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Evaluation of Antidiabetic Effect of Seena occindentalis Flower Extracts On an Experimentally Induced Type 2 Diabetes In Rats

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ABSTRACT

Aim of this study to identify the activity of *Senna occidentalis* flower to the antihyperglycaemic activity and hypolipidemic activity using high fat diet-streptozotocin model. Prepare the aqueous ethanolic extract of *Senna occidentalis* flower 250 and 500 mg/kg dose was used to treat the diabetic rat. Low and high dose of *Senna occidentalis* flower extract to evaluate the body weight, food consumption and activity of blood glucose level, oral glucose tolerance test, kidney function test, and liver function test up to 39 days. Raised glycosylation of haemoglobin, which has been seen to be increased over a lengthy period of time in diabetes, is present in uncontrolled diabetes which worst's the condition of this disease.

Different finding suggests that the SOFE stimulates beta cells to secrete more insulin. They also found that HFD-STZ-induced diabetic rats treated with low and high doses of SOFE had lower levels of triglyceride, total cholesterol, very low-density lipoprotein, and low-density lipoprotein and higher levels of high-density lipoprotein, implying that elevated insulin levels may be responsible for these changes. Different compounds are found by using the technique infrared, thin layer chromatography, and high-performance thin layer chromatography. Higher dose indicate less reduction in serum glutamic pyruvic transaminase and serum glutamic oxaloacetic transaminase as compare to the lower dose may be higher dose produce the liver toxicity. For further study it is concluded that the low dose is effective for the animals that cause no toxicity and did not affect any other parts of the body.

Keywords: *Hypolipidemic, hyperglycaemic activity, Senna occidentalis, Streptozotocin, IR, HFD-STZ.*

1. INTRODUCTION

Diabetes mellitus (DM) is one of the most prevailing global health metabolic disorders characterised by high blood glucose levels, glycosuria, hyperlipidaemia, negative nitrogen balance and ketonaemia. It creates huge burden on health care providers. According to WHO predictions, diabetes will be the seventh greatest cause of death globally in 2030 (McIntyre et al., 2019). In diabetes mellitus increase level of blood glucose may be due to the defects in insulin response, secretion or both (insulin is insufficient or inefficient). Various internal and external factors such as modern lifestyle, obesity and genetic mutations may increase the risk of DM (James et al., 2021).

Diabetes is mainly of two types: T1DM (IDDM) and T2DM (NIDDM). Other diabetic pathological conditions include brittle diabetes, neonatal diabetes mellitus, LADA, diabetes MODY, double diabetes, and diabetes insipidus. They are caused by single genetic mutations. During pregnancy, gestational diabetes develops. T1DM and T2DM are caused by complicated interactions between genes and the environmental factors. It may cause inflammation, autoimmune illness, and metabolic stress. When these factors affect β cell function and mass, insulin levels eventually stop responding as well to the body's need for it, leading to hyperglycaemia levels(Abdel-Moneim et al., 2018).

COMPLICATION OF DIABETES MELLITUS

Diabetes complications are prevalent in people with T1DM or T2DM, and they also cause severe morbidity and death. The mortality rate and the patient's quality of life are significantly impacted by these vasculopathies are given in table 1.1(Yamagishi & Imaizumi, 2005). Diabetes complication classified as diabetic ketoacidosis, microvascular and macrovascular. As a primary cause of lower limb amputation, diabetic foot syndrome is characterised by the development of a foot ulcer along with neuropathy, peripheral vascular dysfunction, and infection (Deshpande et al., 2008).

Diabetic ketoacidosis: Hyperglycaemia with a prolonged insulin shortage can lead to DKA, which is the development of ketones in the blood when the body burns fat for energy instead of glucose. Ketones induce death by turning the blood acidic, slowing down all biological functions, causing a coma, and other effects.

Effect of macrovascular disease: This affects the big blood vessels of the circulatory system and may result in 2-4 times increase in the incidence of cerebrovascular and peripheral vascular disease, which can result in ulceration, gangrene, and lower extremity amputations(Boyle, 2007). These macrovascular consequences are basically accelerated types of atherosclerosis in which leukocytes migrate to the site of arterial damage(Ceriello, 2010).

Cerebrovascular disease: Diabetes mellitus causes cerebrovascular disease, which is a serious consequence. Diabetic people have a greater risk of stroke, as well as a higher death rate and a shorter recovery time following a stroke (Caplan, n.d.).TG are normally mildly to moderately raised, LDL cholesterol is mildly high, and HDL is low in diabetic individuals along with insulin resistance, glycation of LDL particles, and enrichment of HDL particles with triglycerides, the lipid abnormalities are linked to reduced lipoprotein lipase activity, increased hepatic VLDL production, and impaired LDL receptor function. In a prospective study, increased triglycerides and low HDL level were found to predict stroke in T2DM individuals (Haffner, n.d.).

Coronary heart disease: coronary artery disease is more likely to occur in people with diabetes. Hyperlipidaemia, characterised by high triglyceride levels and low HDL levels, has been associated with diabetes. Low HDL levels, high VLDL levels, and high total VLDL triglyceride levels have all been linked to an increased risk of CAD in human with type 2 diabetes (Asghar, 2014).

Peripheral arterial disease: It is characterised by artery blockage, lead to decrease in blood flow to the limbs. Endothelial function is impacted by hyperglycaemia, too many free fatty acids in the blood, increased oxidative stress, and inhibition of endothelial nitric oxide synthase. Endothelin-I and angiotensin-II, two potent vasoconstrictors, are increased, whereas prostacyclin and NO are decreased (Jude et al., 2010).

Due to the non-insulin dependence of glucose absorption, hyperglycaemia increases the intracellular concentration of glucose in platelets. This results in a reduction in platelet-derived NO generation and increase in oxygen free radical productionin a peripheral arterial disease. In diabetic patients, calcium haemostasis, which regulates platelet morphology, secretion, aggregation, and thromboxane's disrupted(Beckman et al., 2002).

Effect of microvascular disease: Microvascular problems are caused by destruction of tiny blood vessels and contribute to diabetic neuropathy, nephropathy, and retinopathy (nerve, eye, and kidney disease).

Neuropathy: Neuropathy condition characterised by peripheral, focal, proximal, or autonomic, is the most prevalent of the diabetes complication, affecting over 60% of patients**.** It is a degenerative condition that causes loss of feeling, discomfort, and weakness, and can result in limb amputations. Hyperglycaemia and other metabolic disturbances can harm neurons and nerve tissue.(Pathak, Gupta, and Gilhotra) Ischemic-neuronal damage may be brought on by changes in neurovascular blood flow. The microvascular pathologic character of diabetic neuropathy has been confirmed by the finding that transfer of VEGF to neuronal tissue in experimental diabetic animal models restores blood flow in neuronal tissues and corrects impaired nerve conductivity in diabetic conditions(Beckman et al., 2002).

Nephropathy: With glomerular hyperfiltration, mesangial enlargement, glomerular hypertrophy, and thickening of the glomerular basement membrane, diabetes nephropathy is the primary cause of ESRD and the most common factor in kidney transplantation worldwide. According to Kirti Kaul, ESRD develops in 30-40% of Type 2 diabetics.(Rawat, Singh Dhramshaktu, et al.) The presence of albumin in the urine and its steady augmentation, together with elevated glomerular blood pressure, are symptoms of neuropathy. This ultimately results in renal failure and ERSD(Selby et al., n.d.).

Retinopathy: The pathophysiology of DR includes hyperglycaemia, inflammation, and neuronal dysfunction.(Rawat, Gupta, et al.) Chronic hyperglycaemia causes reactive oxygen species (ROS) to be activated, which contributes to the development of DR by destroying retinal cells. The production of AGEs, enhance the polyol pathway, activate the PKC, and stimulation of oxidative stress that cause cellular damage.(Khan et al.) Antioxidant therapy are used to improve the condition of retinopathy or other microvascular related disease(Selby et al., n.d.).

Table1: Complication of diabetes.

Organ	Effect	Conclusion
Blood vessels	Slowly healing wounds occur due to poor circulation and they can also cause stroke, heart disease, foot and hand gangrene, infections, and erectile dysfunction.	Small or large arteries in the heart, legs, brain, and penis are the building blocks and growth sites for many fatty substances.(Sharma et al.)
Blood	Patients are capable of contact with infections (urinary tract and skin).	Imbalance between white blood cell functions.
Connective tissue	Development of dupuytren's contracture, or a group of symptoms of carpal tunnel.	When the tissue is thick or expands, glucose is not metabolised.
Eyes	When vision is decreased, then blindness occurs.	Diabetic patients damage the small blood vessels of the retina.
Kidney	In this case kidney failure and kidney malfunction occur.	Protein escape into urine. Kidney blood vessels are thick.(Singh et al.)
Nerves	Legs are weak. Patients reduce their sensation, tingling, and pain in their feet and hands.	When the blood supply is insufficient and glucose is not metabolized then nerves are damged
Skin	Diabetic ulcer is developed and healing is poor.	Injury is occured regularly when the circulation of blood in skin is reduced and sensation is decreased.
Autonomic nervous system	Blood pressure fluctuates. Erectile dysfunction arises as a result of impaired digestive function. It gets tough to swallow.	Nerves that control blood pressure and digestion are damaged.

On the market, there are many drugs (glibenclamide, metformin, pioglitazone, and rosiglitazone) available with many side effects. Today, herbal medicines are being used progressively by the general population in all countries as medicines or dietary supplements, either alone or in combination with modern therapeutic agents. *Senna occidentalis* (Family-Leguminosae) has medicinal value in almost all of its parts and is used to treat a wide range of illnesses. Its stem bark, seeds, and roots, for example, haveanti-inflammatory, antiviral, arthritic, hepatoprotective, and antidepressant activity thanks to the presence of various biomarkers like flavonoids and other phenolic acidic compounds. Beta-sitosterol is present in *Senna occidentalis* flowers. Beta-sitosterol has been demonstrated in clinical and experimental investigations to be a plant molecule that functions similarly to cholesterol. It may help lower cholesterol levels by reducing the amount of cholesterol in the diet (Singh et al., 2019). A "high-fat diet" is the main risk factor for obesity. High-fat diets cause insulin resistance across the body, hyperglycemia, alterations in muscle and liver physiology, and abnormalities in insulin signal transduction. The most commonly used diabetes model includes administering a single dose of STZ to adult animals, which induces pancreatic cell death and hyperglycemia as a direct result of insufficient insulin production. Combination of HFD-STZ model is used in this research work according to previous paper (Srivast et al., 2018).

2. MATERIALS AND METHODS

2.1. Chemicals

Metformin, streptozotocin, ethanol, petroleum ethanol, and chloroform purchased from sigma Aldrich. All the other chemicals used in this protocol were finist analytical grade.

2.2. Collection and extraction process of plant

Senna occidentalis flower were collected between September and October at Prayagraj, Uttar Pradesh and were authorised by the Botanical Survey of India. *Senna occidentalis* is a plant that is found in Africa, Asia, Australia, and India (Jammu and Kashmir to Kanyakumari, Haryana) (Shinde et al., 2019). About 3 kg of flowers of *Senna occidentalis*are shade dried. After that, the dried flowers were put in a desiccator to keep them dry until needed. Unwanted particles were then filtered out using different sieve numbers 24. Then, for three days, the seived flowers were deffated in petroleum ether. The extraction carried out at 80°C for three days using a Soxhlet apparatus and aqueous ethanol (Sharma et al., 2014). Aqueous ethanol was concentrated and evaporated in a water bath to produce a gel-like material.

2.3. Acute Oral Toxicity

According to OECD Guideline 423, the LD50 dose was calculated using animal testing. SOFE was given orally using gavage. Each animal received oral gavage doses of 5, 50, 300, and 2000 mg/kg bwt in addition to a constant supply of food and water. The animals showed no discernible side effects after receiving the plant extract for 72 hours. The rats were inspected for any form of evident abnormalities for fourteen days. The amount of *Senna occidentalis* aqueous ethanolic extract employed in this study was 500mg/kg body weight because no animals were harmed (Yadav et al., 2010). *Senna occidentalis* were given to rats with 2% gum acacia.

2.4. Animal Diet

HFD was made in accordance with the study protocol using 45% fat (Vanaspati ghee), 25% sugar, and 30% commercial diet (Srivast et al., 2018)**.**

2.5. Animals

Thirty male wistar rat weigh 140-180g, divided into five groups. Before the experiment, all rats were moved to a quarantine area to adjust to the animal house for two weeks.(Effect et al.) The animals were housed in polypropylene cages with a 12-hour light/dark cycle and maintained at 25 ± 2^0C under normal conditions. Throughout the experiment, rats were fed commercial food and were given access to unlimited amounts of water (Aragão et al., 2009).

2.6. Diabetes induced by chemicals

All the rats were fasted for 12 hrs before the experiment then rats was injected STZ (40 mg/kg bwt) through intraperitoneally to induce T2DM.(Biharee et al.) After being given a low dose of STZ for 72 hours, experimental animals were categorised as diabetic if their postprandial glycemic levels were greater than or equal to 200mg/dl(De MagalhÃes et al., 2019). Metformin was used as the reference medication.

2.7. Dissolution of chemicals and drug

Streptozotocin is freshly prepared in a 0.01M citrate buffer, 4.5pH and metformin was dissolved in water (Alhaider et al., 2011).

2.8. Experimental design

Animals were further separated into five groups, each of which contained six animals, and each group was given its own label.(Rashid et al.)

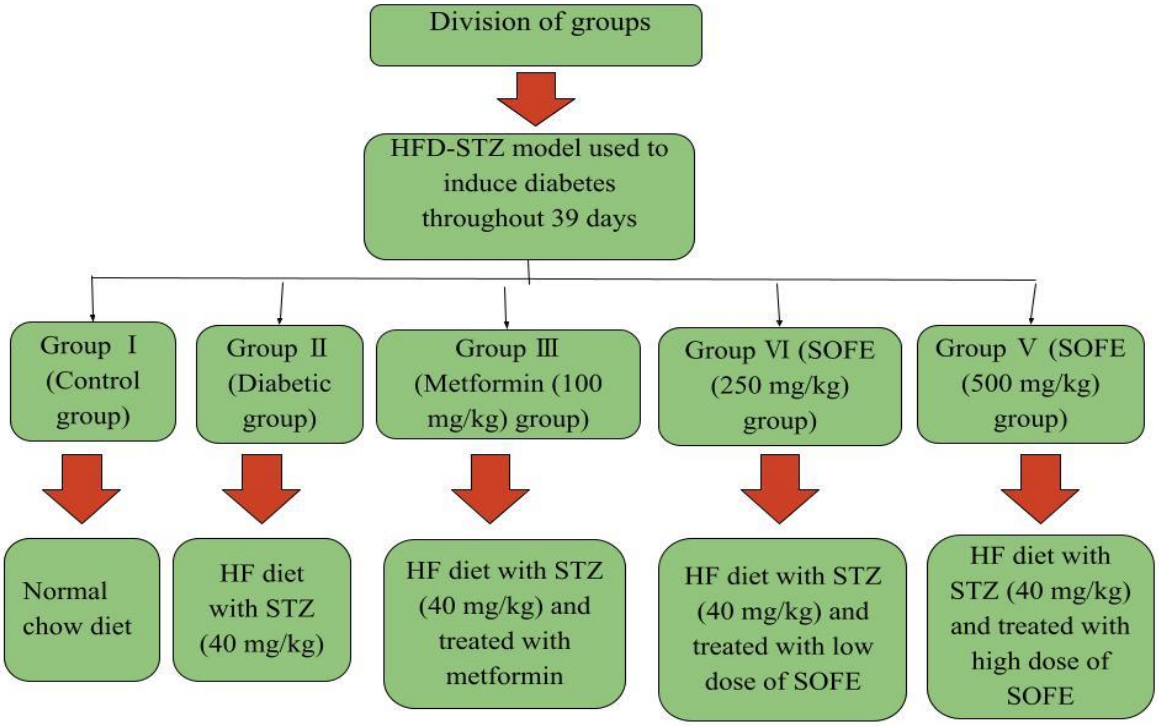


Fig 1: Experimental design

2.9. Estimation of parameters during protocol

Food consumption was record before and after treatment of the animals. Body weights were monitored on the 0, 13th, 16th, 23th, 30th, and 39th day of the experiment.(Of et al.) HF diet was given for 39th days, on thirteenth day STZ was administered. On the sixteenth day blood glucose levels were evaluated. Diabetes and control rats were fasted 15 hours to measure the glycemic activity with the help of OGTT (De MagalhÃes et al., 2019)**.** Blood were collected through the retrobulbar in EDTA tubes on the end of experiment for the biochemical estimation. Animals were dissected and organ (pancreas, liver, kidney) were isolated for histopathology.(Shaikh et al.)

2.10. Biochemical analysis

In lipid profile (TG, TC, HDL, LDL and VLDL) and HbA1C were used enzymatic, glycerol phosphate oxidase techniques, accelerator selective detergent, hplc method.(Javed Shaikh et al.) KFT (serum creatinine and urea levels) were used diagnostic kits based on kinetic alkaline picrate techniques. LFT (total bilirubin, albumin, and globulin) were used several techniques like Diazonium salt, Biuret, and Bromocresol green method (Khadke et al., 2020).

2.11. Histopathology

Organs like pancreas, liver, and kidney were isolated are stored in 10% formalin and then embedded in paraffin wax and tissue sections were stained with H&E under microscope and photomicrographs were observed (Ranajit et al., 2021).

2.12. Statistical analysis

GraphPad Prism 6 was used to calculate the means±SD for six rats in each group. One-way and two-way ANOVA were used to analyse the data.(Chawra et al.) The control, untreated, and treated groups were compared to the test groups. The differences ($P<0.0001$) were significant.(Pathak, Gupta, Thangavelu, et al.)

3. RESULT

3.1 Determination of Acute toxicity study

The OECD recommendations were followed for performing oral acute toxicity tests (423). Where did not exhibit any toxicity and mortality in experimental animals when oral dosing of *Senna occidentalis*flower extract was done up to 5000 mg/kg. Hence on the basis of above result two treatment dose was directly selected for treatment i.e. 250mg and 500mg/ kg body weight.

3.2 Animal feed during experiment

During experiment, control groups were received normal commercial feed was given and other groups received HF diet. Treated with metformin (100mg/kg) and SOFE (250mg/kg & 500mg/kg) showed more significant in consumption of food as compare to the untreated group are showed in fig.2.

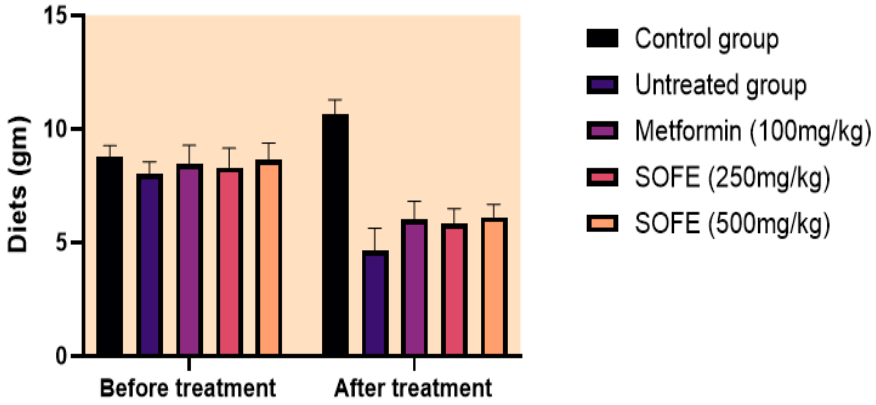


Fig 2: Graph represent food intake of experimental animal. The data represent as mean ± SD of six rats in each group. $^{*}p<0.05$, $^{**}p<0.01$, $^{****}p< 0.0001$ shows the significant difference as compared to the untreated group.

3.3 Body weight

STZ was administered by I.P in rats for the induction of diabetes. It shows more significant reduction after treatment with metformin whereas doses of SOFE (250 and 500mg/kg) showed less reduction in bwt as compared to the untreated group.

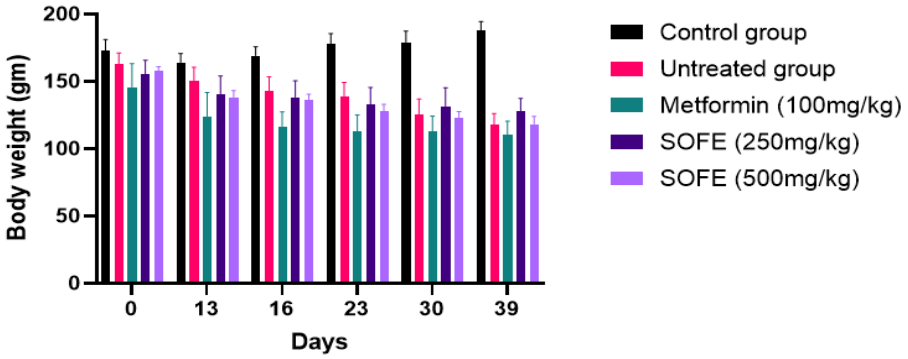


Fig 3: Body mass index graph

3.4 Blood glucose level

The aqueous ethanolic extract of Senna occidentalis flower at low and high doses caused significant changes in BGL in the diabetic rat group on days 0, 13, 16, 23, and 30. The antihyperglycemic effect of low and high doses of SOFE ext. on BGL is shown in the figure. On day 30, rats treated with low-dose SOFE (250 mg/kg), SOFE (500 mg/kg), and standard drug (metformin) (100 mg/kg) experienced a significant fall in BGL.

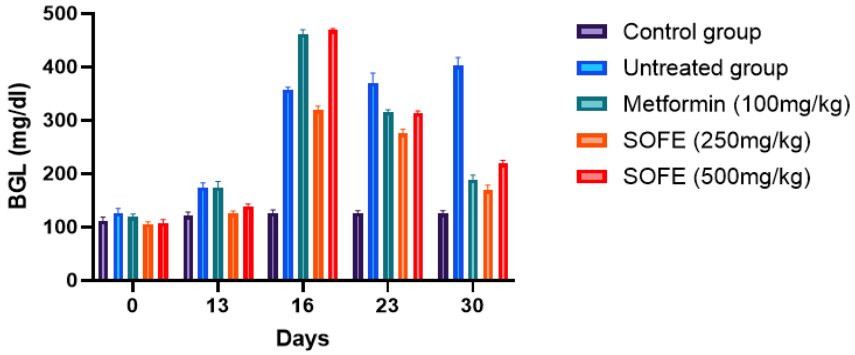


Fig 4: Graphics shows BGL of experimental animal.

3.5 Oral glucose tolerance test

When comparing the treatment group to the untreated group using the OGTT, the treated group explains well-tolerated symptoms. Due to inadequate insulin secretion, the untreated control group lowers its ability to tolerate glucose. In the treated group, the ability of peripheral insulin receptors may be enhanced to enhance the glucose tolerance test in the experimental work, as shown in the figure.

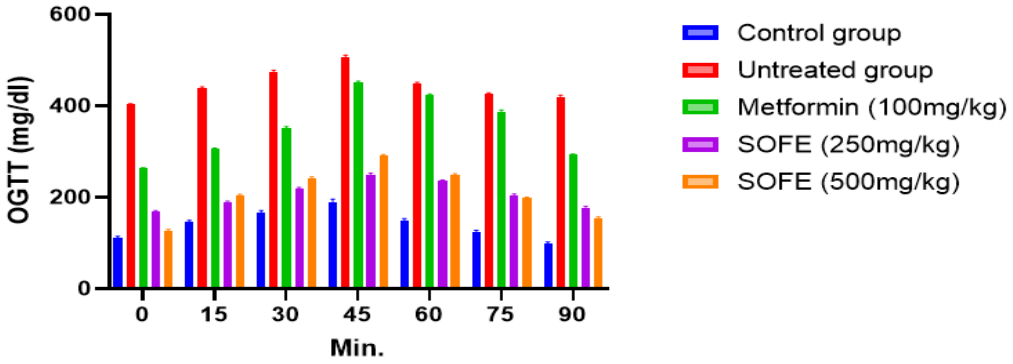


Fig 5: Graphics shows OGTT of experimental animal.

3.6 HbA1C

The results below demonstrate that diabetes was prevented in the five groups of rats who received a 250- or 500-mg/kg aqueous ethanolic extract of the Senna occidentalis flower once daily for 24 days. The HbA1C values are shown in Table.Effect of SOFE on the HbA1C level of HFD-STZ induce diabetic rat.

Table 2: The data represent as mean ± SD of six rats in each group. ****p< 0.0001 shows the significant difference as compared to the untreated group

Group	% Hb
Control group	4.53±0.25****
Untreated group	19.55±0.31
Metformin (100 mg/kg)	5.59±0.28****
SOFE (250mg/kg)	8.86±0.07****
SOFE (500mg/kg)	8.29±0.06****

3.7 Biochemical analysis

Biochemical analysis was estimated via a treatment with standand and test drug after the administered of HFD-STZ are shown in figure. The treated group showed a significant reduction in TC, TG, VLDL, LDL, urea, BUN, creatinine, uric acid total bilirubin, globulin, SGPT and SGOT is compared to the untreated group whereas, HDL, total protein albumin are shown in significantly higher is compared to the untreated group.

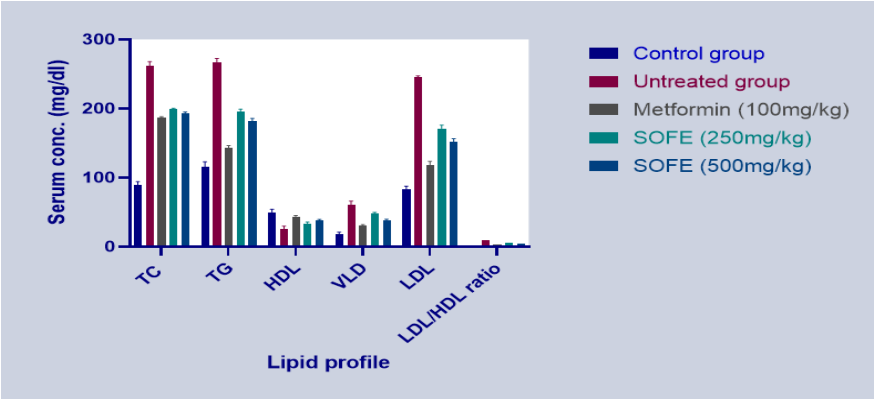


Fig 6: Graph represents lipid profile of experimental animal. The data represent as mean ± SD of six rats in each group. *p<0.05, **p<0.01, ****p< 0.0001 shows the significant difference as compared to the untreated group.

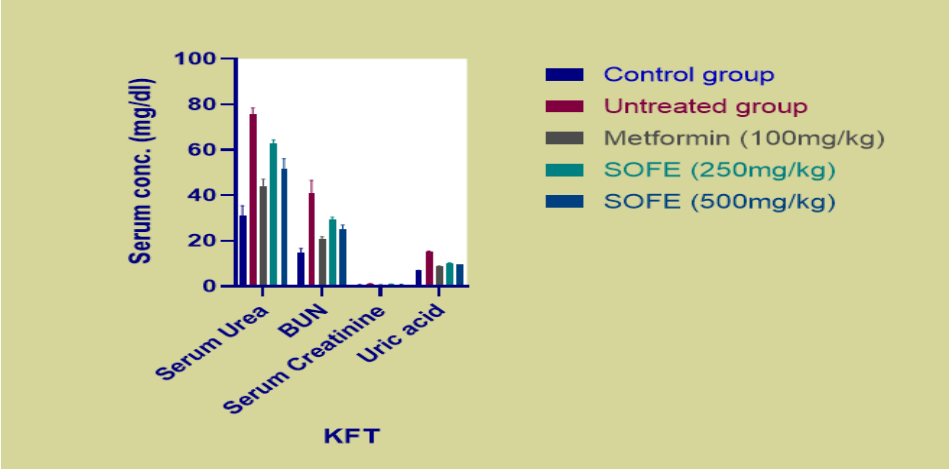


Fig 7: Graph represents KFT of experimental animal. The data represent as mean ± SD of six rats in each group. ****p< 0.0001 shows the significant difference as compared to the untreated group.

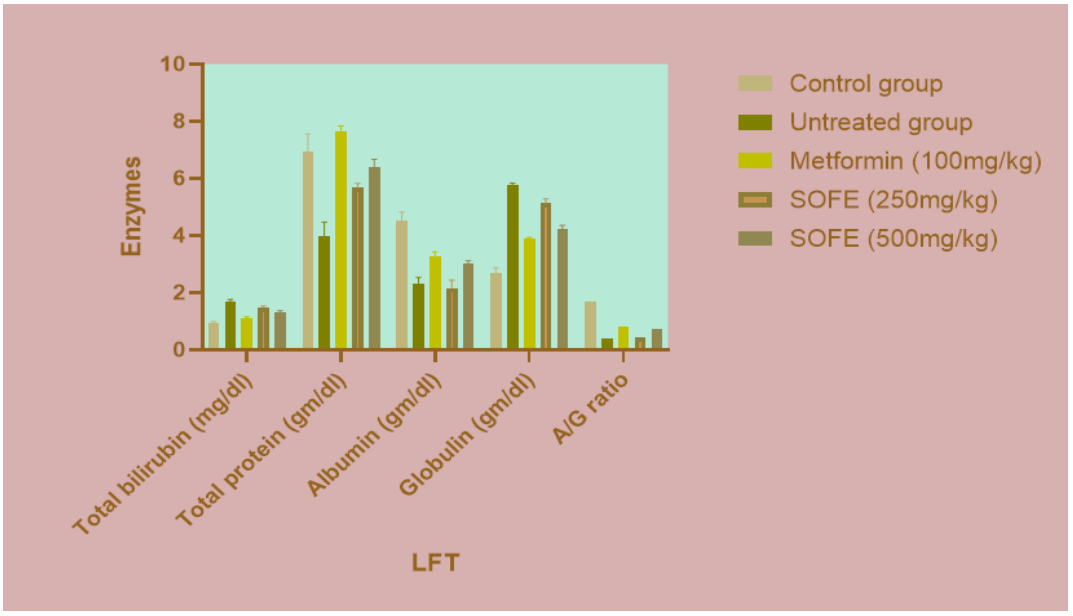


Fig 8: Graph represents LFT of experimental animal. The data represent as mean ± SD of six rats in each group. *p<0.05, **p<0.01, ****p< 0.0001 shows the significant difference as compared to the untreated group.

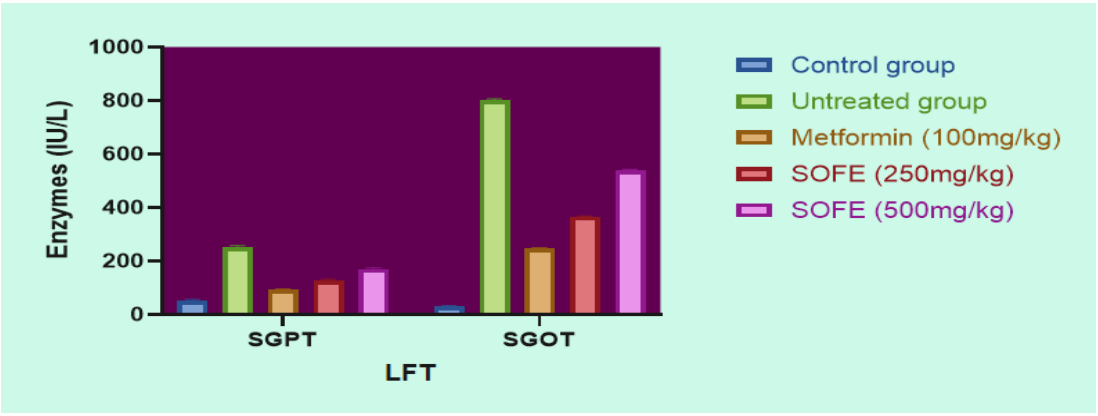
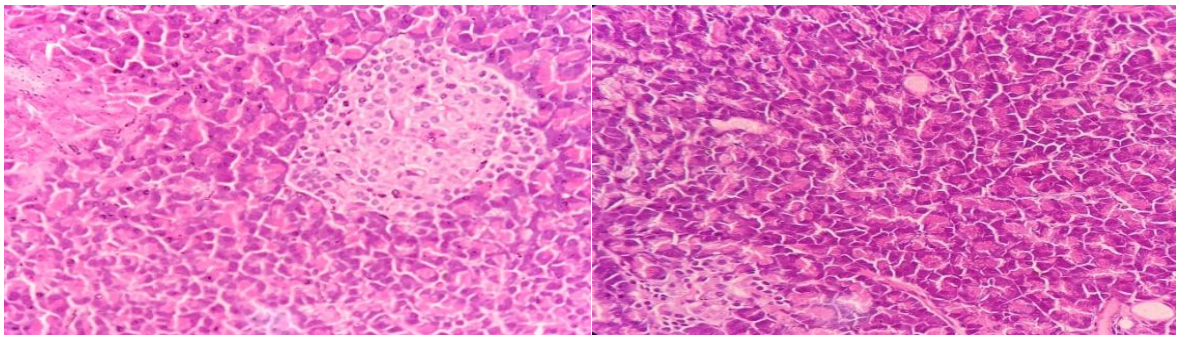


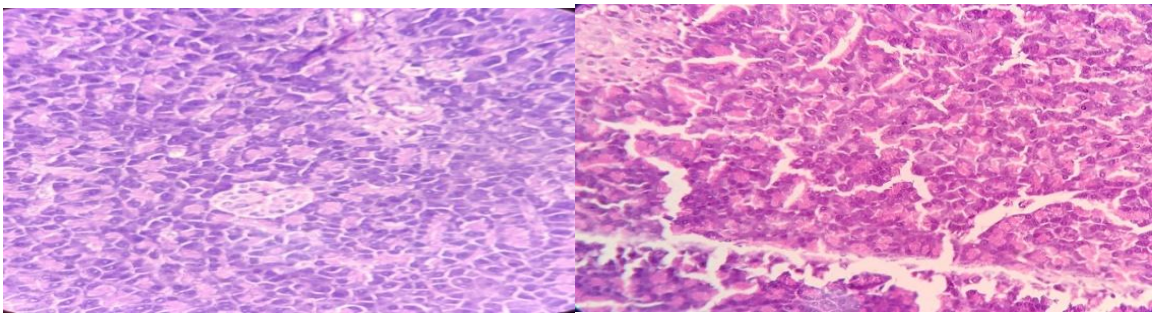
Fig 9: Graph shows SGPT and SGOT of experimental animal. The data represent as mean ± SD of six rats in each group. ****p< 0.0001 shows the significant difference as compared to the untreated group.

3.8 Histopathology

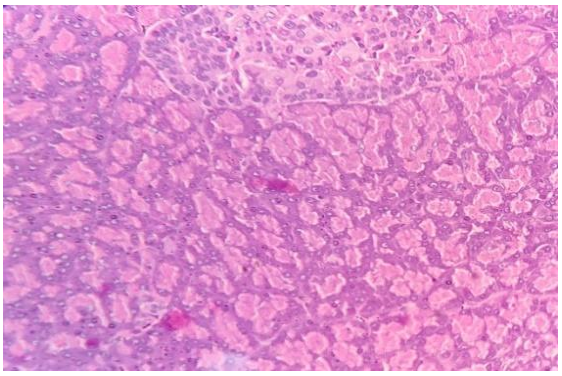
PANCREAS



(A) Negative control **(B) Positive control**



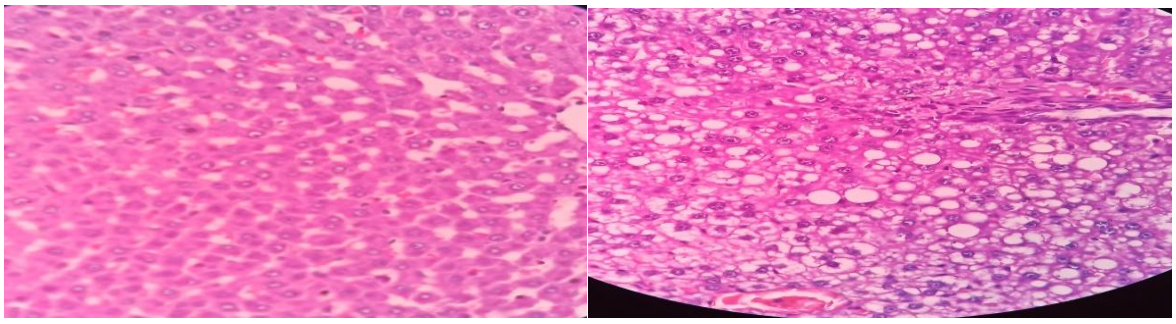
(C) Standard dose **(D) Low dose**



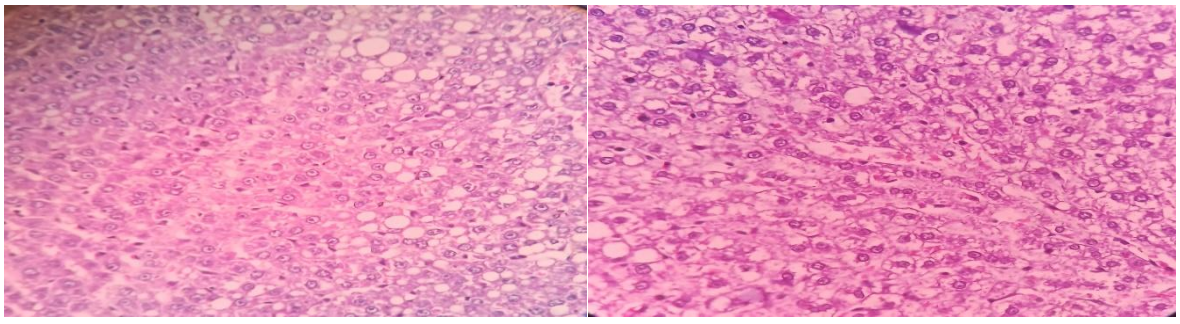
(E) High dose

Fig 10: Under control group (A), the pancreas' picture under a microscope revealed acini of serous epithelial cells and normal architecture. Inflammation or fibrosis was not seen. In the untreated group (B), the islets' breadth and islets' cell population decreased. Metformin (C) group A pancreatic image inspected under a microscope revealed a substantially lower decline in the population of islets and a restoration of the architecture to a level that is close to normal. With low dosages of the drug (D), normal islets were visible, but the stroma showed a light, diffuse infiltration of lymphocytes. High drug dosage (E) A photograph of the pancreas taken under a microscope revealed that there were fewer acinar cells in the islets but that there was either little or no sign of inflammation. The population of islet cells is being destroyed less frequently.

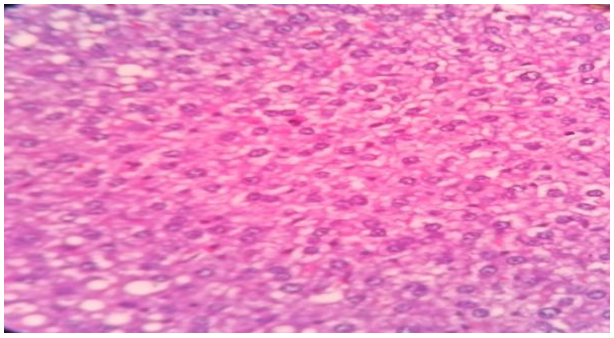
LIVER



(A) Negative control **(B) Positive group**



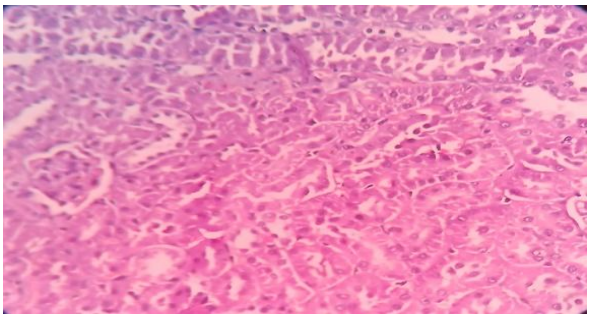
(C) Standard group **(D) Low dose**



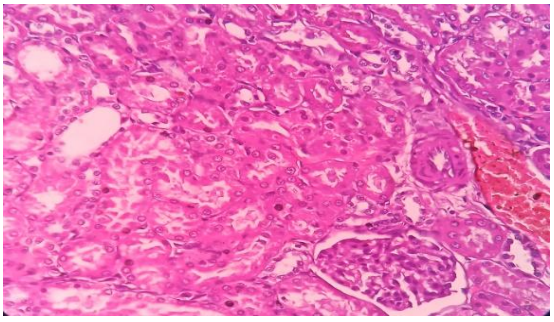
(E) High dose

Fig 11: A control group (A) Hepatocytes with normal cellular architecture and round to oval nuclei in the cytoplasm were visible when viewed under a microscope. There was no evidence of peripheral inflammation. The untreated group (B) microscopically analysed picture revealed a little lymphocyte-based periportal inflammation. The group (C) that received metformin displayed typical lobular architecture. It suggests that when compared to high doses of medication, low doses have a greater hepatoprotective effect. Low dosages of the test (D) produced a significant cytoplasmic effect on hepatocytes. The core veins were normal, but the perivenular region was clogged. The perivenular area was congested, but the core veins were normal. With a higher number of vacuoles and some fatty alterations, the high dose of the medication (E) demonstrated normal lobular architecture.

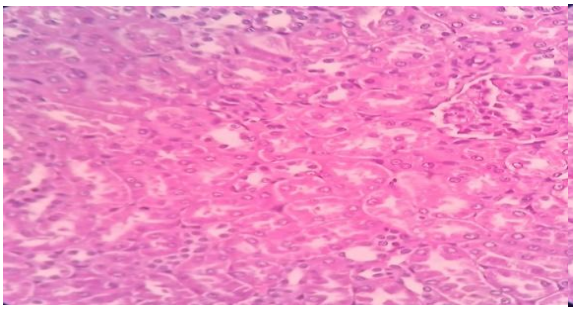
KIDNEY



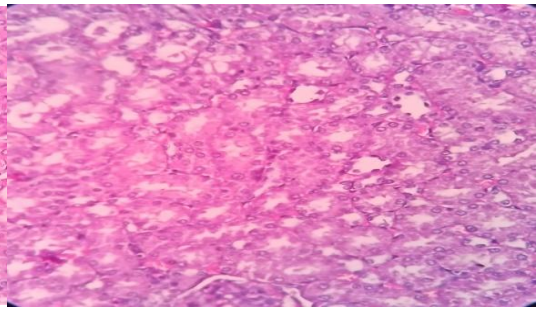
(A) Negative group



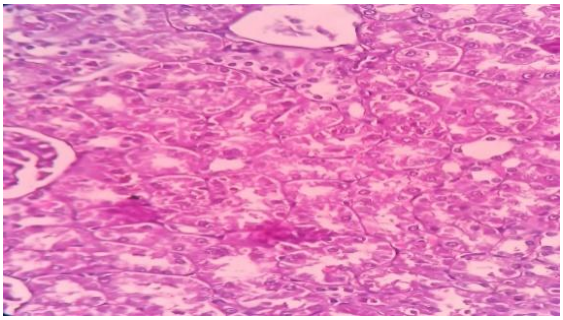
(B) Positive group



(C) Standard group



(D) Low dose



(E) High dose

Fig 12: When the control group (A) image was inspected under a microscope, the tubules, stroma, and glomeruli appeared healthy. The mesangial cellularity and matrix were slightly increased in the diabetic control group (B). Focal lymphoplasmacytic infiltrates were visible in the stroma. Similar to the normal control group, the metformin-treated group (C) displayed normal architecture. Tubules are normal despite the significant increase in cellularity caused by low-dose test medication (D). Glomerulli made a marginal recovery. A test medication at a high dose (E) significantly improved glomerulus recovery. Some tubules seemed normal, although there was a mesenchymal cellularity increase somewhere.

4. DISCUSSION

In T2DM, chronic hyperglycemia, dyslipidemia, and insulin resistance are the main metabolic symptoms. The well-known medication STZ inhibits the synthesis of insulin and causes selective pancreatic islet cytotoxicity. Type-1 diabetes may be brought on by a single high-dose STZ injection, and metformin therapy did not work effectively in these animals. Therefore, STZ at a dose of 40 mg/kg (i.p.) was used in our study along with a high-fat meal. According to the studies, a high-fat diet combined with a STZ has been linked to hyperglycemia, insulin resistance, and insulin insufficiency. In the current study, rats were given a high-fat diet for 39 days before receiving an injection of STZ. Then, using this model, we evaluated SOFE's have antidiabetic, antidyslipidemic, and antioxidant properties. When dosed orally up to 500mg/kg, the aqueous ethanolic extract of *Senna occidentalis*flower did not show any toxicity or fatality. As a result, the two treatment doses of 250 mg/kg and 500 mg/kg were chosen directly.

Up until the 39th day of treatment, the untreated HF-STZ group showed a 42% drop in food consumption. After the treatment of animals with SOFE (low and high dose) food consumption was increased. The HF-STZ untreated group and others did not show a significant difference in body weight after 12 days of diets, but after 16 days of STZ therapy, they did, and they continued to lose weight until the experiment was over (39 days). All high fat-STZ groups of animals lost weight because they ate less than usual.The breakdown of proteins and lipids in the tissues brought on by a lack of insulin is assumed to be the reason for the body's decreased weight. However, SOFE dramatically decreased body weight found in diabetic rats at dosages of 250 and 500 mg/kg. This might be the outcome of better hyperglycemia management in diabetic rats.

Regulations limit a decline in blood sugar levels, but SOFE improved glycemic control and caused hypoglycemia in normal rats. According to the existing research, HF-STZ-induced hyperglycemia in type-2 diabetic rats was successfully decreased by SOFE at low and high doses (250 mg/kg and 500 mg/kg). The hypoglycemic effects of SOFE may be brought about by its activation of GLUT4 transporter activity in adipose tissue. DM and poor lipid metabolism are frequently associated. Impaired insulin production leads to an increase in the metabolism of lipids from adipose tissue to plasma. The accumulation of lipids is caused by a number of disruptive changes to the metabolic and regulatory systems that have been shown to occur as a result of the insulin shortage in diabetes. LDL, TC, VLDL, HDL, and TG levels all significantly decreased as a result of the extract supplementation. These effects could be brought on by low levels of lipolysis or by underactive cholesterol-producing enzymes. After SOFE treatment, dyslipidemic markers returned to values that were almost normal.

Urea, BUN, creatinine, and uric acid levels in serum are significantly improved in this research in SOFE-treated HFD-STZ mice. The HbA1C value was significantly lowered after SOFE was administered in low and high doses, indicating the anti-hyperglycemic efficacy of durgs.

Results from the SGOT and SGPT tests for liver function are widely accepted. In our investigation, higher doses of SOFE result in elevated SGOT and SGPT values compared to lower doses, suggesting that higher doses of SOFE are more toxic to the liver.

Additionally, histopathological examination supports SOFE's anti-hyperglycemic capability in TYPE-2 diabetes.

5. CONCLUSION

A chronic endocrine disease called diabetes mellitus is characterised by hyperglycemia and aberrant insulin production, or the peripheral effects of insulin on tissues. A multitude of complications from diabetes mellitus, such as vascular complications, chronic renal failure, retinal impairment, and increased susceptibility to infection, are considered a global public health concern and may result in disability or even death. As a result, managing diabetes mellitus requires a multidisciplinary approach. The study shows that *Senna occindentalis* flower extract has anti-diabetic effects on diabetic rats treated with the HFD-STZ drug. With doses of 250 mg/kg and 500 mg/kg, Senna occindentalis flower extract reduced BGL and improved metabolic markers. Higher SOFE dosages resulted in higher SGPT and SGOT levels when compared to lower ones. It's possible that bigger doses cause liver damage or put the liver's metabolism under more stress. For the treatment of diabetes, a lower dose is more effective than a higher dose. Histopathological analysis, which is significant for both low and high doses of SOFE in a dose-dependent way, was used to support the aforementioned findings.

6. FUTURE PROSPECT

Senna occidentalis flower extract is a flavonoid, antioxidant and beta sitosterol with potential pharmacological benefits,

including anti-inflammatory, antiviral, arthritic, hepatoprotective, and antidepressant. Moreover, this study has exhibited that SOFE in conjunction with various chemotherapeutic agents and targeted therapies are more effective in the treatment of Type 2 diabetes. Hence, it is important to evaluate the effect of SOFE on other drug metabolism before SOFE can be safely used in combination with other drugs. This paper potently supports the view that SOFE has a broad application prospect. In future prospects these drugs are used in the treatment of Diabetes in osteoporosis and IBD because flavonoid present in *senna occidentalis* flower.

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