Journal or Innovative Development in Pharmaceutical and Technical Science (JIDPTS)
Volume:9, Issue:11, Nov:2026

(J I D P T S)
ISSN(O):2581-6934

EXPLORING THE GLUCOSE LOWERING POTENTIAL OF FICUS CARICA IN EXPERIMENTAL DIABETES

B. MAHESHWARI REDDY*[1], NYALATA ARCHITHA[2], NABIHA[3], SHRUTHI[4], UPENDER[5]

[1]Associate Professor, [2,3,4,5] Students

[1,2,3,4,5] Department of Pharmacology, Joginpally B.R Pharmacy College, Yenkapally(V), Moinabad(M), R.R District, Hyderabad, Telangana-500075 India.

Abstract: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia associated with disturbances in carbohydrate, lipid, and protein metabolism. The present study was undertaken to evaluate the glucose lowering potential of Ficus carica in streptozotocin (STZ)-induced diabetic rats. The plant extract was subjected to preliminary phytochemical screening, which revealed the presence of flavonoids, phenolic compounds, tannins, alkaloids, glycosides, saponins, and terpenoids. Experimental diabetes was induced in Wistar rats by a single intraperitoneal injection of STZ (45–55 mg/kg). The animals were divided into five groups consisting of normal control, diabetic control, standard-treated (Metformin), and two extract-treated groups receiving Ficus carica extract at doses of 200 mg/kg and 400 mg/kg, respectively. The treatment was continued for 21 days, and various biochemical parameters including fasting blood sugar, oral glucose tolerance test, serum insulin, lipid profile parameters (TC, TG, LDL, HDL, VLDL), and antioxidant markers such as Superoxide Dismutase (SOD), Reduced Glutathione (GSH), and Glutathione-S-Transferase (GST) were evaluated. The results showed that Ficus carica extract significantly reduced elevated blood glucose levels and improved glucose tolerance in diabetic rats. The extract also improved serum insulin levels and restored altered lipid profile parameters toward normal values. Furthermore, treatment with Ficus carica significantly enhanced antioxidant enzyme levels, indicating its protective effect against oxidative stress induced by diabetes. The higher dose (400 mg/kg) exhibited more pronounced pharmacological activity comparable to the standard drug Metformin. Ficus carica possesses significant antihyperglycemic, antihyperlipidemic, and antioxidant activities and may serve as a potential natural therapeutic agent for the management of diabetes mellitus and its associated complications.

Keywords : Ficus carica, Diabetes mellitus, Streptozotocin, Antihyperglycemic activity, Superoxide dismutase, Glutathione, Experimental diabetes.

INTRODUCTION

DIABETES MELLITUS

Diabetes mellitus is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin production, insulin action, or both, altered metabolism of lipids, carbohydrates, and proteins, and an increased risk of complications of vascular diseases [1]. It is the most common endocrine disorder and can be associated with serious complications and premature death.

HISTORY [2, 3]

Knowledge of diabetes mellitus dates back to many centuries. Eber's Egyptian Papyrus (1500 BC) described it as an illness associated with the passage of much urine. A renowned Greek physician Arataeus of Cappodica coined the name diabetes (a siphon which described it as melting down of flesh and limbs into urine. Scholars in China, Japan, and India during the 3rd and 6th centuries AD wrote of a condition with polyurea in which urine was 'sweet and sticky'. Although it has been for centuries, it was until 1674, that Willis added the observation

All rights reserved by www.jidps.com

'as it imbued with honey and sugar'. The name diabetes mellitus (mellitus- honey) was thus established. A century after Willis, Dobson demonstrated that the sweetness was due to sugar. From the earliest recorded history of diabetes, progress in understanding came slowly until the middle of the 19th century. An association was established with a disturbance in the beta cells, clustered as tiny islets of tissue in the exocrine pancreas. Brockman first noticed the presence of these islets in fish during the 19th century. Soon after, the German scientists, Mering and Minkowski, found that surgical removal of the pancreas produced diabetes in dogs. The breakthrough of the discovery of insulin was by Fredrick Banting and Charles Best in 1921. By 1952, various purified modified versions of insulin were available and by 1982, recombinant DNA insulin became available. Thus diabetes, which was synonymous with an inevitably fatal disease, became a more benign controllable disease.

EPIDEMIOLOGY [4]

In the year 2000, according to the World Health Organization, at least 171 million people worldwide suffered from diabetes. Its incidence is increasing rapidly, and it is estimated that by 2030, this number will almost double. Diabetes mellitus occurs throughout the world but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in the incidence of diabetes in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented. For at least 20 years, diabetes rates in North America have been increasing substantially. In 2010 nearly 26 million people had diabetes in the United States alone, and from those 7 million people remain undiagnosed. Other 57 million people are estimated to have pre-diabetes. The Centers for Disease Control has termed the change an epidemic. The National Diabetes Information Clearinghouse estimates that diabetes costs $132 billion in the United States alone every year. About 5%–10% of diabetes cases in North America are type 1, with the rest being type 2. The fraction of type 1 in other parts of the world differs. Most of this difference is not currently understood. The American Diabetes Association cites the 2003 assessment of the National Centered for Chronic Disease Prevention and Health Promotion (Centers for Disease Control and Prevention) that 1 in 3 Americans born after 2000 will develop diabetes in their lifetime. The diabetes epidemic was more pronounced in India as the World Health Organization (WHO) reports showed that 32 million people had diabetes in the year 2002 and expected that it may rise to 80 million in 2030. According to the American Diabetes Association, approximately 18.3% (8.6 million) of Americans age 60 and older have diabetes. Diabetes mellitus prevalence increases with age, and the numbers of older persons with diabetes are expected to grow as the elderly population increases in number. The National Health and Nutrition Examination Survey (NHANES III) demonstrated that, in the population over 65 years old, 18% to 20% have diabetes, with 40% having either diabetes or its precursor form of impaired glucose tolerance. Indigenous populations in first-world countries have a higher prevalence and increasing incidence of diabetes than their corresponding non-indigenous populations.

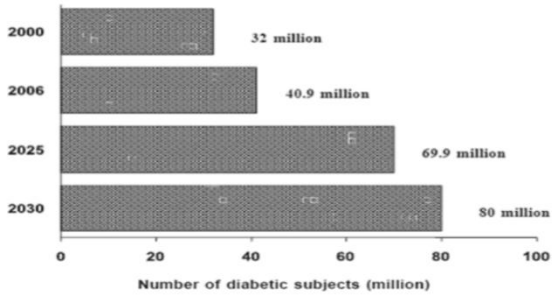


Figure 1.1: Estimated number of diabetic subjects in India

CLASSIFICATION OF DIABETES MELLITUS [5]

Although all forms of diabetes mellitus share hyperglycemia as a common feature, the pathogenic process involved in the development of hyperglycemia varies widely. Diabetes mellitus can be classified as follows:

1) Type-I diabetes

(i) Immune-mediated

(ii) Idiopathic

2) Type-II diabetes 3) Other specific types of diabetes

(i) Genetic defects of β-cell function

(ii) Genetic defects in insulin action

(iii) Exocrine pancreatic defects

(iv) Endocrinopathies

(v) Drug- or chemical-induced

(vi) Infections

(vii) Genetic syndromes associated with diabetes

(viii) Gestational diabetes mellitus

1. Type 1 (previously called Insulin Dependent Diabetes mellitus (IDDM) or juvenile-onset Diabetes)

Causes

- Genetic predisposition.
- Environmental exposure: virus, toxin, stress
- Autoimmune reaction: beta-cells that produce insulin in the pancreas are destroyed. When 80-90% of the beta-cells are destroyed, over symptoms occur.

Characteristics

- Usually occurs before 30 years of age, but can occur at any age. Peak incidence occurs during puberty, around 10-12 years of age in girls and 12-14 years in boys.
- Abrupt onset of signs and symptoms of hyperglycemia: increased thirst and hunger, frequent urination, weight loss, and fatigue.
- Ketosis prone.

Treatment

- Insulin by injection with syringes or pumps.
- Diet
- Exercise

2. Type 2 (previously called Non-Insulin Dependent Diabetes mellitus, NIDDM, or adult-onset diabetes)

Causes

- Insulin resistance: unable to utilize insulin that the body makes because of cell-receptor defect; glucose is unable to be absorbed into cells for fuel.
- Decreased insulin secretion: The pancreas does not secrete enough insulin in response to glucose levels.
- Excess production of glucose from the liver: result of defective insulin secretory response; dawn phenomenon is an example.

Characteristics

- Usually occurs after 30 years of age, but sometimes also observed in children and adolescents.
- Increased prevalence in some ethnic groups, e.g., African Americans, Hispanic/Latino, Native Americans, Asian Americans, and Pacific Islanders.
- Strong genetic predisposition.
- Frequently obese.
- Not prone to ketoacidosis until late in the course or with prolonged hyperglycemia.
- May or may not have symptoms of hyperglycemia.
- May also have extreme tiredness, blurred vision, delayed healing, numbness and tingling of hands and feet, and recurring yeast infection.
- Children between the ages of 10-19 years that have one or more of the following are at an increased risk:
- Family history.
- Member of certain ethnic populations.
- Overweight.
- Sedentary lifestyle.
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans [dirty-neck syndrome], hypertension, dyslipidemia, and polycystic ovarian syndrome.

Treatment

- Diet/weight management.
- Exercise/increase physical activity.
- Oral hypoglycemic/antihyperglycemic agents, insulin sensitizers, or insulin.
- Treatment of comorbid conditions (e.g., hypertension, lipid abnormalities).

3. Gestational Diabetes Mellitus (GDM)

Causes

- Insulin resistance due to pregnancy.
- Genetic predisposition

Characteristics

- Carbohydrate intolerance during pregnancy was identified via a 1-hour screen using a 50-g oral glucose load (performed between the 24th and 28th week of gestation unless otherwise indicated).
- If the 1-hour screen for glucose is >140 mg/dl (>7.8 mol/l), a full diagnostic 100-g, 3-hour oral glucose tolerance test (OGTT) is indicated.

Treatment

- Diet: provide adequate calories without hyperglycemia or ketonemia.
- Exercise: program that does not cause fetal distress, contractions, or hypertension (>140/ 90 mmHg).
- Insulin: if unable to consistently maintain blood glucose <95 mg/dl fasting (<5.3 mmol/l) and <140 mg/dl (<7.8 mmol/l) 1 hour postprandial and <120 mg/dl (<6.7 mol/l) 2 hours postprandial.

SYMPTOMS OF DIABETES MELLITUS [6-10]

The common symptoms are the presence of high amount of glucose in the blood and urine of the patient. Symptoms of type 1 diabetes usually develop over a short period, although beta cell destruction can begin years earlier. Symptoms may include increased thirst and urination, constant hunger, weight loss, blurred vision, and extreme fatigue. If not diagnosed and treated with insulin, a person with type 1 diabetes can lapse into a life-threatening diabetic coma, also known as diabetic ketoacidosis. Symptoms of type II may include fatigue, frequent urination, increased thirst and hunger, weight loss, blurred vision, and slow healing of wounds or sores.

MATERIALS AND METHODS

Collection and Authentication of plant material:

The plant fig was collected from natural habitat of Ranga Reddy District, Telangana, India. The taxonomic identification of the plant was confirmed by Department of Botany, Government Degree College, Kukatpally, Medchal District, Telangana State. The fig was cleaned and drying under sunlight. The dried plant was ground with mortar pestle and passed through sieve no. 14. The powdered plant was kept in airtight container for extraction.

Extraction

The figs are collected and shade dried for one week, the dried leaves are pulverized by a mechanical grinder reduced to coarse powder and around 50g of powder material was subjected to successively hot continuous extraction .a weight quantity of each of the plant powdered material was extracted by Soxhlet with ethanol of 200ml for 24hrs with intermediate heating at 40 0 c after that the residues were extracted the extract was filtered using Whatmann filter paper and then the extract was evaporated in a rota evaporator and further dried under vacuum.

In-vivo activity:

Animals: Wistar rats (weighing 250-300 gm). They were kept under controlled conditions (temperature: 28-30°C, photoperiod: roughly 12 hours of natural light per day, relative humidity: 50-55%) with free pellet food and water. From Jeeva Life Sciences, Hyderabad Animal Ethics Committee and the Institutional Animal Ethical Committee approved the experimental protocol.

Animal Husbandry Conditions

The animals will be housed under controlled temperature (24 ± 2∘ C) and relative humidity (45% ± 10%).

Table Animal Husbandry Conditions

	Conditions
Temperature	28-30°C
Relative humidity	50-55%
Air changes	10 to 15 air changes per hour.
Housing	Standard polypropylene rat cages with stainless steel top grill were used to house the animals. The cages were washed; clean paddy husk was used as the bedding material.
Sanitation	Bedding material will be changed on alternative days.
Light/dark cycle	12-hourly
Feed & water	Standard pelleted feed and Filtered water was provided ad libitum. The diet and water were routinely analysed for any contaminants that could reasonably be expected to affect the purpose or integrity of the study

Drug used: Test drug: Extract of fig

Standard drug: metformin

Induction of Diabetes

Experimental diabetes was induced in overnight fasted Wistar rats by a single intraperitoneal injection of Streptozotocin (STZ) at a dose of 45–55 mg/kg body weight. STZ was freshly prepared in cold 0.1 M citrate buffer (pH 4.5) and administered immediately after preparation. Following STZ administration, animals were provided with 5% glucose solution for 24 hours to prevent sudden hypoglycemia. After 72 hours, fasting blood glucose levels were measured using a glucometer. Animals showing fasting blood glucose levels above 250 mg/dL were considered diabetic and included in the study.

Animal grouping

Group I Normal Control Normal rats treated with vehicle (0.5% CMC, 1 mL/kg, p.o.)

Group II Diabetic Control Diabetic rats receiving streptozotocin (STZ) + vehicle

Group III Standard Treatment Diabetic rats treated with Metformin (100 mg/kg, p.o.)

Group IV Ficus carica Low Dose Diabetic rats treated with Ficus carica extract (200 mg/kg, p.o.).

Group V Ficus carica High Dose Diabetic rats treated with Ficus carica extract (400 mg/kg, p.o.).

PARAMETERS FOR EVALUATION [11]

Fasting Blood Sugar (FBS):

Fasting blood sugar level was determined by using glucose oxidase peroxidase reactive strips.

Lipid Profile:

The lipid profiles viz Serum cholesterol, Serum triglycerides, and HDL Cholesterol were estimated by using an auto analyzer. On the 15th day, animals were sacrificed by cervical dislocation, and the following parameters were monitored.

Liver Glycogen Content:

The liver glycogen was estimated by the Anthrone method.52

Reagents:

1. Anthrone reagent 1 liter of 72 % v/v sulphuric acid was prepared by placing 280 ml of distilled water in a suitable flask and then cautiously adding 720 ml of concentrated (11 N) sulphuric acid to it. Then, 500 mg of AR grade anthrone as well as 10 g of highest purity thiourea was added to this. The mixture was then warmed at 80-90oC, in a hot water bath, with occasional shaking, till the anthrone and thiourea were dissolved. Then the mixture was cooled and stored in a refrigerator.
2. Trichloroacetic acid 5%: 5 g of Trichloroacetic acid crystals were accurately weighed and dissolved in 100 ml of distilled water.
3. 95% ethanol
4. Standard glucose solution A stock solution of (1 mg/ml) glucose solution was prepared by dissolving 100 mg glucose in 100 ml saturated benzoic acid solution. A saturated solution of benzoic acid was prepared by dissolving excess of benzoic acid in distilled water by heating on a water bath. On cooling overnight crystals of benzoic acid separate. This is then filtered to obtain a saturated benzoic acid solution. 2.5 ml of glucose stock solution was then diluted to 100 ml in a volumetric flask with saturated benzoic acid solution. 2 ml of this solution (containing 0.05mg glucose) was used as a reference-working standard.

Procedure: Excision of the liver: The animals were sacrificed by decapitation and the livers were excised and placed in separate beakers. Each beaker was weighed and noted.

Estimation of liver glycogen [12]

Each liver tissue was minced and placed in an efficient blender containing an approximate volume (about 5ml) of 5% Trichloroacetic acid and homogenized for 3 minutes. The homogenate was centrifuged at 3000 rpm for 5 minutes. The supernatant was decanted upon an acid-washed filter paper (glass wool was used) in a funnel, draining into a graduated cylinder. The residue was then transferred into the blender with an appropriate volume of TCA (5 ml) and homogenized again for 1 minute. The homogenate was centrifuged and the supernatant was poured through the same filter. This was repeated two more times. The total volume of filtrate collected in the graduated cylinder was noted. 10µl of this filtrate was pipetted into 15-ml Pyrex centrifuge tubes. To each tube, 5 ml of 95% ethanol was added and the tubes were allowed to stand overnight at room temperature. After completion of the precipitation of glycogen, the tubes were centrifuged at 3000 rpm for 15 minutes. The clear liquid was gently decanted out from the packed glycogen and the tubes were kept in an inverted position for 10 minutes to make the packed glycogen free from alcohol. The glycogen was dissolved in 2 ml of distilled water. A reagent blank was prepared by pipetting 2 ml of distilled water into a clean boiling tube. A standard was prepared by pipetting out 2 ml of standard glucose solution (containing 0.1mg glucose), into another tube. The dissolved glycogen was added to different boiling tubes. Then to each tube, 10 ml of anthrone reagent was added. All the tubes were capped tightly with an air condenser and placed in the cold-water bath. After allowing the contents of the tubes to reach the temperature of cold water, (20 minutes) all tubes were taken out and immersed in a boiling water bath to a depth, a little above the level of contents in the tubes for 15 minutes. They were taken out again immersed in a cold-water bath and cooled to room temperature (about 10 minutes). Then the contents of each were transferred to colorimeter tubes and the optical density was read at 620 nm, after adjusting the colorimeter with reagent blank.

Calculation:

$$mg\ of\ glycogen/gm\ of\ liver \frac{DU}{DS} \times 0.05 \times \frac{Total\ volume\ of\ extract\ (ml)}{Weight\ of\ tissue\ (g)} \times \frac{0.9}{0.01}$$

Where,

DU = Optical density of unknown

DS = Optical density of standard

0.05 = mg of glucose in 2 ml of standard solution

0.9 = Conversion factor.

Changes in Body Weight

The changes in the body weight were calculated by checking the weights of individual animals on the 0th, 5th,10th, and 15th day.

Estimation of Total Cholesterol (TC) [49]

Total cholesterol levels in serum were estimated by the enzymatic cholesterol oxidase–peroxidase (CHOD–POD) method using a commercially available diagnostic kit. Serum samples were obtained by centrifuging the collected blood at 3000 rpm for 10 minutes. In this method, cholesterol esters present in the serum were hydrolyzed by cholesterol esterase to free cholesterol, which was then oxidized by cholesterol oxidase to form hydrogen peroxide. The hydrogen peroxide formed reacted with phenol and 4-aminoantipyrine in the presence of peroxidase enzyme to produce a red-colored quinonimine complex. The intensity of the color produced was measured spectrophotometrically at 505 nm against a reagent blank. The total cholesterol concentration was expressed in mg/dL.

Estimation of Triglycerides (TG) [13]

Serum triglyceride levels were estimated by the enzymatic glycerol phosphate oxidase–peroxidase (GPO–POD) method using a commercially available diagnostic kit. Blood samples collected from overnight fasted experimental animals were centrifuged at 3000 rpm for 10 minutes to separate the serum. For the assay, working reagent was added into labeled test tubes for blank, standard, and test samples. Standard solution and serum samples were added separately to the respective tubes and mixed thoroughly. The reaction mixture was incubated at 37°C for 10 minutes. After incubation, the absorbance of the colored complex formed was measured spectrophotometrically at 505 nm against the reagent blank.

Estimation of Low-Density Lipoprotein (LDL) [14-15]

Low Density Lipoprotein (LDL) cholesterol levels were estimated indirectly using Fried Ewald's formula after determining serum Total Cholesterol (TC), Triglycerides (TG), and High-Density Lipoprotein (HDL) levels. Blood samples collected from overnight fasted experimental animals were centrifuged at 3000 rpm for 10 minutes to obtain serum. Serum TC, TG, and HDL were estimated using standard enzymatic methods with commercially available diagnostic kits. LDL cholesterol concentration was then calculated mathematically and expressed in mg/dL.

Estimation of High-Density Lipoprotein (HDL) [16]

High Density Lipoprotein (HDL) cholesterol was estimated using a precipitation method followed by enzymatic CHOD–POD analysis with a commercially available diagnostic kit. Blood samples collected from overnight fasted experimental animals were centrifuged at 3000 rpm for 10 minutes to obtain serum. In this method, Low Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL) fractions were precipitated using a precipitating reagent containing phosphotungstic acid and magnesium chloride. The mixture was centrifuged to obtain a clear supernatant containing HDL cholesterol. The HDL cholesterol present in the supernatant was then estimated enzymatically by the cholesterol oxidase–peroxidase method. The intensity of the colored complex formed was measured spectrophotometrically at 505 nm. The HDL cholesterol concentration was expressed in mg/dL.

Estimation of Very Low-Density Lipoprotein (VLDL) [17]

Very Low-Density Lipoprotein (VLDL) cholesterol levels were estimated indirectly from serum triglyceride values using Fried Ewald's formula. Blood samples collected from overnight fasted experimental animals were centrifuged at 3000 rpm for 10 minutes to separate the serum. Serum triglyceride levels were determined by the enzymatic GPO–POD method using a commercially available diagnostic kit. VLDL cholesterol concentration was then calculated mathematically and expressed in mg/dL.

Serum Insulin Estimation [18]

Serum insulin levels were estimated to assess the effect of Ficus carica extract on insulin secretion in streptozotocin-induced diabetic rats. At the end of the experimental period, blood samples were collected from overnight fasted animals through retro-orbital plexus or cardiac puncture under light anesthesia. The collected blood was allowed to clot and centrifuged at 3000 rpm for 10 minutes to obtain serum. Serum insulin concentration was determined using a commercially available rat insulin ELISA kit according to the manufacturer's instructions. The absorbance was measured using a microplate reader, and insulin levels were expressed as µIU/mL. The

obtained values were compared among all experimental groups to evaluate the antidiabetic potential of the test extract.

Estimation of Total Proteins [19]

Total protein levels were estimated to evaluate the metabolic status and hepatic function in experimental diabetic rats treated with Ficus carica extract. At the end of the treatment period, blood samples were collected from overnight fasted animals and centrifuged at 3000 rpm for 10 minutes to separate the serum. Serum total protein concentration was determined by the Biuret method using a commercially available diagnostic kit. In this method, proteins present in the serum react with copper ions in alkaline medium to form a violet-colored complex, and the intensity of the color produced was measured spectrophotometrically at 540 nm. The total protein concentration was expressed in g/dL and compared among different experimental groups.

Estimation of Superoxide Dismutase (SOD) [20]

Principle: This method is based on the inhibition of NADH-dependent nitro blue tetrazolium reduction by dismutase. Inhibition of the chromogen formation by superoxide dismutase was linear with an increase in enzyme concentration.

Specimen: The liver and kidney were homogenized in sodium pyrophosphate buffer PH 8.3 and the homogenates were used for the assay.

Reagents: Sodium pyrophosphate buffer 0.052M pH 8.3. Phenazine methosulfate (186 µM). NBT (300µM) 2.6034g in 10 ml water. NADH (780µM) 9 mg in 10 ml water.

Procedure: 1.2ml sodium pyrophosphate buffer, 0.1ml of Phenazine metho sulfate, and 0.3ml of NBT were added to the test tube. 1.2ml homogenate was added to the test tube. The reaction was started by the addition of 0.2 ml of NADH. After incubation at 30°C for 90 sec, the reaction was stopped by the addition of 1ml glacial acetic acid. The reaction mixture was stirred vigorously and shaken with 4ml butanol. The mixture was allowed to stand for 10 minutes, centrifuged and the butanol layer was taken out. The color intensity of the chromogen in the butanol was measured at 560 nm.

Calculation: The Superoxide dismutase activity was determined in the tissue and the results were expressed in U/gm.

Estimation of Glutathione Synthetase (GSH) [21-25]

Principle: Virtually all of the non-protein sulfhydryl groups of RBCs are in the form of reduced GSH. 5, 5' – Di Thio bis (2-Nitro Benzoic acid (DTNB) is a disulfide chromogen that is readily reduced by sulfhydryl compounds to an intensely yellow compound. The absorbance of the reduced chromogen is measured at 412 nm and is directly proportional to the GSH concentration.

Specimen: The intensity of the chromogen in the butanol was measured at 560 nm.

Calculation: The Superoxide dismutase activity was determined in the tissue and the results were expressed in U/gm.

Glutathione - S – Transferase (GST)

Reagents:

1. **Phosphate buffer pH 6.5:** 1.7418 gm of potassium dihydrogen phosphate in 100 ml of distilled water.
2. **GSH (30mM):** 16 mg of GSH in 2 ml of double distilled water.
3. **CDNB (1- chloro – 2,4, dinitrobenzene):** 62 mg CDNB in 10 ml ethanol.

Procedure: 1 ml of CDNB solution was added to 0.6 ml of supernatant of kidney homogenate. 2.2 ml of phosphate buffer pH 6.5 was added to it. This was then incubated at 37 °C for 5 minutes. 0.1 ml of 30 mM GSH solution was added. The absorbance was read at 340 nm at intervals of 1, 2, 3, 4, and 5 minutes. The blank reading was carried out in the same manner without the homogenate.

Staining process

The histopathological examination included Haematoxylin and Eosin staining of the tissues to observe any morphological changes in the cells present. The same tissue blocks were used for triple staining to differentiate between alpha, beta, and delta cells.

a) Haematoxylin and Eosin staining Preparation of Haematoxylin solution:

Haematoxylin (2 g) was dissolved in absolute alcohol followed by the addition of glycerol (100 ml), distilled water (100 ml), glacial acetic acid (100 ml), and potash alum in excess. The solution was allowed to stand for a few days. Preparation of Eosin solution: A 5% eosin solution in distilled water was made with eosin G.

b) Triple staining

The following reagents were prepared for the procedure. 0.03 % of silver nitrate solution by dissolving 30 mg of silver nitrate in distilled water. This solution was prepared freshly. Reducing solution: This was prepared freshly by dissolving 1g of hydroquinone and 5 g of sodium sulfite in 100 ml of distilled water. Aldehyde Fuchsin solution: This was prepared three days before the experiment. 0.5% of basic fuchsin in 60% alcohol was prepared (500mg in 100 ml of 60% alcohol). To this solution, 1.5 ml of concentrated hydrochloric acid and 1 ml of paraldehyde solution were added. This was then stored in the refrigerator for three days to make ready when the color changed to gentian violet. Lead Haematoxylin: 50 ml 5% lead nitrate solution was mixed with the same volume of saturated ammonium acetate solution. This was filtered and 2 ml of 37% formaldehyde solution was added to it. 0.2 g of haematoxylin was dissolved in 1.5 ml of 95% alcohol 10 ml of the above solution and 10 ml of distilled water was added to it. This was filtered and the volume was made up to 75 ml. The tissue was washed, dehydrated with alcohol, cleared with xylene, and paraffin blocks were made. Serial sections of 5-micron thickness were cut using a rotary microtome. The sections were then deparaffinized with xylene and hydrated in descending grades of alcohol. The slides were then placed in 0.03% of solution silver nitrate overnight at 37 oC. They were then transferred to freshly prepared reducing solution followed by rinsing in aldehyde fuchsin solution for 30 seconds and rinsing in three changes of distilled water. The tissues were then rinsed in lead hematoxylin solution and finally rinsed in three changes of water. The sections were then dehydrated in ascending grades of alcohol (50, 70, 90 %, and ending in absolute alcohol for 2 minutes each) and then cleared in xylene and mounted using DPX mounting.

STATISTICAL ANALYSIS

The results of biochemical estimations were reported as mean ± S.E.M The total variation present in the data was analyzed by one-way analysis of variance (ANOVA). Differences among the means were analyzed by Dunnett's test. For this, a window-based PRISM computer package was used.

RESULTS

Percentage of yield

$$Percentage\ of\ yield = \frac{Weight\ of\ crude\ extract}{Weight\ of\ dried\ material} \times 100$$

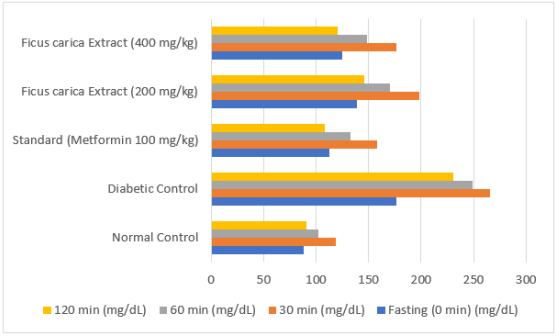
$$Percentage\ of\ yield = \frac{26g}{200g} \times 100 = 13\%$$

50gms of drug dissolved in 200ml of solvent in 1:4 Ratio

Oral Glucose Tolerance Test (OGTT)

Group	Fasting (0 min) (mg/dL)	30 min (mg/dL)	60 min (mg/dL)	120 min (mg/dL)
Normal Control	88.4 ± 2.1	118.6 ± 3.4	102.3 ± 2.8	90.5 ± 2.2
Diabetic Control	176.5 ± 4.6	265.8 ± 5.2	248.7 ± 4.9	230.4 ± 4.3
Standard (Metformin 100 mg/kg)	112.3 ± 3.2	158.6 ± 4.1	132.5 ± 3.5	108.7 ± 2.9
Ficus carica Extract (200 mg/kg)	138.7 ± 3.8	198.5 ± 4.6	170.2 ± 4.0	145.6 ± 3.4
Ficus carica Extract (400 mg/kg)	124.6 ± 3.5	176.4 ± 4.2	148.3 ± 3.7	120.8 ± 3.1

The diabetic control group showed significantly elevated blood glucose levels at all time intervals compared to the normal control group. Treatment with Ficus carica extract produced a dose-dependent reduction in blood glucose levels during the OGTT. The higher dose (400 mg/kg) showed better glucose lowering activity, comparable to the standard drug Metformin.

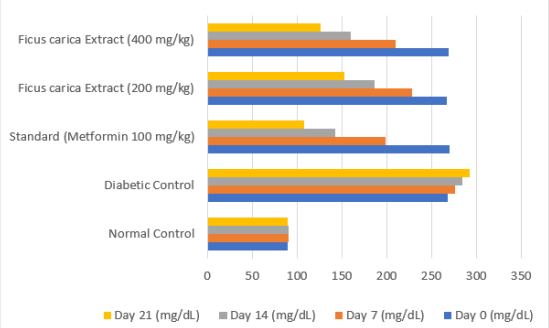


Fasting Blood Sugar (FBS)

Group	Day 0 (mg/dL)	Day 7 (mg/dL)	Day 14 (mg/dL)	Day 21 (mg/dL)
Normal Control	89.2 ± 2.3	90.4 ± 2.1	91.1 ± 2.4	89.8 ± 2.0
Diabetic Control	268.5 ± 5.6	276.4 ± 6.2	284.8 ± 5.9	292.3 ± 6.5
Standard (Metformin 100 mg/kg)	270.2 ± 5.1	198.6 ± 4.8	142.5 ± 3.9	108.4 ± 3.1
Ficus carica Extract (200 mg/kg)	267.4 ± 5.3	228.7 ± 4.9	186.3 ± 4.4	152.6 ± 3.8
Ficus carica Extract (400 mg/kg)	269.1 ± 5.5	210.4 ± 4.6	160.2 ± 4.1	126.8 ± 3.5

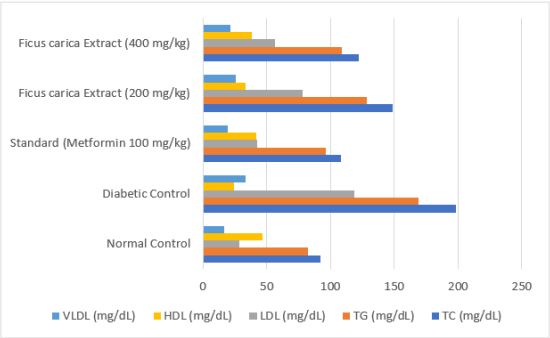
The diabetic control group exhibited persistent elevation in fasting blood glucose levels throughout the experimental period. Treatment with Ficus carica extract significantly reduced fasting blood glucose levels in a dose-dependent manner. The higher dose (400 mg/kg) showed greater

antihyperglycemic activity and produced results comparable to the standard drug Metformin.



Lipid profile (TC, TG, LDL, HDL, VLDL) in diabetic

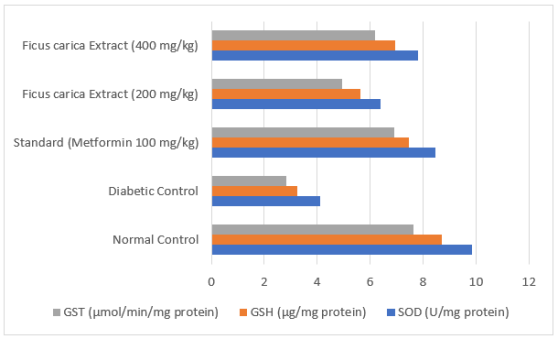
Group	TC (mg/dL)	TG (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	VLDL (mg/dL)
Normal Control	92.4 ± 2.6	82.4 ± 2.3	28.6 ± 1.4	46.8 ± 1.9	16.5 ± 0.8
Diabetic Control	198.7 ± 5.2	168.7 ± 4.8	118.4 ± 3.7	24.3 ± 1.2	33.7 ± 1.0
Standard (Metformin 100 mg/kg)	108.5 ± 3.1	96.5 ± 3.1	42.7 ± 1.8	41.6 ± 1.6	19.3 ± 0.7
Ficus carica Extract (200 mg/kg)	148.6 ± 4.0	128.4 ± 3.9	78.5 ± 2.6	33.2 ± 1.4	25.7 ± 0.8
Ficus carica Extract (400 mg/kg)	122.3 ± 3.5	108.6 ± 3.4	56.4 ± 2.1	38.5 ± 1.5	21.7 ± 0.7



The diabetic control group showed significant elevation in serum TC, TG, LDL, and VLDL levels with a reduction in HDL levels compared to the normal control group. Treatment with Ficus carica extract significantly improved the lipid profile in a dose-dependent manner. The higher dose (400 mg/kg) produced better antihyperlipidemic activity and showed results comparable to the standard drug Metformin.

(SOD), (GSH), Glutathione - S – Transferase (GST)

Group	SOD (U/mg protein)	GSH (µg/mg protein)	GST (µmol/min/mg protein)
Normal Control	9.84 ± 0.32	8.72 ± 0.28	7.65 ± 0.24
Diabetic Control	4.12 ± 0.18	3.26 ± 0.14	2.84 ± 0.11
Standard (Metformin 100 mg/kg)	8.46 ± 0.27	7.48 ± 0.25	6.92 ± 0.20
Ficus carica Extract (200 mg/kg)	6.38 ± 0.21	5.64 ± 0.19	4.96 ± 0.16
Ficus carica Extract (400 mg/kg)	7.82 ± 0.25	6.95 ± 0.23	6.18 ± 0.18



The diabetic control group exhibited a significant decrease in antioxidant enzyme levels such as Superoxide Dismutase (SOD), Reduced Glutathione (GSH), and Glutathione-S-Transferase (GST) compared to the normal control group, indicating oxidative stress associated with diabetes. Treatment with Ficus carica extract significantly restored antioxidant enzyme levels in a dose-dependent manner. The higher dose (400 mg/kg) showed marked antioxidant activity comparable to the standard drug Metformin.

DISCUSSION

The present study was carried out to evaluate the glucose lowering and antioxidant potential of Ficus carica extract in streptozotocin-induced diabetic rats. Streptozotocin administration successfully induced experimental diabetes, as evidenced by persistent hyperglycemia, altered lipid profile, and reduction in antioxidant enzyme levels in the diabetic control group. STZ is known to selectively damage pancreatic β-cells through oxidative stress and free radical generation, resulting in impaired insulin secretion and elevated blood glucose levels. Preliminary phytochemical screening of Ficus carica extract revealed the presence of flavonoids, phenolic compounds, tannins, glycosides, saponins, alkaloids, and terpenoids. These phytoconstituents are well known for their antidiabetic, antihyperlipidemic, and antioxidant activities. Flavonoids and phenolic compounds particularly contribute to free radical scavenging and protection against oxidative damage. The oral glucose tolerance test demonstrated that treatment with Ficus carica extract improved glucose utilization and reduced elevated blood glucose levels in diabetic rats. Similarly, fasting blood sugar levels were significantly reduced in extract-treated groups when compared to the diabetic control group. The higher dose (400 mg/kg) showed better antihyperglycemic activity, which may be attributed to

enhanced insulin secretion, improved peripheral glucose uptake, or inhibition of intestinal glucose absorption. Diabetes is commonly associated with disturbances in lipid metabolism leading to hypercholesterolemia and hypertriglyceridemia. In the present study, diabetic rats showed elevated serum levels of total cholesterol, triglycerides, LDL, and VLDL with decreased HDL levels. Treatment with Ficus carica extract significantly improved these lipid abnormalities, indicating its antihyperlipidemic potential. The improvement in lipid profile may be due to better glycemic control and the presence of bioactive phytoconstituents capable of modulating lipid metabolism. Oxidative stress plays a crucial role in the progression of diabetes and its complications. The diabetic control group exhibited a marked reduction in antioxidant enzymes such as Superoxide Dismutase (SOD), Reduced Glutathione (GSH), and Glutathione-S-Transferase (GST). Administration of Ficus carica extract restored these antioxidant parameters toward normal levels, suggesting significant antioxidant activity. This protective effect may be due to the presence of flavonoids and phenolic compounds that neutralize reactive oxygen species and reduce oxidative stress.

The present study suggests that Ficus carica possesses significant antihyperglycemic, antihyperlipidemic, and antioxidant activities in experimental diabetic rats. The observed pharmacological effects support the traditional use of Ficus carica in the management of diabetes and related metabolic disorders.

Conclusion

The present study extract possesses significant antihyperglycemic, antihyperlipidemic, and antioxidant activities in streptozotocin-induced diabetic rats. Treatment with the extract effectively reduced fasting blood glucose levels, improved oral glucose tolerance, and restored serum insulin levels. In addition, the extract significantly improved altered lipid profile parameters such as total cholesterol, triglycerides, LDL, and VLDL while increasing HDL levels. The study also revealed that Ficus carica enhanced antioxidant defense mechanisms by increasing the levels of Superoxide Dismutase (SOD), Reduced Glutathione (GSH), and Glutathione-S-Transferase (GST), thereby reducing oxidative stress associated with diabetes. The pharmacological effects observed may be attributed to the presence of bioactive phytoconstituents such as flavonoids, phenolics, tannins, and glycosides identified during preliminary phytochemical screening.

Ficus carica has promising therapeutic potential in the management of diabetes mellitus and its associated complications. Further studies involving isolation of active constituents and clinical investigations are required to establish its exact mechanism of action and therapeutic efficacy.

REFERENCES

[1]. Tripathi KD. Essentials of Medical Pharmacology. 5th edition, Jaypee Brothers Medical Publishers Pvt Ltd, New Delhi. 2003. PP 264 – 281.

[2]. Tornsten D, Grenfell A. In: Text Book of Diabetes. John Pickup & Gareth Williams. Blackwell Scientific Publications. Vol- 2. 2003. PP 1991, 651.

[3]. Donald M, Barnette LP, Kral LP. Joslin's Diabetes Mellitus, 14thEd Lippincott Will, and Wilkins, New York. 2003. PP- 2-7.

[4]. Clifford JB, Caroline D. Antidiabetic drugs. British Journal of Cardiol. 10. 2003. PP 128–136.

[5]. Goodman, A., and Gilman. The Pharmacological Basis of Therapeutics, 10th Edition. Mc-Graw Hill Medicinal Publishing Division. 2001. PP 1141-71.

[6]. Douglas R S, Larry W O. Analytical Biochem. 179, 1989, PP 8-18.

[7]. Gupt R, Johri S, Saxena AM. Diabetes mellitus: The Pandemic of 21st century. Asian Journal of Experimental Science. 23(1). 2009. PP 261-68.

[8]. Guyton CA, Hall EJ. Textbook of Medical Physiology, 9th Edition. WB Saunders, Philadelphia. 1996. PP 868-73.

[9]. International Diabetes Fact Sheet. Department of Health and Human Services-Centre for Disease Control and Prevention. 2003.

[10]. Kamboj V.P. Herbal medicine. Current Science. 78. 2000. PP 35- 38.

[11]. Ananthan R, Ramkumar KM, Pari L, Baskar C, Bai VN. Modulatory effects of Gymnema montanum leaf extract on alloxan-induced oxidative stress in Wistar rats. Nutrition. 20. 2004. PP 280-285.

[12]. Ballard AM. Pathophysiology of diabetes. The Diabetes Ready- Reference Guide for Health Care Professionals.

American Diabetes Association. Vol II. 2000. PP 201-217.

[13]. Aneesh TP, Hisham M, Shekar MS, Madhu M. Deepa TV. An international market scenario of traditional Indian herbal drugs- India declining. International Journal of Green Pharmacy. 3(3). 2009. PP184-190.

[14]. Gupta R K, Kesari A N, Murthy P.S., Chandra R, Tandon V, Watal G. Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of Annona squamosa L. in experimental animals. Journal of Ethnopharmacology 99. 2005. PP 75–81.

[15]. Barik R, Jain S, Qwatra D, Joshi A, Tripathi GS, Goyal R. Antidiabetic activity of aqueous root extract of Ichnocarpus frutescens in streptozotocin-nicotinamide induced type-II diabetes in rats. Indian Journal of Pharmacology. 40. 2008. PP 19-22.

[16]. Farnsworth NR. Biological and phytochemical screening of plants. J Pharm Sci. 1966;55(3):225–76.

[17]. Szkudelski T. The mechanism of alloxan and streptozotocin action in β-cells of the rat pancreas. Physiol Res. 2001;50(6):537–46.

[18]. Szkudelski T. The mechanism of alloxan and streptozotocin action in β-cells of the rat pancreas. Physiol Res. 2001;50(6):537–46.

[19]. Gornall AG, Bardawill CJ, David MM. Determination of serum proteins by means of the biuret reaction. J Biol Chem. 1949;177(2):751–66.

[20]. Misra HP, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. J Biol Chem. 1972;247(10):3170–5.

[21]. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem. 1972;18(6):499–502.

[22]. Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. St Louis: Elsevier Saunders; 2012.

[23]. Varley H, Gowenlock AH, Bell M. Practical Clinical Biochemistry. 5th ed. London: William Heinemann Medical Books Ltd; 1980.

[24]. Tietz NW. Fundamentals of Clinical Chemistry. 6th ed. Philadelphia: Saunders Elsevier; 2008.

[25]. Rifai N, Warnick GR, Dominiczak MH. Handbook of Lipoprotein Testing. 2nd ed. Washington DC: AACC Press; 2000.