ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 9, Issue, 11(B), pp. 29570-29578, November, 2018

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

PROTECTIVE ROLE OF *FISCUS BENGALENSIS* LEAF EXTRACT AGAINST STREPTOZOTOCIN INDUCED BIOCHEMICAL ALTERATIONS AND BODY WEIGHTS IN MUSCLE TISSUE OF ALBINO RATS

Obaiah Jamakala

Department of Zoology, Sri Venkateswara University, Tirupati - 517502 A.P. India

DOI: http://dx.doi.org/10.24327/ijrsr.2018.0911.2884

ARTICLE INFO

Article History:

Received 10th August, 2018
Received in revised form 2nd September, 2018
Accepted 26th October, 2018
Published online 28th November, 2018

Key Words:

Diabetes, Streptozotocin, *Fiscus bengalensis,* Blood glucose, Body weight, Oxidative enzymes, Rats.

ABSTRACT

Diabetes mellitus is a chronic disease characterized by high blood glucose levels due to an absolute or relative deficiency of circulating insulin levels. *Fiscus bengalensis* leaf has several biological properties, including anti-diabetic and antioxidant activity. The present study was designed to investigate the anti-diabetic effect of *Fiscus bengalensis* leaf extract against streptozotocin (STZ) induced alterations in blood glucose, body weights and oxidative enzymes in muscle tissues of albino rats. Adult male albino Wister rats, weighing 180 ± 20 g was made diabetic by injecting STZ (40mg/kg body weight) intraperitoneally. Diabetic rats were supplemented with ethanolic extract of *Fiscus bengalensis* leaf extract (250 mg/kg body weight) for a period of three weeks. After this period, rats were decapitated and blood was collected. Fresh muscle tissue was also isolated for the assay of oxidative enzymes such as lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), malate dehydrogenase (MDH) and glucose-6-Phosphate dehydrogenase (G-6-PDH) status in control and experimental rats. Blood glucose and LDH activity levels were significantly elevated in diabetic rats with decreased body weight, SDH, MDH and G-6-PDH activity levels when compared with control. The above mentioned parameters were significantly restored to near normal by oral administration of *Fiscus bengalensis* leaf extract once daily for three weeks as compared to untreated rats. The results obtained indicated that ethanolic extract has more potent protective action against hyperglycemic condition.

INTRODUCTION

Diabetes mellitus (DM) is a chronic and life long metabolic disorder characterized by hyperglycemia due to disturbance in the group of metabolism of carbohydrates, fat and protein (Koukhdan and Khaksar, 2015). This disease mainly related to insulin deficiency and can involve many organs (Georg and Ludvik, 2000; Nyholm *et al.,* 2000; Palanisamy *et al.,* 2011). In diabetes, the deficiency of insulin leads into a complex series of reactions, which are clinically manifested as hyperglycemia and is characterized by a loss of glucose homeostasis (Shyam *et al.,* 2013). Persistent hyperglycemia in diabetes causes increased production of oxygen free radicals from autoxidation of glucose (Hunt *et al.,* 1990) and glycosylation of protein (Wolff and Dean, 1987) which lead to oxidative stress which is associated with several health complications including antipathies, cardiovascular disorders, blindness, renal failure, neuropathies and cancers (American Diabetes Association, 2006; Mansour *et al.,* 2002; Ashraf and Zare, 2015; Sheweita *et al.,* 2016).

Diabetes mellitus is one of the major global public health problem. The number of people suffering from diabetes is increasing worldwide at an alarming rate. It is a long considered disease of minor significance to world health which is now taking its place as one of the major threats to human health in the 21st century. The past two decades have seen as explosive diabetes worldwide. Pronounced changes in the human environment, in human behavior, lifestyle and accompanied globalization have resulted in escalating rates of both obesity and diabetes. Currently there are over 150 million diabetics worldwide and this number is likely to increase due to increase in sedentary lifestyle, consumption of energy rich diet and obesity (Yajnik, 2001). Recently, a survey estimated that there will be more than 439 million people suffering from diabetes in nearly all countries by the year 2030 (Shaw *et al.,* 2010). The countries with the largest number of diabetic people

Corresponding author:* **Obaiah Jamakala
Department of Zoology, Sri Venkateswara University, Tirupati - 517502 A.P. India

will be India, China and USA by 2030. India has today become the diabetic capital of the world with over 20 million diabetics and this number is set to increase to 57 million by 2025 (Sharma *et al.*, 2010).

In modern medicine, there is still no satisfactory effective therapy available to cure diabetes (Piedrola *et al.,* 2001). Many synthetic remedies like sulfonylurea, insulin injection are used which are associated with various undesirable side effects (Patil *et al*., 2011). Management of diabetes without any side effect is still a challenge to the medical community. There is continuous search for alternative drugs. Therefore it is prudent to look for options in herbal medicines for diabetes (Prasad *et al.*, 2009). Thus due to an increase in demand by patients to use natural products with anti-diabetic activity investigations on hypoglycemic agents derived from medicinal plants have gained popularity in recent years (Mohd *et al.*, 2009). Compared to synthetic drugs, herbal preparations are frequently considered to be less toxic with fewer side effects (Osadolor *et al.*, 2011).

The tribal and rural population of India is highly dependent on the medicinal plant therapy for meeting their health care needs. There is an urgent need to formulate some effective herbal medicinal preparations either with single plant or in combination with different plants after clinical trials for effective treatment and control of diabetes mellitus. Many indigenous medicinal plants have been found to be useful for the successful management of diabetes (Joy *et al.*, 1999). Among the several available medicinal plants, *Fiscus bengalensis* is the most effective medicinal plant to control the diabetes.

Ficus bengalensis is a large tree with aerial roots. It is an Indian Banyan tree and grows wild in lower Himalayas and is found all over India. Different parts of the tree have been found to possess medicinal properties: leaves are good for ulcers and diabetic, aerial roots are useful in treating gonorrhea, seeds and fruits are used as cooling agent and tonic as well (Gayathri and Krishnan, 2008; Ahmed *et al.,* 2011). *F. benghalensis* is one of the most widely explored medicinal plants for the antidiabetic activity wherein, the antidiabetic potential of various parts of *F. benghalensis*, particularly of the bark and leaves have been evaluated in experimental diabetes using alloxan/ streptozotocin as diabetogenic compounds in animal models. It is one medicinal plant whose active components such as perlargonidin derivatives, leucopelargonin derivatives and α-amyrin acetate have been extensively evaluated for the anti-diabetic activity *in vivo*.

Based on the medicinal importance of *Fiscus bengalensis,* the present study was designed to investigate the anti-diabetic effect of *Fiscus bengalensis leaf* extract against streptozotocin (STZ) induced alterations in blood glucose, body weights and oxidative enzymes in muscle tissues of albino rats.

MATERIALS AND METHODS

Chemicals

All the chemicals used in the present study were Analar Grade (AR) and were obtained from Sigma (St. Louis, MO, USA), Fisher (Pitrsburg, PA, USA), Merck (Mumbai, India), Ranbaxy (NEW Delhi, India), Qualigens (Mumbai, India) scientific companies.

Preparation of Fiscus bengalensis leaf extract

The fine powder of *Fiscus bengalensis* leaf were purchased (AGMARK symbol) in Tirupati, Andhra Pradesh. The power is extracted by cold percolation with 95% ethanol for 24h. The extract was recovered and 95% ethanol was further added to the plant material and the extraction was continued. The process was repeated three times. The three extractions were pooled together, combined, filtered and the filtrate was concentrated to dryness under reduced pressure in rotary evaporator. The resulting ethanol extract was air dried. Finally crude ethanol extract of *Fiscus bengalensis* leaf was obtained. Without any further purification the plant crude ethanol extract was used in the present study. Dose equivalent to 250mg kg/body was calculated and suspended in 2% V/V Tween 80 solution for the experiment.

Animals

Three months old Wistar strain albino rats weighing 180 ± 20 g were chosen for the present study. The animals were obtained from Sri Venkateswara Traders, Bangalore, Karnataka, India and were kept in stainless steel mesh cages, housed under standard laboratory conditions (23 ± 2°C, 50 ± 20% relative humidity, 12‑h light‑dark cycle) with standard rat chow (Sai Durga Feeds and Foods, Bangalore, India) and drinking water ad libitum. The rats were acclimatized to the laboratory conditions for 10 days. The protocol and animal use has been approved by the Institutional Animal Ethics Committee (Resol. No. 10(ii)/a/CPCSCA/ IAEC/SVU/AUR‑JO dt 22‑12‑2008), Sri Venkateswara University, Tirupati, Andhra Pradesh, India.

Induction of Diabetes

Diabetes was induced in overnight fasted male Wistar rats by a single intraperitoneal injection (I.P.) of freshly prepared solution of streptozotocin (40 mg/kg body weight) in 0.1 M cold sodium citrate buffer (pH 4.5). After injection, they had a free access to food, water and were given 5% glucose solution to drink overnight to counter hypoglycemic shock. Diabetes in rats was identified by moderate polydipsia and marked polyuria. From the second day onwards fasting blood samples were collected from the rats by tail vein and blood glucose was measured by Accu chek Sensor comfort glucometer (Manufacture-Johnson and Johnson) to know the induction of diabetes. If the blood glucose levels were more than 300mg/dL, insulin (IIU Protamine Zinc Insulin) is given to the diabetic rats for diabetic condition for one week. After one week the rats with hyperglycemia (blood glucose level 250mg/dL) were selected and used for the experiment (Radha Madhavi *et al.,* 2012).

Experimental design

In the present experiment totally 18 rats were used. They were separated into three groups of 6 rats each.

Group -1 : Normal Control rats (were given 0.5 mL of 0.9% saline orally for 21 days).

Group- 2 : Diabetic rats (STZ 40 mg/kg body weight)

Group -3 : Diabetic rats treated with 250 mg/Kg body weight of *Fiscus bengalensis* leaf extract orally for 21 days.

Toward the study's end (21 days), the animals were sacrificed by cervical decapitation between 9:00 and 11:00 am to minimize diurnal variation. The blood was gathered. The muscle tissue was dissected and washed with ice-cold saline immediately to remove blood.

Estimation of Blood glucose

Blood glucose levels were Estimated by using Accu Chek glucometer (Sensor Comfort).

Body Weight Changes

Body weights of all groups (three) of rats were recorded before and after treatments. The body weights of all groups were recorded at an interval of one week till the completion of the experiential period (21 days).

Glucose-6-Phosphate dehydrogenase (G-6-PDH) (E.C: 1.1.1.49)

Glucose-6-posphate dehydrogenase activity was assayed by the method of Lohr and Waller (1965), as modified by Mastanaiah *et al.,* (1978). 10% (W/V) Muscle tissue homogenates were prepared in ice cold sucrose 0.25 M solution and centrifuged at 1000g for 15 min at 4^0C. The reaction mixture in a total volume of 2 ml contained 100µ moles of sodium phosphate buffer (pH 7.4), 20µ moles of glucose-6-phosphate, 2µ moles of INT and 0.3µ moles of NADP. The reaction was initiated by adding 0.5ml containing 50mg of tissue as an enzyme source. The reaction mixture was incubated at 37°C for 30 min and the reaction was stopped by the addition of 5 ml of glacial acetic acid. The formazan formed was extracted with 5 ml of toluene at 5°C. The optical density of the formazan was read at 495nm against the toluene blank. The activity was expressed in µ moles of formazan formed/ mg protein / hour.

Lactate dehydrogenase (LDH) (L-lactate: NAD^+ Oxidoreductase - E.C: 1.1.1.27)

Lactate Dehydrogenase activity was determined by the method described by Nachlas *et al.,* (1960) as suggested by Prameelamma and Swami (1975) with slight modifications. 10% (W/V) homogenates of the Muscle tissues were prepared in ice cold 0.25 M sucrose solution and centrifuged at l000g for 15 minutes at 4°C. The supernatant fraction was used for enzyme assay. The reaction mixture in a final volume of 2 ml contained 40 (µ moles of sodium lactate, 100 µ moles of phosphate buffer (pH 7.4), 0.1 µ mole of NAD and 4 µ moles of INT. The reaction was initiated by the addition of 0.2 ml of homogenate containing 20 mg of tissue as an enzyme source and incubated for 30 minutes at 37°C and the reaction was stopped by the addition of 5 ml of glacial acetic acid. Zero time controls (ZTC) were maintained by addition of 5 ml of glacial acetic acid prior to the addition of the enzyme source to the incubation mixture. The formazan formed was extracted over night into 5 ml of toluene at 5^0C. The color developed was measured at 495nm in a Spectrophotometer against the toluene blank. The enzyme activity was expressed in µ moles of formazan formed / mg protein / hour.

Succinate dehydrogenase (SDH) (Succinate acceptor oxidoreductase - E.C: 1.3.99.1)

The specific activity of SDH was assayed by the method of Nachlas *et al.,* (1960) as suggested by Prameelamma and Swami (1975) with slight modifications. 10% (W/V) homogenates of the Muscle tissues were prepared in ice cold 0.25 M sucrose solution and centrifuged at l000g for 15 minutes at 4°C. The supernatant fraction was used for enzyme assay. The reaction mixture in a final volume of 2 ml contained 40µ moles of sodium succinate and 100µ moles of phosphate buffer (pH 7.0) and 4µ moles of INT. The reaction was initiated by adding 0.2 ml of homogenate containing 20 mg of tissue as an enzyme source. The incubation was carried out for 15 min at 37°C and the reaction was stopped by the addition of 5 ml of glacial acetic acid. The subsequent steps were followed same as described for LDH. The activity was expressed in µ moles of formazan formed / mg protein / hour.

Malate dehydrogenase (MDH): (L-Malate NAD^+ Oxidoredutase (E.C.1.1.1.37)

Malate dehydrogenase activity was assayed by the method of Srikanthan and Krishna murthy (1955). Muscle tissue homogenate was prepared in ice-cold 0.25M sucrose solution and centrifuged at 2000 rpm for 15 minutes. The supernatant fraction was used for the assay of the enzyme. The final 2.0 ml volume reaction mixture containing 40µ moles of sodium malate, 100µ moles of phosphate buffer (pH 7.4) and 4µ moles of INT. The reaction was initiated by the adding of 0.5 ml of enzyme source. The incubation was for 30 minutes at 37^0C and the reaction was blocked by the addition of 5 ml of glacial acetic acid. The formazan formed was extracted over night in 5 ml of toluene at 5^oC. The color developed was measured at 495nm in spectrophotometer against a toluene blank and the activity of MDH was expressed as µ moles of formazan formed / mg protein / hour.

Statistical analysis

All values were expressed as mean ± SD. The statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS and the Duncan's Multiple Range Test (DMRT). A value of $p < 0.05$ was considered to indicate a significant difference between groups.

RESULTS

Body weights and Blood glucose levels were measured in control, diabetic, diabetic treated with *Fiscus bengalensis leaf* extract groups before and after treatment. Oxidative enzymes such as lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), malate dehydrogenase (MDH) and glucose-6-Phosphate dehydrogenase (G-6-PDH) status were estimated in control and experimental rats.

Body Weights

Body weights of rats were measured using a digital balance at an interval of 10 days during the experimental period. The initial average weight of animals was in the range of 180 ± 20g. A vast reduction in the body weight was seen in STZ prompted untreated diabetic control (Group II) rats when compared with normal rats (Group I). Whereas significant increment observed in the body weight of diabetic rats treated with *Fiscus bengalensis leaf* extract.

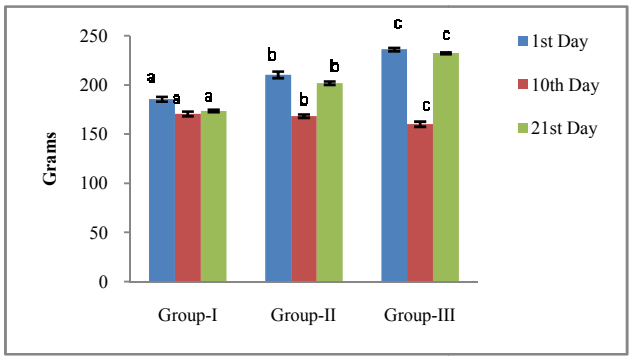


Fig 1 Effect of *Fiscus bengalensis leaf* extract on body weight in normal and experimental rats

- Values are expressed as Mean ± SD (n = 6 rats in each group).
- Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT).
- $^{b}p < 0.05$ as compared with normal rats^{a}.
- $^{c}p < 0.05$ as compared with diabetic control^{b}.

Blood Glucose

Blood glucose levels were measured in control, diabetic, diabetic treated with *Fiscus bengalensis leaf* extract groups before and after treatment. Blood glucose of the diabetic rats (Group II) was higher than the normal rats (Group I). Following oral administration of *Fiscus bengalensis leaf* extract at the dose of 250 mg/kg the blood glucose levels were significantly (P<0.05) reduced.

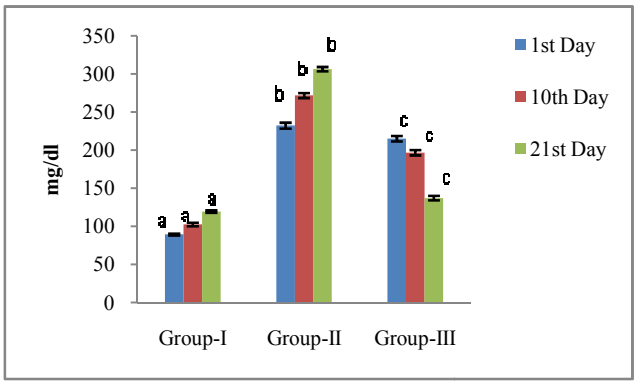


Fig 2 Effect of *Fiscus bengalensis leaf*extract on blood glucose level of normal and experimental rats

- Values are expressed as Mean ± SD (n = 6 rats in each group).
- Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT).
- $^{b}p < 0.05$ as compared with normal rats^{a}.
- $^{c}p < 0.05$ as compared with diabetic control^{b}.

Oxidative enzymes status

Fig.3 explains the oxidative enzymes status in control and experimental groups of rats. LDH activity was significantly ($p < 0.05$) elevated in group II (Diabetic) rats when compared with the control (group I) rats. However, SDH, MDH and G-6-PDH activities were significantly ($p < 0.05$) decreased in STZ induced rats (group II) when compared to the control group. Administrations of ethanolic extract of *Fiscus bengalensis* leaf to diabetic rats (Group III), the elevated LDH activity was progressively decreased to near normal level when compared with the diabetic group. Whereas the decreased SDH, MDH and G-6-PDH enzymes activities were significantly ($p < 0.05$) elevated in *Fiscus bengalensis* leaf extract supplemented rats.

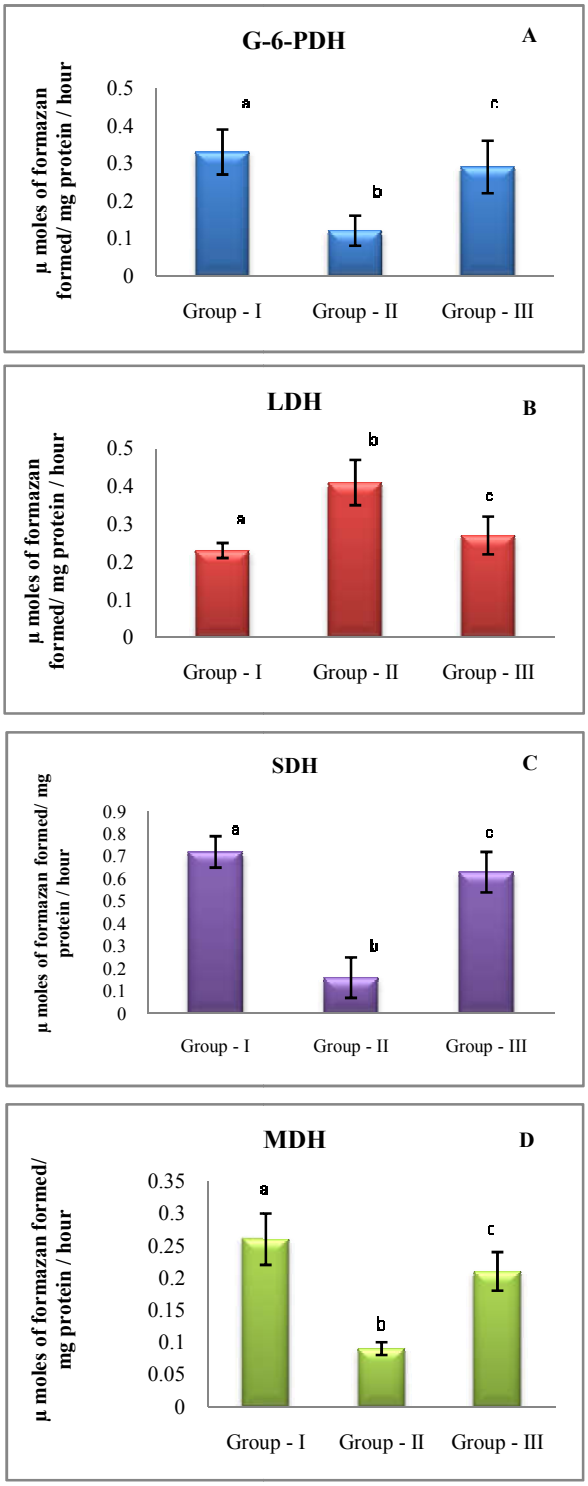


Fig 3 (A-D) Effect of *Fiscus bengalensis* leaf extract on the activities of G-6-PDH, LDH, SDH and MDH respectively in the muscle tissue of normal and experimental rats

- Values are expressed as Mean ± SD (n = 6 rats in each group).
- Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT).
- [b]$p < 0.05$ as compared with normal rats[a].
- [c]$p < 0.05$ as compared with diabetic control[b].

DISCUSSION

Diabetes mellitus is the most common metabolic disorder that impairs glucose homeostasis resulting in severe diabetic complications due to perturbation in utilization of glucose. The present study was mainly focused on the alterations of blood glucose, body weights and oxidative enzymes status.

Most of the body cells use the sugar called glucose as their major source of energy. Glucose molecules are broken down within cells in order to produce adenosine triphosphate (ATP), energy-rich molecules that power numerous cellular processes. Glucose molecules are delivered to cells by the circulating blood and therefore, to ensure a constant supply of glucose to cells, it is essential that blood glucose levels be maintained at relatively constant levels. Level constancy is accomplished primarily through negative feedback systems, which ensure that blood glucose concentration is maintained within the normal range of 70 to 110 mg/dl. The levels of glucose in the blood are monitored by the cells in the pancreas. If the blood glucose level falls to dangerous levels (as in very heavy exercise or lack of food for extended periods), the Alpha cells of the pancreas release glucagon, a hormone which alerts the liver to increase blood glucose levels and converts stored glycogen into glucose (Glycogenesis). Thus glucose is released into the blood stream, increasing blood sugar levels. There are several other causes for an increase in blood sugar levels. Among them accumulation of reactive oxygen spices is a major cause to increase blood sugar levels under diabetic stress.

In the present study blood glucose levels were maintained at normal levels in control rats. After induction of diabetes by STZ, the blood glucose levels were significantly elevated. This may be due to rapid depletion of pancreatic beta cells by DNA alkylation and accumulation of cytotoxic free radicals that is suggested to result from initial islet inflammation, followed by infiltration of activated macrophages and lymphocyte in the inflammatory focus. It leads to a reduction in plasma insulin concentration leading to a stable hyperglycemia state (Szkudelski, 2001). In diabetes, enzymes of glucose and fatty acid metabolism are markedly altered; hence blood glucose levels were increased (Gottried and Rosenberg, 1973; Sochar *et al.,* 1985).

In case of rats which were subjected to both STZ and plant extracts, the decrease in blood glucose was due to the hypoglycemic activity of the plant extracts. Changes of blood glucose levels in the group III where diabetic rats were treated with *Fiscus bengalensis* leaf extract is due to the active components such as perlargonidin derivatives, leucopelargonin derivatives and α-amyrin acetate and bioactive glycoside compounds in them. A number of investigations had reported that the bioactive compounds present in plants such as tannins, 6-gingerol, polyphenolic compounds, flavonoids, triterpenoids posses analgesic, hypoglycemic and other pharmacological actions in various experimental animal models (Jiang *et al.,* 2006; Ojewole, 2006). The plant favorably affected glycolytic, gluoneogenic and liogenic enzymes to restore glucose homeostasis in STZ-induced diabetic rats (Raju *et al.,* 2001). The administration of plant extract to diabetic animals has been shown to lower blood glucose levels and partially restore the activities of key enzymes of carbohydrate and lipid metabolism close to normal levels in animal model systems (Raju *et al.,* 2001; Vats *et al.,* 2003). Various reports demonstrated that the *Fiscus bengalensis* have hypoglycemic, hypocholesterolemic and hyperinsulinomic effects on type 1 and type 2 diabetes mellitus patients and experimental diabetic animals (Shukla *et al.,* 1994; Puri *et al.,* 1995; Gayathri and Krishnan, 2008; Ahmed *et al.,* 2011; Chikezie *et al.,* 2015). Oral administration of *Fiscus bengalensis* leaf extract lowers blood glucose and attenuates STZ induced hyperlipidemia in diabetic rabbits (Shukla *et al.,* 1994; Mahesh *et al.,* 2005; Nishiyama *et al.,* 2005; Sarah Nwozo, *et al.,* 2009). Hence, in the present investigation administration of an ethanolic extract of *Fiscus bengalensis* resulted in a significant reduction in the blood glucose due to the presence of bioactive glycoside which stimulated insulin secretion in the experimental animals (Chikezie *et al.,* 2015).

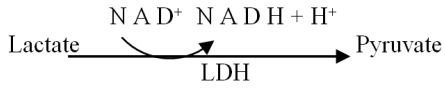
In the present study, STZ induced diabetic rats showed decreased level of body weights. The decrease in body weight in diabetic rats clearly shows a loss or degradation of structural proteins. Weight loss which is one of the clinical features of diabetes mellitus may be due to the degeneration of the adipocytes and muscle tissues to make up for the energy lost from the body due to frequent urination and over conversion of glycogen to glucose. Weight loss is a very serious issue in the management of diabetes mellitus (Akbarzadeh *et al.,* 2007). The control diabetic animals showed a significant decrease in body weight compared with normal rats (Al -Amin *et al.,* 2006). Weight loss during diabetes is mainly related to urinary glucose excretion because cells become to use glucose. Another factor could be also the osmotic diuresis resulting in hyper osmotic dehydration (Kaplan *et al.,* 1982).

In the case of diabetic rats treated with *Fiscus bengalensis* extract (group III), the levels of body weights were increased. They showed almost same response as that of control rats. This shows that *Fiscus bengalensis* plant extract apposes degeneration of the adipocytes and muscle tissues which occurs during diabetic stress in order to make up for the energy lost from the body due to frequent urination and over conversion of glycogen to glucose.

G-6-PDH as an important enzyme in hexose monophosphate (HMP) shunt pathway occurs in the cytosol of the cell and is an alternate pathway of glucose oxidation. This pathway provides a major portion of the cell NADPH, which functions a biochemical reluctant. The activity of G-6-PDH is an index for determining the efficiency of HMP shunt. The activity of G-6-PDH was found to be lowered in the STZ induced diabetic rat tissues (Saraswathi and Swaminathan, 2002; Ashok kumar and Pari, 2005). The same was found in the present study of STZ induced rats. The decrease in the activity of this enzymes in diabetic condition may result in the diminished functioning of HMP shunt and there by the production of reducing equivalents such as NADP and NADPH. The hyperglycemia results in decreased levels of citric acid cycle enzymes and pentose phosphate pathway enzymes as the

phosphorylated glucose enters into the other pathways like gluconeogenesis (Hue, 1987; Gomathy *et al.,* 1990) and glycoprotein synthesis (Rathi *et al.,* 1981). The decreased activity of G-6-PDH affects the concentration NADPH and increases oxidative stress, leading to diabetic complications (Ugochukwu and Babady, 2003). With the treatment of *Fiscus bengalensis* extract to diabetic rats, the G-6-PDH activity was increased. This may be due to the role of antioxidants, which are present in plant extract that elevate the G-6-PDH in diabetic rats and also could be due to elevation of mitochondrial enzymes by plant extract. Hence, the diabetic rats treated *Fiscus bengalensis* extract showed increased activity of G-6-PDH in the present study.

LDH is a key enzyme of anaerobic glycolysis and catalyses the reversible oxidation of lactate to pyruvate in the terminal step of glycolysis. The reaction catalyzed by LDH interlinks anaerobic and aerobic oxidation of glucose. In view of its role in glucose oxidation, the NAD dependent LDH activity was assayed to assess the metabolic significance of this enzyme in compensatory mechanism operating in the tissues of diabetic (STZ induced) and plant extract treated diabetic rats.



In the present investigation, LDH activity was significantly elevated in the diabetic rats when compared to control. The significant increase in the activity of LDH in STZ induced diabetic rats could be due to excessive accumulation of pyruvate. This excessive pyruvate is converted to lactate for which LDH is needed and therefore the activity of LDH may be increased due to less production of insulin in diabetes. Previously several authors have been reported increased LDH activity in diabetes (Goldberg *et al.,* 1977; Jones *et al.,* 1988; Awaji *et al.,* 1990; Ramachandran *et al.,* 2003). Increased activity of LDH interferes with normal glucose metabolism and insulin secretion in the *β*-cells of pancreas and it may therefore be directly responsible for insulin secretory defects in diabetes (Ainscow *et al.,* 2000). When STZ subjected rats were treated with *Fiscus bengalensis* extract, the activity was decreased due to the regulation of NAD^+/NADH ratio following stimulation of oxidation of NADH thereby removing the oxidative stress.

SDH is a key enzyme in Krebs cycle, that catalyses the reversible oxidation of succinate to fumarate. It is the only enzyme in TCA cycle which is an inner membrane bound and involves the direct transfer of hydrogen atoms from the substrate, succinate to flavoprotein FAD.

In the present study, STZ treated rats showed decreased activity of SDH in the muscle tissue. This may be due to the STZ induced oxidative stress condition indicates reduction in the conversion of succinate to fumarate resulting in decreased in oxidative metabolism. During stress condition diversion of phosphoenolpyruvate leads to increased formation of fumarate resulting in product inhibition of SDH (Moorthy, 1983). The decrease in the activities of SDH in tissues of diabetic rats can be associated with enzyme dysfunction due to activation of lipid peroxidation. This may be due to excess production of free radicals to counter these toxic effects. Previously several researchers reported decreased SDH activity in tissues of diabetic animals (Rathi *et al.,* 1981; Chen and Ianuzzo, I982; Hue, 1987; Gomathy *et al.,* 1990; Oexle *et al.,* 1994; Saraswathi and Swaminathan, 2002; Lashin *et al.,* 2006). The decreased activity of SDH in diabetic condition affecting succinate-fumarate conversion indicates the depressed oxidative metabolism at the level of mitochondria. A similar decrease in the activities of citric acid cycle enzymes were also observed by Sener *et al.,* (1990).

The deleterious effects of oxidative stress on mitochondrial respiration, ATP synthesis and membrane properties are mainly connected with extensive peroxidation of membranous polyunsaturated phospholipids, the integrity of which is important for functioning of mitochondrial respiratory chain. The damage of these lipids surrounding membrane bound enzymes alters the function of these enzymes (Narabayashi *et al.,* 1982), primarily those of mitochondrial dehydrogenases (Padma and Setty, 1997: Ramanathan *et al.,* 2003). Long term reactive oxygen species exposure to oxidative stress resulted in oxidative damage of mitochondrial proteins that caused disturbances in mitochondrial energy production.

When STZ subjected rats were treated with *Fiscus bengalensis* extract, the SDH activity was increased. This elevation is due to the antioxidant compounds present in these plant extracts which have the capacity of normalizing the levels of lipid peroxidation. Increase in SDH activity in plant extract treated rats indicates better utilization of energy yielding intermediates by TCA cycle. Same results were seen in UDCA (Ursodeoxycholic acid) treated diabetic and ethanol treated rats. This acid ameliorates the oxidative phosphorylation and normalizing mitochondrial enzymes (Tabouy *et al.,* 1998).

MDH enzyme oxidizes malate into oxaloacetate in the presence of NAD^+, which was the last step of citric acid cycle and plays an important role in citric acid cycle. The study of MDH also has diagnostic significance in several clinical investigations.

In the current study MDH activity was decreased in diabetic rat muscle tissue. The decrease in specific activity of MDH as a consequence of diabetes suggests decreased utilization of malate. The decrease in the activity levels of dehydrogenases is in consistent with the decreased conformation (Cederbaum and Rubin, 1976). An increase in proteolytic activity during diabetes may also be responsible for the decreased MDH activity. MDH activity was decreased in the tissues of diabetic animals in several studies (Ianuzzo and Armstrong, 1976; Saraswathi and Swaminathan, 2002). The increased production of free radicals in mitochondrial cells in the tissue, also a decrease in oxygen consumption respiratory ratio was observed in mitochondria of diabetic rats (Puckett and Reddy, 1979). Lowering in the activity of MDH and increase in NAD^+ / NADH were reported by Obrosova *et al.,* (1999). It has been suggested that the diabetogenecity of STZ is dependent on the inhibition of the activities of citric acid enzymes like MDH, α-ketoglutarate dehydrogenase (Boquist *et al.,* 1985). Diabetes decreased the expression of genes involved in carbohydrate and energy metabolism through effects on known pathways such as glycolysis, TCA cycle and oxidative phosphorylation. In the present study, MDH levels were elevated in *Fiscus bengalensis*

extract treated diabetic rats. This may be due to decreased oxidative stress and increased activities of mitochondrial enzymes. *Fiscus bengalensis* extract has the capacity to increase the activities of mitochondrial enzymes and decrease the oxidative stress. This may due to the antioxidant compounds which are present in *Fiscus bengalensis* extract.

CONCLUSION

This study drawn a conclusion, stating that *Fiscus bengalensis* treatment to diabetic rats may be beneficial to improve the metabolic efficiency and thereby improve the health status. Thus *Fiscus bengalensis* may be useful in the formulation of herbal drugs which can be used in the treatment of diabetes. Since *Fiscus bengalensis* exhibited anti-diabetic activity; it might be clinically useful in the control of human diabetes.

References

Ahmed, F., Chavan, S., Satish, A. and Punith Kumar, R. (2011). Inhibitory activities of *Ficus benghalensis* bark against carbohydrate hydrolyzing enzymes - An *in vitro* study. *Pharmacognosy Journal*, 3 (20): 33-37.

Ainscow, E.K., Zhao, C. and Rutter, G.A. (2000). Acute overexpression of lactate dehydrogenase-A perturbs beta-cell mitochondrial metabolism and insulin secretion. Diabetes, 49: 1149-1155.

Akbarzadeh, A., Norouzian, D., Mehrabi, M.R., Jamshidi, S.H., Farhangi, A., Allah Verdi, A., Mofidian, S.M. and Lame Rad, B. (2007). Induction of diabetes by Streptozotocin in Rats. *Indian Journal of Clinical Biochemistry*, 22: 60-64.

Al-Amin., Martha Thomson Khaled, K., Al-Qattan, Peltonen-Shalaby, R. and Muslim All. (2006). Antidiabetic and hypolipidaemic properties of ginger (Zingiber officinale) in Streptozotocin-induced diabetic rats. *British Journal of Nutrition*, 96: 660-666.

American Diabetes Association. (2006). Diagnosis and classification of diabetes mellitus. Diabetes Care, 29 (1): s43-s48.

Arun Narayannasamy. (2002). Effect of Turmeric on the Enzymes of Glucose Metabolism in Diabetic Rats. The Haworth Press publishers, 10(1): 75 - 84.

Ashok kumar, N. and Pari, L. (2005). Effect of N-benzoyl-D-phenlalanine and metformin on carbohydrate metabolic enzymes in neonatal streptozotoein diabetic rats. Clin Chim Acta, 351:105-13.

Ashraf, H. and Zare, S. (2015). Preventive effects of aqueous extract of *Berberis integerrima* Bge. root on liver injury induced by diabetes mellitus (Type 1) in rats. *Iranian Journal of Pharmaceutical Research*, 14 (1): 335-343.

Awaji, Y., Hastimoto, H., Matsui, Y., Kawaguchi, K., Okumura, K., Lto, T. and Stake, T. (1990). Isoenzyme profiles of creatine kinase, lactate dehydropgenase and aspartate aminotransferase in diabetic heart: comparison with hereditary and catecholamine cardiomyopathies. Cardivasc Res, 24: 547-554.

Boquist, L., Ericsson, I., Lorentzon, R. and Nelson, L. (1985), Alterations in mitochondrial aconitase activity and respiration, and in concentration of citrate in some organs of mice with experimental or genetic diabetes. FEES Lett, 183: 173 - 176.

Cederbaum, A.I. and Rubin, E. (1976). Mechanism of the protective action of cysteine and pencillamine against acetaldehyde-induced mitochondrial injury. Biochem Pharmacol, 25: 2179-2185.

Chen, V. and Ianuzzo, C.D. (I982). Metabolic alterations in skeletal muscle of chronically streptozotocin-diabetic rats. Arch Biochem Biophys, 217: 131-138.

Chikezie, P.C., Ojiako, O.A. and Nwufo, K.C. (2015). Overview of anti-diabetic medicinal plants: The Nigerian Research Experience. *J Diabetes Metab*, 6: 546. doi:10.4172/2155-6156.1000546.

Gayathri, M. and Krishnan, K. (2008). Antidiabetic and ameliorative potential of *Ficus bengalensis* bark extract in streptozotocin induced diabetic rats. *Indian Journal of Clinical Biochemistry*, 23 (4): 394-400.

Georg, P. and Ludvik, B. (2000). Lipids and Diabetes. *J Clin Basic Cardiol*, 3: 159-162.

Goldberg, D.M., Martin, J.V. and Knight, A.H. (1977). Elevation of serum alkaline phosphate activity and related enzymes in diabetes mellitus. Clin Biochem, 10: 8-11.

Gomathy, R., Vijayalekshmi, N.R. and Kurup, P.A. (1990). Hypoglycemic action of the pectin present in the juice of the inflorescence stalk of plantain-mechanism of action. *J Biosci*, 15: 297-303.

Gottried, S.P. and Rosenberg, B. (1973). Improved manual spectrophotometric for determinatiopn of serum triglycerides. Clin Chem, 19:107-108.

Hue, L. (1987). Gluconeogenesis and its regulation. Diabetes Metab Rev, 3: 111-126.

Hunt, J.V., Smith, C.C.T. and Wolff, S.P. (1990). Autoxidative glycosylation and possible involvement of peroxides and free radicals in LDL modification by glucose. Diabetes, 39 (11): 1420-1424.

Ianuzzo, C.D. and Armstrong, R.B. (1976). Phosphofructokinase and succinate dehydrogenase activities of normal and diabetic rat skeletal muscle. Horm Metab Res, 8: 244-245.

Jiang, H., Xie, Z., Koo, H.J., McLaughlin, S.P., Timmermann, B.N. and Gang, D.R. (2006). Metabolic profiling and phylogenetic analysis of medicinal Zingiber species: Tools for authentication of ginger (Zingiber offlcinale Rose). Phytochemistry, 67: 232-244.

Jones, R.G., Grant, P.G., Brown, D., Stickland, M. and Wiles, P.G. (1988). Arise in the plasma activities of hepatic enzymes is not a common consequence of hypoglycaemia. Diabetes Med, 5(3): 253-255.

Joy, K.L. and Kuttan, R. (1999). Antidiabetic activity of Picorrhizakurroaextract. *Journal of Ethnopharmacology*, 167:143-148.

Kaplan, S.A., Lippe, B.M., Brinkman, C.R., Davidson, M.B. and Geffher, M.E. (1982). Diabetes mellitus. Ann Intern Med, 96: 635-649.

Koukhdan, E.T. and Khaksar, Z. (2015). Study of fenugreek seed extract effect (*Trigonella foenum-graecum* L) on histomorphic structure of cervical enlargement of the spinal cord development during gestational age of 20 day offspring of diabetic rats. *Biomedical and Pharmacology Journal*, 8(2): 1333-1340.

Lashin Ossama, M., Pamela, A., Szweda Luke, I. and Szweda Andrea, M.P. (2006). Romani decreased

complex II respiration and HNE-modified SDH subunit in diabetic heart. Free Rad Biol Med, 40: 886-896.

Lohr, G.W. and Waller, H.D. (1974). Glucose-6-phosphate dehydrogenase. In: Bergmeyer, H.U. (ed.), Methods of Enzymatic Analysis. Verlag Chemie, Weinheim, pp636-643.

Mahesh, T., Balasubashini, M. and Menon, V. (2005). Effect of pholo-irradiateit cur¬cumin treatment against oxidative stress in slrcptozolocin-induced diabetic rats. *Journal of Medicinal Food*, 8: 251-255.

Mansour, H.A., Newairy, A.S.A., Yousef, M.I. and Sheweita, S.A. (2002). Biochemical study on the effects of some Egyptian herbs in alloxan-induced diabetic rats. Toxicology, 170 (3): 221-228.

Mastanaiah, S., Chengal Raju, D. and Swami, K.S. (1978). Orcadian rhythmic activity of lipase in scorpion, heterometry fulvipes (C. Koch). Curr Sci, 20(47): 130-131.

Mohd, M., Alam, K.S., Mohd, A., Abhishek, M. and Aftab, A. (2009). Antidiabetic activity of the aqueous extract of Annona squamosa in Streptozotocin induced-hyperglycemic rats. The Pharm Res, 2: 59-63.

Nachlas, M.M., Marguil, S.I. and Seligman, A.M. (1960). A colorimetric method for determination of succinate dehydrogenase activity. *J Biol Chem*, 235: 499-505.

Narabayashi, H., Takeshige, K. and Minakami, S. (1982). Alteration of inner membrane components and damage of electron-transfer activities of bovine heart submitochondrial particles induced by NADPH-dependent lipid peroxidation. The Biochemical Journal, 202: 97-105.

Nishiyama, T., Mae, T., Kishida, H., Tsukagawa, M., Mimaki, Y., Kuroda, M., Sashida, Y., Takahashi, K., Kawada, T., Nakagawa, K. and Kitahara, M. (2005). Curcuminoids and sesquiterpenoids in turmeric (*Fiscus bengalensis* leaf L) suppress an increase in blood glucose level in type 2 diabetic KK-Ay mice. *Journal of Agriculture Food and Chemistry*, 53(4): 959-963.

Nyholm, B., Porksen, N., Juhl, C.B., Gravholt, C.H., Butler, P.C., Weeke, J., Veldhuis, S., Pincus, S. and Schimtz, O. (2000). Assessment of insulin secretion in relatives of patients with type2 (non□insulin dependent) diabetes mellitus: evidence of early beta cell dysfunction. Metabolism, 49: 896-905.

Obrosova, I., Fathallah, L., Lang, H.J. and Greene, D.A. (1999). Evaluation of sorbitol dehydrogenase inhibitor on diabetic peripheral nerve metabolism; a preventive study. Diabetologia, 42: 1187-1194.

Oexle, K., Obserle, J. and Hibner, C. (1994). Insulin-dependent diabetes mellitus in melas-mitochondiropathy: discussion of possible causal relations. Modern Trends Biothermo Kinetics, 3: 279-289.

Ojewole, A. (2006). Analgesic, anti-inflammatory and hypoglycemic effects of ethanol extract of *Zingiber officinale* (Roscoe) and *Rhizomes* (Zingiberaceae) in mice and rats. Phytother Res, 20: 764-772.

Osadolor, H.B., Ariyo, I.I., Emopae, M.C. and Anukam, K.C. (2011). Hypoglycemic effect of unripe pawpasw on streptozotocin induced diabetic albino rats. *Res J Med plants*, 90 - 94.

Padma, G. and Setty, O. H. (1997). Effect of administration of galactosamine hydrochloride on rat liver motochondria. *Indian Journal of Biochemistry and Biophysics*, 34: 296-301.

Palanisamy, M., Ganesan, K. and Murugan, R. (2011). Antibiabetic efficacy of ellagic acid in streptozotocininduced diabetes mellitus in albino wistar rats. *Asian J Pharm Clin Res*, 4(3): 124 - 128.

Patil, S.B., Ghadyale, V.A., Taklikar, S.S., Kulkarni, C.R. and Arvindekar, A.U. (2011). Insulin secretagogue, alpha-glucosidase and antioxidant activity of some selected spices in streptozotocin-induced diabetic rats. Plant Foods Hum Nutr, 66: 85-90.

Piedrola, G., Novo, E., Escober, F. and Garcia Robles, R. (2001). White blood cell count and insulin resistance in patients with coronary artery disease. Ann Endocrinol, 62: 7-10.

Prameelamma, Y. and Swami, K.S. (1975). Gluthathione dehydrogenase activity in normal and denervated gastocnemius muscle of frog, *Rana hyxadactyla*. Curr Sci, 44: 739-740.

Prasad, A.S.K., Kulshreshtha, A. and Qureshi, N. (2009). Antidiabetic activity of some herbal plants in streptozotocin induced diabetic albino rats. *Pak J Nutr*, 8(5): 551-557.

Puckett, S.W. and Reddy, W.J. (1979). A decrease in the malate-aspartate shuttle and glutamate translocase activity in heart mitocbondfia from alloxan-diabetic rats. *J Mol Cell Cardiol* 11: 173-187.

Puri, D., Prabhu, K.M. and Murlhy, P.S. (1995). Hypocholesterolemic effect of the hy-poglycemic principle of fenugreek fTngonelia foenum gmecum) seeds. *Indian J Clin Bioehem*, 9: 13-16.

Radha Madhavi, Y.R., Swapna Rekha, S., Pradeepkiran, J.A., Ismail, S.M., Madhuri, E. and Bhaskar, M. (2012). Protective role of ethanolic extract of *Aloe vera* antioxidant properties on liver and kidney of streptozotocin-induced diabetic rats. *Digest Journal of Nanomaterials and Biostructures*, 7 (1): 175-184.

Raju, J., Gupta, D., Rao, A.R., Yadava, P.K. and Baqucr, N.Z. (2001). *Trigtmella foenumgraecum* (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. Mol Cell Biochem, 224(1-2): 45-51.

Ramachandran, B., kandaswamy, M., Narayanan, V. and Subramanian, S. (2003). Insulin mimetic effects of macrocyclic binuclear oxovanadium complexes on streptozotocin induced experimental diabetes in rats. Diabetes Obes Metab, 5: 455-461.

Ramanathan, K., Shila, S., Kumaran, S. and Paneerselvam, C. (2003). Ascorbic acid and alpha-tocopherol as potent modulators on arsenic induced toxicity in mitochondria. *Journal of Nutritional Biochemistry*, 14: 416-420.

Rathi, A.N., Aruna, V. and Radha Shanmugasundaram, K. (1981). Studies on protein-bound polysaccharide components & glycosaminoglycans in experimental

diabetes-Effect of Glymnema sylvestre, J Exp Biol, 19: 715-721.

Sarah, N., Oluwatosin, A. and Edith, A. (2009). Oral administration of extract from *Fiscus bengalensis* leaf lowers blood glucose and attenuates alloxan induced hyperlipidemia in diabetic rabbits. *Pakistan Journal of Nutrition*, 8 (5): 625-628.

Saraswathi, P. and Swaminathan, G. (2002).Effect of sodium molybdate on carbohydrate metabolizing enzymes in alloxan induced diabetic rats. *The Journal of Nnutritional Biochemistry*, 13(1): 21-26.

Sener, A., Rasschaert, J. and Malaisse, W.J. (1990). Hexose metabolism in pancreatic islets: participation of Ca+2 sensitive to α-ketoglutarate dehydrogenase in the regulation of mitochondrial function. Biochem Biophy Acta, 101(9): 42-50.

Sharma, V.K., Suresh, K., Patel, H.J., Shivakumar, H. (2010). Hypoglycemic activity of *Ficus glomerata* in alloxan induced diabetic rats. *Int J Pharm Sci Rev Res*, 1(2):18-22.

Shaw, J.E., Sicree, R.A. and Zimmet, P.Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Research and Clinical Practice, 87: 4-14.

Sheweita, S.A., Mashaly, S., Newairy, A.A., Abdou, H.M. and Eweda, S.M. (2016). Changes in oxidative stress and antioxidant enzyme activities in streptozotocin induced diabetes mellitus in rats: role of *Alhagi maurorum* extracts. Oxidative Medicine and Cellular Longevity, 1-8.

Shyam, T., Ganapaty, S. and Balakrishnaiah, P. (2013). Antidiabetic activity of *Rotula aquatic* lour roots in streptozotocin induced diabetic rats. American Journal of Phytomedicine and Clinical Therapeutics, 1(7): 530-535.

Sochar, M., Baquer, N.Z. and Mclean, P. (1985). Glucose under utilization in diabetes. Comparative studies on the changes in the activities of enzymes of glucose metabolism in rat kidney and liver. Mol Physiol, 7: 51-68.

Szkudelski, T. (2001). The mechanism of alloxan and streptozotocin action in β-cells of the rat pancreas. Physiol Res, 50: 536-537.

Tabouy, L., Zamora, A.J., Oliva, L., Montet, A.M., Beauge, F. and Montet, J.C. (1998). Ursodeoxycholate protects against ethanol-induced liver mitochondrial injury. Life Scienes, 63: 2259-2270.

Ugochukwu, N.H. and Babady, N.E. (2003). Antihyperglycemic effect of aqueous and ethanolic extracts of *Gongronema latifolium* on glucose and glycogen metabolism in livers of normal and streptozotocin induced diabetic rats. Life Sci, 73:1925-1938.

Vats, V., Yadav, S.P. and Grover, J.K. (2003). Effect of *Trigonella foenumgraecum* on glycogen content of tissues and the key enzymes of carbohydrate metabolism. *J Ethnopharmacol*, 85(2-3): 237-242.

Wolff, S.P. and Dean R.T. (1987). Glucose autoxidation and protein modification: the potential role of autoxidative glycosylation in diabetes. *Biochemical Journal*, 245 (1): 243-250.

Yajnik, C.S. (2001). The insulin resistance epidemic in India: fetal origins, later lifestyle, or both? Nutr Rev, 59:1-9.

Shukla, R., Prabhu, K.M. and Murthy, P.S. (1994). Hypoglycaemic effect of the water extract of *Ficus bengalensis* in alloxan recovered, mildly diabetic and severely diabetic rabbits. *Intl J Diabetes Dev Count*, 14: 78-81.

How to cite this article:

Obaiah Jamakala.2018, Protective Role of Fiscus Bengalensis Leaf Extract Against Streptozotocin Induced Biochemical Alterations and Body Weights In Muscle Tissue of Albino Rats. *Int J Recent Sci Res.* 9(11), pp. 29570-29578.
DOI: http://dx.doi.org/10.24327/ijrsr.2018.0911.2884

****