expressed as Mean±S.E.M. from n=8 rats in each group. Data were analysed using statistical software GraphPad Prism version 5. The significance of difference among the groups was assessed using one-way analysis of variance, followed by Tukey's test, compared between Normal control (Untreated) versus all groups, $p<0.05$ was considered significant.

## RESULTS AND DISCUSSION

In the present study, methanolic extraction of *A. fruticosa* leaves produced a yield of 14.38%, and preliminary phytochemical analysis revealed the presence of triterpenoids, flavonoids, tannins, alkaloids, saponins, and anthraquinones. Similar phytoconstituents have been reported in several plants with antidiabetic activity. Flavonoids and tannins present in medicinal plants such as *Momordica charantia* and Pterocarpus marsupium have been shown to possess hypoglycemic and antioxidant activities by enhancing glucose utilization and protecting pancreatic β-cells from oxidative damage [31]. These bioactive compounds may contribute to the therapeutic potential observed in the present study.

Streptozotocin-induced diabetic rats in the present investigation exhibited characteristic symptoms such as body weight loss, increased water intake, and metabolic disturbances. These observations are consistent with earlier reports describing STZ-induced diabetes, where destruction of pancreatic β-cells leads to insulin deficiency and increased catabolism of proteins and lipids, resulting in progressive weight loss [32]. Administration of the MeAF significantly prevented body weight loss, particularly at the higher dose (500 mg/kg) (Table 2). Similar improvements in body weight have been reported with plant extracts such as *Gymnema sylvestre* and *Trigonella foenum-graecum*, which were shown to improve metabolic homeostasis in diabetic animal models [33].

The present study demonstrated that MeAF significantly reduced blood glucose levels and improved serum and pancreatic insulin levels in diabetic rats (Figure 1). Comparable results have been reported with several medicinal plants known to possess insulinotropic activity. For example, *M. charantia* extract has been reported to enhance insulin secretion and reduce hyperglycemia in diabetic models [34]. Likewise, *G. sylvestre* has been shown to promote regeneration of pancreatic β-cells and increase insulin secretion [35]. These findings suggest that the antidiabetic activity of *A. fruticosa* may be partly mediated through preservation or stimulation of pancreatic β-cell function.

Oxidative stress is a major contributor to the pathogenesis and complications of diabetes. In the present study, diabetic rats showed increased LPO and reduced antioxidant enzyme activities, indicating enhanced oxidative stress. Treatment with MeAF significantly decreased LPO levels in pancreatic and liver tissues and increased the activities of antioxidant enzymes such as SOD and CAT, along with elevated levels of reduced GSH (Table 3). Similar antioxidant effects have been reported for medicinal plants such as *Curcuma longa* and *Azadirachta indica*, which have been shown to restore antioxidant defense systems and protect tissues from oxidative damage in diabetic conditions [36].

Inflammatory pathways also play a critical role in diabetes progression. In the present study, MeAF significantly reduced inflammatory cytokines such as TNF-α, IL-6, and TGF-β in diabetic rats (Figure 2). Previous studies have demonstrated that phytochemicals such as flavonoids and polyphenols possess strong anti-inflammatory properties. For example, curcumin derived from *C. longa* has been reported to suppress proinflammatory cytokines and improve insulin sensitivity in experimental diabetes [37]. The reduction of inflammatory markers observed in this study suggests that *A. fruticosa* may exert protective effects through modulation of inflammatory pathways.

Biochemical analysis further revealed that MeAF improved liver function markers, including ALP, SGPT, and SGOT levels, which were elevated in diabetic rats (Figure 3). Similar hepatoprotective effects have been reported with medicinal plants such as *Tinospora cordifolia and Phyllanthus amarus*, which reduce liver enzyme levels and improve hepatic metabolism under diabetic conditions [38]. In addition, MeAF restored liver glycogen levels, indicating improved glucose utilization and glycogen storage, which is consistent with previous studies involving antidiabetic plant extracts.

Histopathological examination of pancreatic tissue supported the biochemical findings. Diabetic rats showed significant pathological changes, including lymphoid infiltration, acinar atrophy, and a reduction in β-cell population. However, treatment with MeAF, particularly at the higher dose, preserved pancreatic architecture and protected the islets of Langerhans (Figure 4). Similar protective effects on pancreatic tissue have been reported with plant extracts such as *M. charantia,* which have been shown to regenerate β-cells and restore pancreatic function in diabetic animals [39].

## CONCLUSION

The study suggests that *A. fruticosa* extract (MeAF) has potential as an antidiabetic agent, improving glucose metabolism, reducing oxidative stress, and providing moderate protection to pancreatic and liver tissues in diabetic rats. MeAF, while less potent than insulin, offers a natural and complementary therapeutic approach for diabetes management, particularly in reducing oxidative stress and inflammation, which contribute to diabetes-related complications. Further research is needed to understand the mechanisms of action, long-term efficacy, and safety of MeAF for potential clinical applications. The findings support MeAF as an adjunct or complementary therapy to conventional antidiabetic drugs.

## ETHICAL ISSUE

The experimental protocol was duly approved by the IAEC (Institutional Animal Ethical Committee) of Karnataka College of pharmacy, Bangalore (Sl. No. KCP/IAEC/15/24–25/01/01/07/24).

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**AUTHOR CONTRIBUTIONS**

Suri CR – Laboratory work and prepared the manuscript, Amol S. Rakte – Final review and supervised of project, Chandanam Sreedhar – Contributed to the Final review and supervision of project, Harsha K Tripathy – Statistical work, contributed to reviewing, and editing, P.K. Choudhury – Involved in Statistical work, reviewing, and editing, and Deepak Kumar Jha – Laboratory work and supervised the project work.

**CONFLICTS OF INTEREST**

The authors declare that they have no financial, personal, or professional conflicts of interest that could influence the interpretation or presentation of the research findings.

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