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ANTIDIABETIC, ANTIHYPERLIPIDEMIC, ANTIOXIDANT, HEPATOPROTECTIVE AND RENAL PROTECTIVE EFFECT OF *LUFFA CYLINDRICA* EXTRACT AGAINST THE STREPTOZOTOCIN-INDUCED DIABETES MELLITUS IN RATS

Vastvikta Sahai and Vikas Kumar *

Department of Pharmaceutical Sciences, Shaloam Institute of Health Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, Prayagraj - 211007, Uttar Pradesh, India.

Keywords:

Diabetes mellitus, *Luffa cylindrica*, Blood glucose level, Inflammation, Antioxidant

Correspondence to Author:
Dr. Vikas Kumar

Department of Pharmaceutical Sciences, Shaloam Institute of Health Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, Prayagraj - 211007, Uttar Pradesh, India.

E-mail: phvikas@gmail.com

ABSTRACT: The main objective of the current study was to see whether SG peel methanolic extract had antidiabetic and hepatoprotective results in streptozotocin-induced diabetic rats. Streptozotocin was administered intraperitoneally to rats to trigger diabetes. When rats had an elevated blood sugar level three days after acquiring streptozotocin, it was determined that they were diabetic. Diabetic rats were given pre-determined doses of a methanolic extract of SG. Our experimental study took 28 days to complete. Rats were fasted overnight for an oral glucose tolerance test, and antioxidant parameters were measured. Rats were euthanized after 28 days to perform histopathological tests. One of the three doses of methanolic extract of SG peels (50, 100 and 200 mg/kg) showed nearly identical findings to Glibenclamide (2.5 mg/kg). After administering sponge gourd peel extract doses, blood glucose levels were found to be depleted. The positive impact on HOMA-IR and HOMA- β, plasma insulin levels, glycated haemoglobin, and several other variables. Furthermore, antioxidant parameters, including GLUT2 and SGLT1, significantly improved in diabetic rats. Finally, in Streptozotocin-induced rats, methanolic sponge gourd concentrate had a major effect. The 200mg/kg dose, in specific, had incredible effects. Elevated concentrations of GLUT2 and SGLT1 in diabetic rats treated with SG extract relieved the pressure. Based on the result, we can conclude that SG has a potential antidiabetic effect against STZ-induced diabetes.

INTRODUCTION: Nature has bestowed us with a vast storehouse for the therapeutic cure of ailments of mankind [1, 2]. Medicinal plants have been used for ages as therapy for poisonous bites as they accommodate the component of remedial values and have also been employed in labour during childbirth [3-6].

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A long-established traditional healing system is essential in maintaining the physical and psychological wellness of the innumerable tribal people in India. The ancestral system of medicine consists of enormous plants with several medicinal and pharmacological importance and, on that account, represents a rich tank of new bioactive molecules [7].

Natural or herbal products obtained from plants are a priceless resource employed for centuries to cure enormous ailments [8, 9]. The utility of the bioactive plant-derived product is on an up-scale because the prime concern with the utilization of synthetic drugs is the side effects or after-effects, which can

be even more fatal than the diseases claimed to be cured. On the contrary, plant-derived medications are based upon the fact that they contain natural substances that will boost health and alleviate illness. They are proven safe, have finer patient tolerance, and are quite barely expensive yet globally competitive [10]. Hence, given the healing potency of plants, returning to natural medicaments is a rigid requirement.

Diabetes mellitus (DM) is a widespread metabolic disorder and a health problem affecting an innumerable proportion of our global population [11–13]. It is characterized by hyperglycaemia, dyslipidemia, renal failure, and hepatic damage. Hyperglycaemia induces oxidative stress and leads to cell damage and the progression of DM-associated complications [14–16]. Plants are major sources of drugs that are readily available and have very few side effects. Diabetes mellitus is a bunch of disorders with many different etiologies. Diabetic patients show disarrangements in the carbohydrates, fat metabolism, and proteins due to total or partial slippage of insulin secretion and/or its action. In 2016, it was estimated that 1.6 million lives were lost due to diabetes. 2.2 million demises were attributable to the increased blood glucose level in 2012. Approximately 50% of deaths due to elevated blood glucose were aroused before age 70. World Health Organisation had appraised that diabetes would be the seventh major reason for demise of human beings in the year 2016 [17]. According to estimation, the number will elevate to approximately 552 million people by 2030, mostly due to the elevating burden of diabetes in developing nations [18–21].

Luffa (*Luffa cylindrica)* (Sponge gourd (SG)) belong to the Cucurbitaceae family and have the following common names such as sponge gourd, loofa, vegetable sponge, bath sponge dish [22–24]. *Luffa cylindrica* has approximately 7 varieties in the genus. Luffa fibres are obtained from the grown and dried fruit of *Luffa cylindrica* (sponge-gourd), which is a yearly crop that is cultivated in the sub-tropical countries. These fibers are easy to get as they are inexpensive, lightweight, biodegradable, possess high economic significance, and are reported that the fibers are friendly for the environment [25, 26].

It has found its use as a medicinal herb to treat diseases such as bronchial asthma, worms in the intestinal, sinusitis, edema, sore throat and rhinitis. Leaves can be employed in amenorrhea, decaying teeth, parasitic affections, skin diseases, chronic bronchitis pain, inflammation, carbuncles, and abscesses. The stem is utilized in respiratory complaints, while its fruits are helpful in hemorrhage of the bowels or bladder, hernia, hemorrhoids, jaundice, menorrhagia, scarlet fever, bronchitis, leprosy and syphilis. Flowers have found use in migraine treatment [25, 27, 28].

METHODS:

Plant Components: Raw and clean sponge gourds were purchased from a marketplace in Prayagraj, Uttar Pradesh, India, in July 2017. Dr. Imran Kazmi identified the raw and fresh fruits, Pharamcognoist at Glocal University, and a reference sample was preserved in the department for reference purposes (GU/19/02/004).

Acquiring the Crude Extract: The fruits of the sponge gourd were peeled. The peels were then taken and dried, avoiding direct sunlight. Once the peels had dried, they were brought into the lab for extraction. The total weight of the peel post-drying was 255 gm. The *Luffa cylindrica* peels were placed in a Soxhlet, and petroleum ether was applied to it to perform the collection. The extraction exercise took 11 hours to accomplish. The crude extract of sponge gourd peels was then removed from the Soxhlet apparatus and allowed to dry 24 hours at room temperature. The filtrate generated was concentrated by constructing a distillation assembly to bring out the distillation process. The same crude extract was dried before being put in the Soxhlet apparatus, which was then filled with methanol. As per Kumar *et al.,* the extract was extracted for 10 hours, then condensed in a Petri dish, scraped off, and placed in a cool position to prevent oxidation [29–31].

Animals: Albino Wistar rats in good health, weighing around 150 and 200 gm, were bought and sheltered. The rats were regularly given a normal pellet diet of Hindustan Lever Limited in Mumbai, India. Water was always available. The Animal Ethical Committee (AEC) guidelines were followed for all analyses and tests.

Induction of Diabetes: Before the induction of diabetes in rats, they had abstained from eating overnight. Streptozotocin (STZ) was dissolved in the citrate buffer and administered intraperitoneally in rats to cause diabetes mellitus. Both groups of rats received STZ citrate buffer, except for the normal control rats, which received saline injections. Diabetes was induced in the second group, the normal control group, but no treatment was provided. The four categories that remained were those that were given diabetes and medication. The research and analysis were carried out for the next 28 days, with one of the five groups receiving a regular antidiabetic drug, Glibenclamide, and the other three receiving a varying dosage of sponge gourd extract, 50, 100, and 200 mg [32–35].

Antioxidant Parameters: For antioxidant specifications, the liver homogenate was developed in an icy solution of 10% potassium chloride was used for appraisal. It was deployed to gauge malondialdehyde (MDA) levels and activity using the previously reported method but with few alterations [36, 37].

Glycated Haemoglobin: Glycated haemoglobin (HbA1c) levels in rats were calculated using standard protocols. The procedure was as follows: 4 mL of blood was taken and placed in an EDTA-containing bulb, from which plasma was separated. The packed cell was washed six times with normal saline to decontaminate it. The hemolysate was then made by mixing equal parts of distilled water and carbon tetrachloride (1/4th part) in a packed cell and centrifuging it at 3000 rotations per minute for 20 minutes. The amount of haemoglobin in hemolysate was determined using the cyanmethemoglobin process. An isotonic saline solution balanced the hemoglobin concentration to 10 mg/dl (which contained 0.9 percent sodium chloride). Hemolysate was prepared with 2 ml of 10 mg/dl haemoglobin and 1.0 ml of oxalic acid with a normality of 0.3 and then mixed. After cooling the mixture to room temperature and adding 1 ml of 40 percent trichloroacetic acid, it was kept in a water bath for around 1 hour. The tube contents were thoroughly mixed before being centrifuged at 3000 RPM. The floating part (supernatant) was collected in a 2 ml container, and 0.5 ml of 0.7 percent thiobarbituric acid solution was applied to it and held at 37 °C for 40 minutes. At 443 nm, a reading was obtained for the solution mentioned above and compared to a blank solution (which contains 2 mL distilled water and 0.5 mL thiobarbituric acid). GHb percent was used to express glycosylated haemoglobin [38, 39].

Hexokinase Concentration: Using an assay blend, spectroscopy determines hexokinase activity in hepatic tissues (flesh). The assay was conducted with 3.7 mM glucose, 7.5 mM magnesium chloride, 11 mM thio-glycerol and 45 mM HEPES (4-(2-hydroxyethyl)-1-piper-azineethanesulfonic acid) buffer. At a tissue sample concentration of 50 mg/ml, tissue was homogenised in cooling 0.1 M phosphate buffer saline (pH-7.4). In a cuvette, we combined 0.9 ml of the assay blend with 0.22 M 0.03 ml ATP completely. 0.1 mL of tissue supernatant was added to the cuvette containing the above solution after thoroughly combined, and the absorbance was recorded at 340 nm. Measurements of hexokinase were calculated as a ratio of g/mg of tissues [40].

Glucose-6 Phosphate Level: A common protocol was used to assess the impact on hepatic glucose-6-phosphatase. In a freeze solution of 0.1 M phosphate buffer saline, tissues were incorporated at a concentration of 50 mg/ml (pH-7.4). In the centrifugation tube, 0.1 ml of glucose-6-phosphate solution having 0.1 M molarity and 0.3 ml of maleic acid buffer of molarity 0.5 M (pH-6.5) were mixed and stirred in a water bath to 37 °C for 15-20 minutes. We used 1 mL of 10% trichloroacetic acid solution (TCA) and ice to halt the reaction, accompanied by 10 minutes of centrifugation at 3000 RPM. At a wavelength of 340 nanometres, the optical density was measured. The enzyme activity was evaluated in milligrams of inorganic phosphate per gram of tissue [29, 41, 42].

Biological Assays / Bioassays: All Wistar strain rats were given diethyl ether to render them unconscious. These rats' blood samples were collected through retro-orbital puncture, and anti-coagulating agents were used to store the blood samples. The samples were held in a centrifugation tube and centrifuged at 4000 revolutions per minute for exactly 15 minutes at 25 °C to see whether there were any improvements in biochemical parameters. Using standardized kits containing serum insulin,

total cholesterol concentration, total HDL *i.e.* High-density lipoprotein cholesterol total LDL *i.e.,* Low-density lipoprotein cholesterol and total triglycerides were spectrophotometrically measured at Span Diagnostic, India [43–45].

Histopathology: Following the completion of the study, all rats were sacrificed under mild anaesthetic, and their organs (pancreas) were segregated for histological analysis. The quarantine organ tissues were retained in formalin (40 percent natural buffered formaldehyde), with hydration extracted by streaming it through the different components of alcohol before being immersed in paraffin wax and cut into 5 mm pieces employing semi-au for staining [29, 46].

Statistical Assessment: All statistics in this research study were presented as Mean ±SEM using ANOVA, also known as one-way analysis of variance. Graph Pad Prism Version 5.0 (San Diego, California) was used to conduct all statistical analyses. The important, more significant and extremely significant values were assigned to each value. P values of 0.05, 0.01 and 0.001 were used [29, 47, 48].

RESULTS:

Screening for Phytochemicals in the Preliminary Stage: Terpenoids, flavonoids, phenolic compounds, tannins and saponins were identified in screening for phytochemicals in the preliminary stage of the *Luffa cylindrical* peel extract. However, the extract's flavonoids and phenolic compounds were found to be more prevalent **Table 1.**

Studies on Acute Toxicity: To determine the non-toxic nature of our extract compound, an acute toxicity analysis of the sponge gourd peel methanolic extract was conducted. Numerous doses of sponge gourd peel extract showed no hazardous reaction or fatal impact until the experiment was completed.

The acute toxic effects of methanol extracts of sponge gourd peel showed that perhaps the doses were safe. Until the end of our study period, there were no positive inferences about the lethality or toxic behaviours of the chosen group who were given different doses of extract (data not presented).

Tolerance Screening for Oral Glucose: When different doses of sponge gourd extract were given 30 minutes before inducing glucose loading, there was a substantial depletion ($P < 0.001$) in blood glucose concentrations after the glucose was given **Fig. 1**. When compared to a vehicle monitor, the different doses of sponge gourd extract resulted in a decrease in blood glucose levels after 6 hours. In contrast to the blood control group's vehicle glucose level, Glibenclamide's blood glucose level was lower.

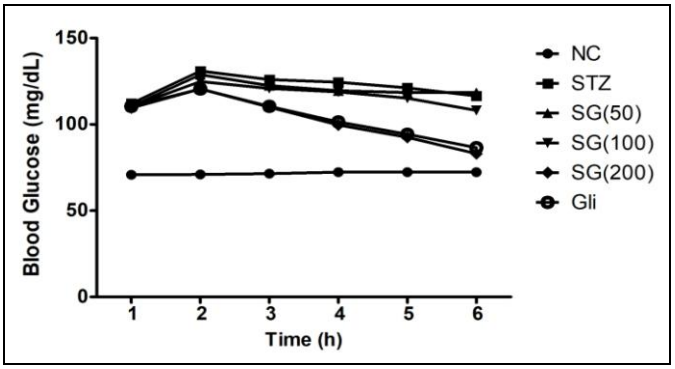

FIG. 1: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE ORAL GLUCOSE TOLERANCE TEST

Glucose Level in the Blood: Fig. 2 depicts the antidiabetic impact of the extract or sponge gourd peels on the level of difference in blood glucose levels in rats struggling with STZ (streptozotocin)-induced diabetes. The various concentrations of 50, 100 and 200 mg/kg extract were dispensed to rats. In the initial days of the experiment, there was not much alteration in the blood glucose proportion. Some notable level of alteration was observed on the 10^{th} day of the study, and then the change in blood glucose level was observed on consecutive days. On the final day of the study, the blood glucose level had fallen significantly. The extract's maximum dose produced almost identical results to the typical antidiabetic drug Glibencamide. Because of the above results, we can conclude that different concentrations of sponge gourd extract had a dose-dependent effect. When STZ/streptozotocin-induced diabetes rats received distinct concentrations of *Luffa cylindrica*/ sponge gourd peels extract and Glibenclamide, the *Luffa cylindrica* peel extract at a concentration of 200mg/kg had the most effective glucose-lowering effect.

Impact on HOMA-IR (Homeostatic model assessment for Insulin Resistance) and HOMA-β: The results of different quantities of sponge gourd peels extract on HOMA-IR are shown in **Fig. 2**. Insulin sensitivity was higher in STZ-induced diabetic rats relative to normal control rats, but it was significantly lower at 50 mg/kg and 100 mg/kg extract concentrations. The Glibenclamide-treated rats were also smaller. **Fig. 2** also displays the results of HOMA, a homeostatic model assessment for cell function).

The function of cells in STZ-induced diabetic rats was significantly diminished compared to Normal Control rats. Diabetic rats given sponge gourd or *Luffa cylindrica* peels extract showed an improvement, and rats assigned a 200 mg/kg dose, which was close to Glibenclamide, showed a large increase.

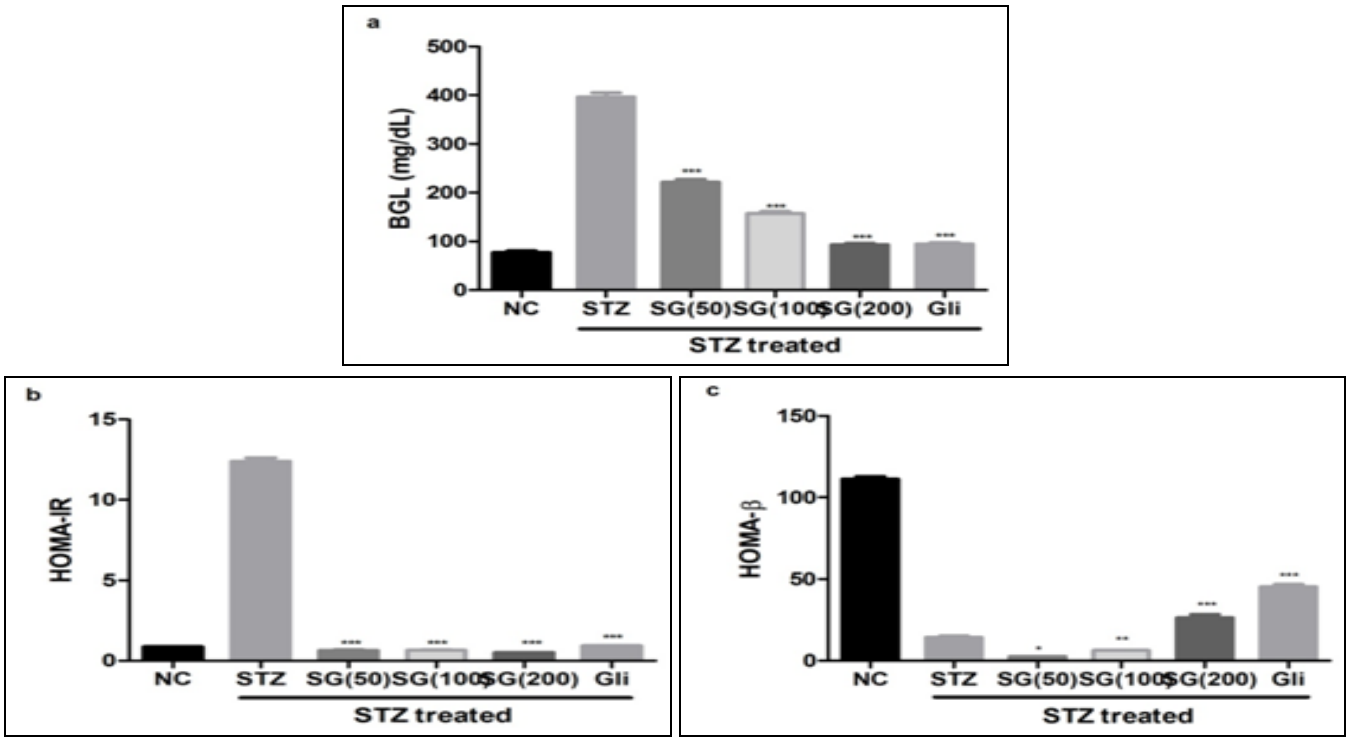

FIG. 2: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE BLOOD GLUCOSE LEVEL, HOMA-IR AND HOMA-B OF STZ-INDUCED DIABETIC RATS. A: bgl, b: homa-ir and c: homa-β as described in the material and method section. where *p<0.05 consider as significant, **p<0.01 consider more significant and ***p<0.001 consider as extreme significant.

Influence on Insulin Levels in the Blood: Fig. 3 depicts the effect of various sponge gourd peel extract doses on plasma insulin levels. In diabetic rats treated with STZ (streptozotocin), plasma insulin levels were significantly lower than in rats treated with vehicle only.

Plasma insulin values were significantly enhanced (P 0.001) when groups were orally treated with various sponge Luffa cylindrica peels extract doses. When compared to other doses of sponge gourd peel extract and the regular drug glibenclamide, the 200 mg/kg dose of sponge gourd peel extract had the greatest effect in raising plasma insulin levels.

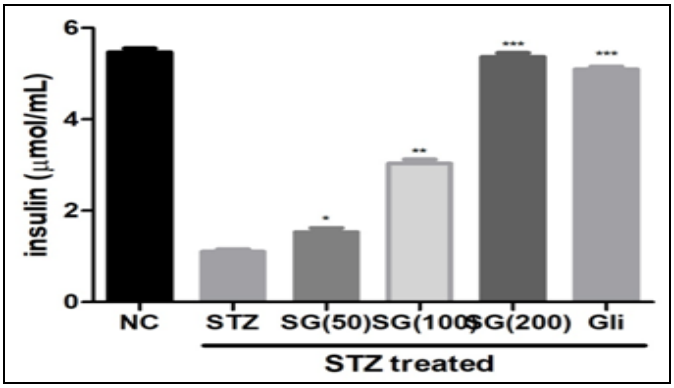

FIG. 3: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE PLASMA INSULIN OF STZ-INDUCED DIABETIC RATS. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extreme significant.

Effect on Glycated Haemoglobin: In diabetic rats, the amount of glycated haemoglobin was found to have increased (which was induced by streptozotocin). Group rats received three concentrations of SG peel extract as follows, 50 mg/kg, 100 mg/kg and 200 mg/kg) as well as glibenclamide (2.5 mg/kg) for the research. Compared to the diabetic control group rats, there was a substantial deficiency (P 0.001) in the amounts of glycated haemoglobin on the research's 28th day (**Fig. 4.**

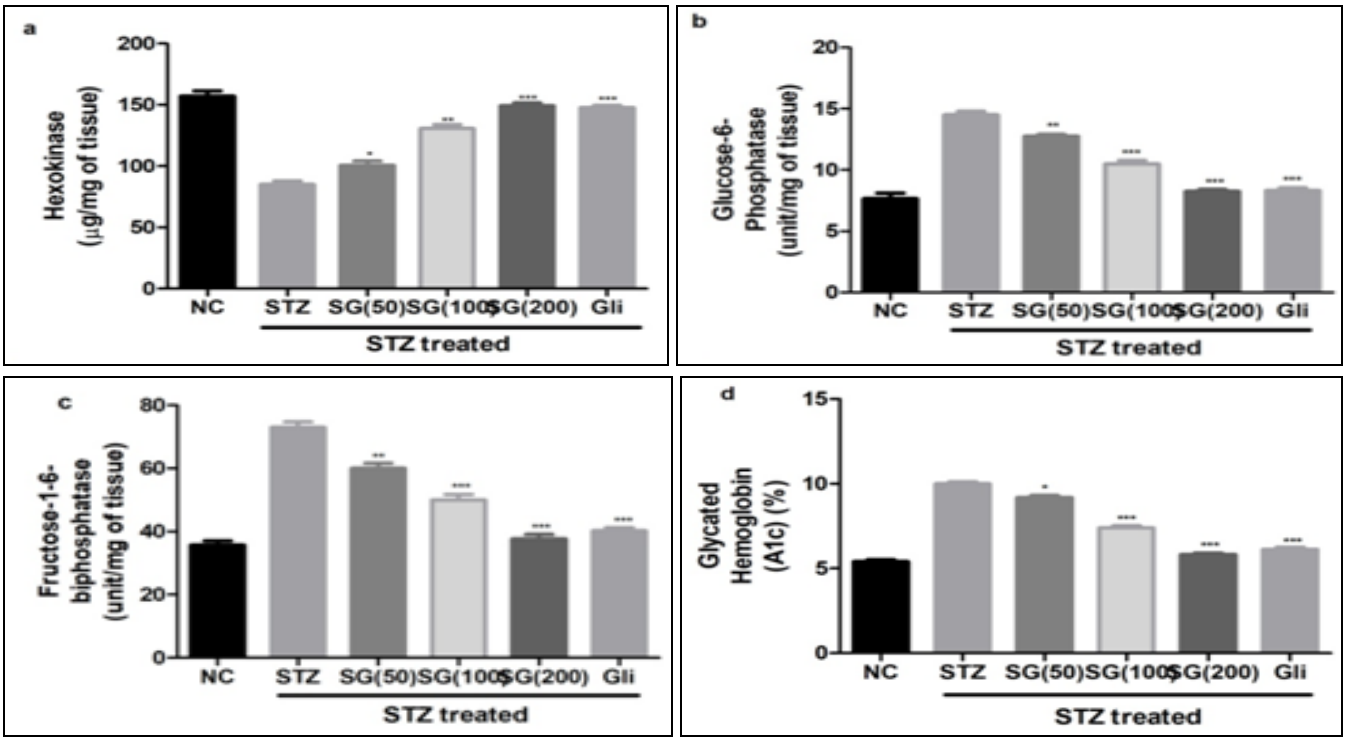

FIG. 4: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE BIOCHEMICAL PARAMETERS OF STZ-INDUCED DIABETIC RATS. A: Hexokinase, b: Glucose-6-phosphatase, c: Fructose 1,6, biphosphatase and d: Glycated haemoglobin as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extreme significant.

Impact on the Amount of Hexokinase: When rats are induced with diabetes, the amount of hexokinase is decreased, according to our findings. For distinct groups of rats, different doses of sponge gourd peels (50, 100, 200 mg/kg) and the standard treatment glibenclamide (2.5 mg/kg) were given, and a dramatic rise in hexokinase was detected (P 0.001) **Fig. 4**. The *Luffa cylindrica* peels extract dose of 200 mg/kg had the maximum level of hexokinase of the three concentrations and the usual standard drug glibenclamide.

Impact on the Concentration of Glucose-6-Phosphate: In diabetic Wistar rats, glucose-6-phosphate levels increased dramatically (streptozotocin-originated diabetes). Different rat groups were given three doses of sponge gourd peels (*Luffa cylindrica*) extract (50 mg/kg, 100 mg/kg, 200 mg/kg) and a single group was provided with a dosage of glibenclamide (2.5 mg/kg), which is the standard antidiabetic drug. This indicates that diabetic rats had lesser glucose-6-phosphate amounts than non-diabetic rats **Fig. 4**. When comparing the various doses of sponge gourd peel extract, the dose of 200 mg/kg was the most effective.

Effect on Cholesterol Concentration: A rise in cholesterol concentration was observed in Streptozotocin-induced diabetic rats. The use of multiple doses of sponge gourd or *Luffa cylindrica* peels extract resulted in a decrease in total cholesterol levels **Fig. 5**. Diabetic rats who had not been treated had significantly elevated serum cholesterol levels than normal control rats' group (group I) and usual control rats provided with sponge gourd peels (*Luffa cylindrica*) extract (group II). When sponge gourd (*Luffa cylindrica*) peels extract was administered to STZ-

induced diabetic rats in various concentrations (*i.e.*, 50 mg/kg, 100 mg/kg and 200 mg/kg) for 4 weeks, serum cholesterol levels declined substantially, with the biggest influence seen throughout the population of rats given 200 mg/kg of sponge gourd (*Luffa cylindrica*) peels extract. The group of rats that only obtained Glibenclamide (2.5 mg/kg) had minimum to no shifts or changes in serum cholesterol levels **Fig. 5.**

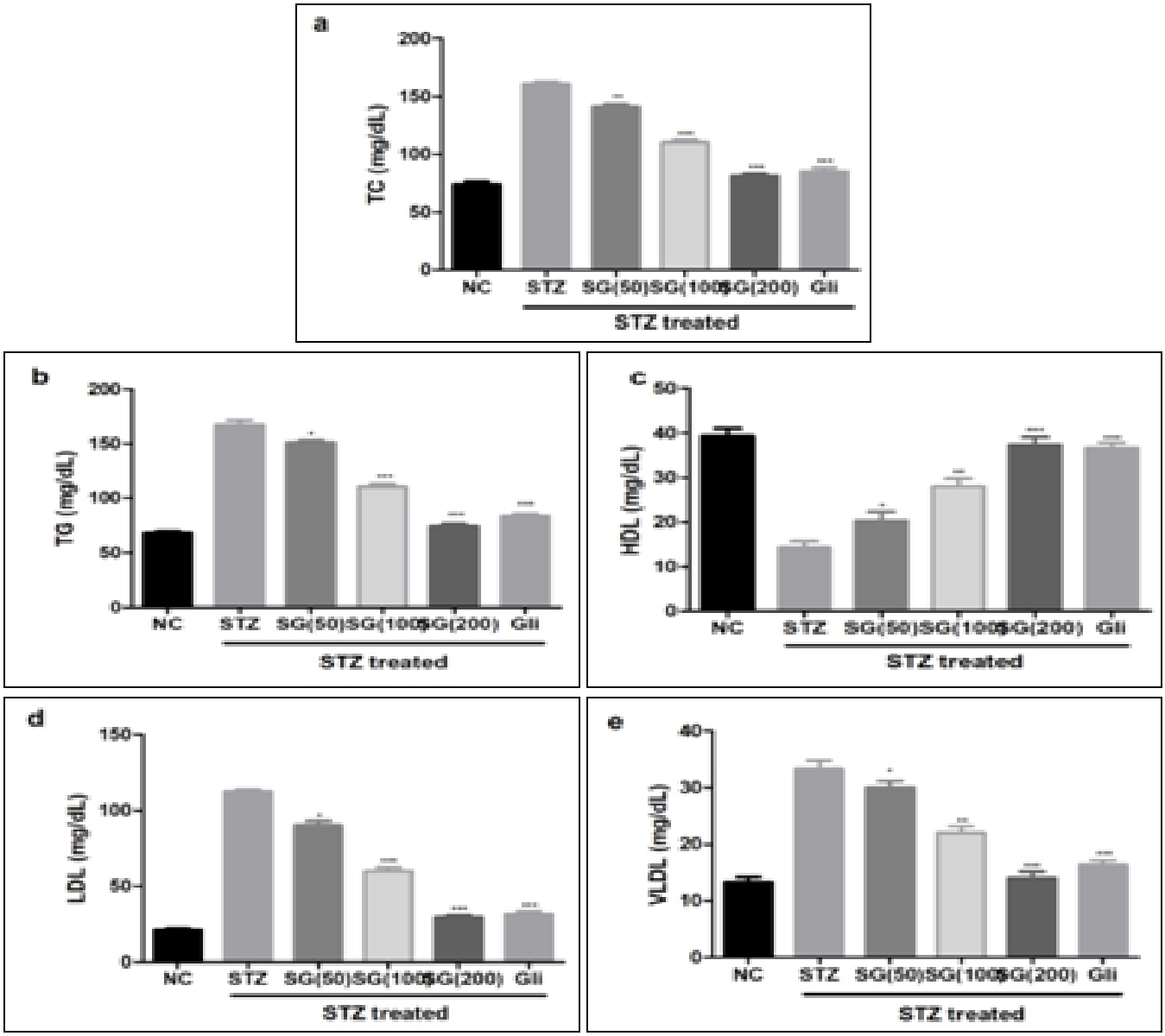

FIG. 5: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE LIPID PARAMETERS OF STZ-INDUCED DIABETIC RATS. A: TC, b: TG, c: HDL, d: LDL and e: VLDL as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extremely significant.

Impact on HDL (High-Density Lipoprotein) Cholesterol: The amount of HDL cholesterol in Streptozotocin-induced diabetic rats is likely to have declined.

When diabetic rats were offered various doses of sponge gourd peel extract, there was a significant increase in HDL cholesterol levels **Fig. 5.**

Impact on LDL (Low-Density Lipoprotein) Cholesterol: The LDL cholesterol of diabetic rats provided with streptozotocin increased. This elevation is shown to decrease after oral administration of different doses of sponge gourd peel extract. Furthermore, the data indicates that the sponge gourd peel extract (200 mg/kg) dose

resulted in the greatest reduction in LDL cholesterol quantity **Fig. 5.**

Effect on Concentration of VLDL (Very Low-Density Lipoprotein) Cholesterol: Diabetic Wistar rats given streptozotocin had a higher level of VLDL cholesterol *i.e.,* very low-density lipoprotein cholesterol **Fig. 5**. Following the administration of different doses of sponge gourd peel extract and the regular medication glibenclamide, the amount of VLDL was found to be lower ($P < 0.001$). The dose of sponge gourd peel extract that had the best impact on preventing VLDL cholesterol was 200 mg/kg.

Impact on Hepatic Functions: Alkaline Phosphatase (ALP), Aspartate Aminotransferase (AST) and Alanine Aminotransferase (AAT) levels are all high (ALT). The ALP (IU/L) amounts in numerous rats' groups are shown in Graph A. When a person has diabetes, their ALP levels rise dramatically, but this rise is decreased after antidiabetic drugs are taken. On giving the 3 different doses of sponge gourd peel extract and a dose of the standard drug Glibenclamide, the level of ALP reduced, in which maximum deflation was seen for 200mg/kg dose of sponge gourd peel extract amongst all three of its doses. Graph B shows AST levels in rats on treating them with the three concentrations of sponge gourd peel extract and Glibenclamide. The graph clearly shows that the concentration of AST rises in diabetic rats.

The doses given of the extract reduced the level of AST in diabetic rats. The best result was observed in a group of rats administered 200mg/kg of the sponge gourd peel extract. Graph C demonstrates ALT level in rats, which rises in diabetic rats. On providing doses of sponge gourd peel extract, the level deflated. 200 mg/kg dosage of the *Luffa cylindrica* peels extract showed a remarkable outcome as it was somewhat similar to Glibenclamide (**Fig. 6).**

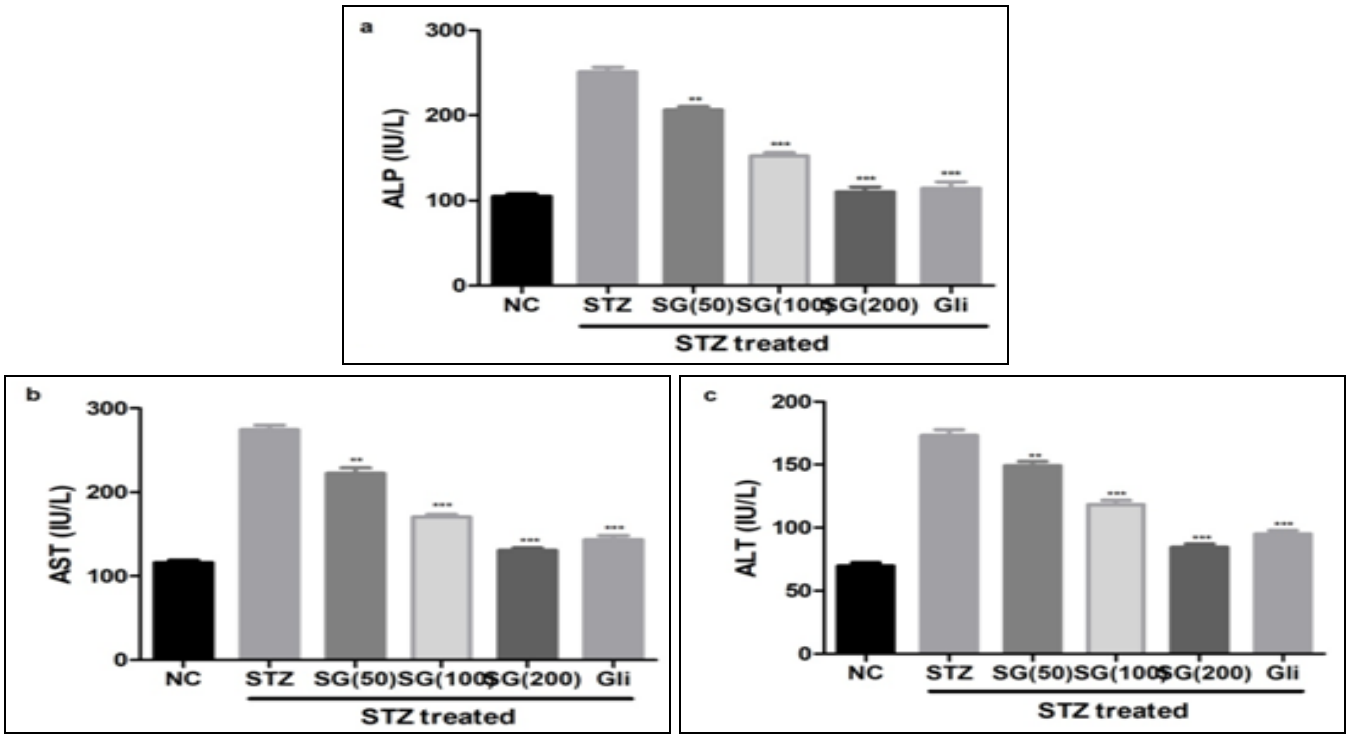

FIG. 6: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE HEPATIC PARAMETERS OF STZ INDUCED DIABETIC RATs. A: ALP, b: AST and c: ALT as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider extremely significant.

Impact on Antioxidant Parameters: Fig. 7 indicates the amount of malonaldehyde (MDA) in the blood. MDA amount grows in diabetic rats. MDA concentrations were reduced in rats given Sponge gourd peel extract and Glibenclamide. This amount nearly stabilized in rats given a 200 mg/kg dose of Luffa cylindrica peels extract and the standard drug glibenclamide.

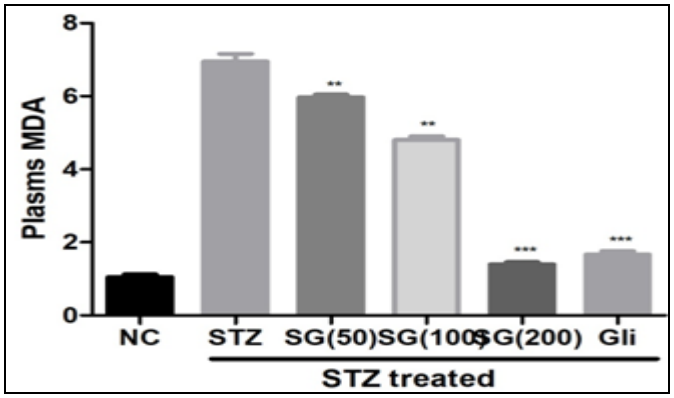

FIG. 7: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE PLASMA MALONALDEHYDE OF STZ-INDUCED DIABETIC RATS AS DESCRIBED IN THE MATERIAL AND METHOD SECTION. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extremely significant.

Impact on Renal Parameters: Creatinine amount, overall protein concentration and Blood Urea Nitrogen are examples of renal parameters (BUN). In contrast to the Normal Control rats, STZ-induced diabetic rats have an elevated Creatinine level, as shown in Graph A. Due to the induction of diabetes, the creatinine level in all such rats increased. Still, on administering doses of the extract, there was a reduced amount of creatinine in rats.

Maximum effect was noted for 200mg/kg dose amongst the three doses of the extract. Graph B is about Total protein concentration, which reportedly reduces in diabetic rats; administration of extract doses and standard drugs aids in increasing the total protein. An increased level of BUN is shown in Graph C due to the induction of diabetes.

But on treating the rat's groups with doses of extract and standard drug glibenclamide, the level reduced considerably Best result was again seen for the group of rats which were given 200mg/kg dose of the sponge gourd peel extract **Fig. 8.**

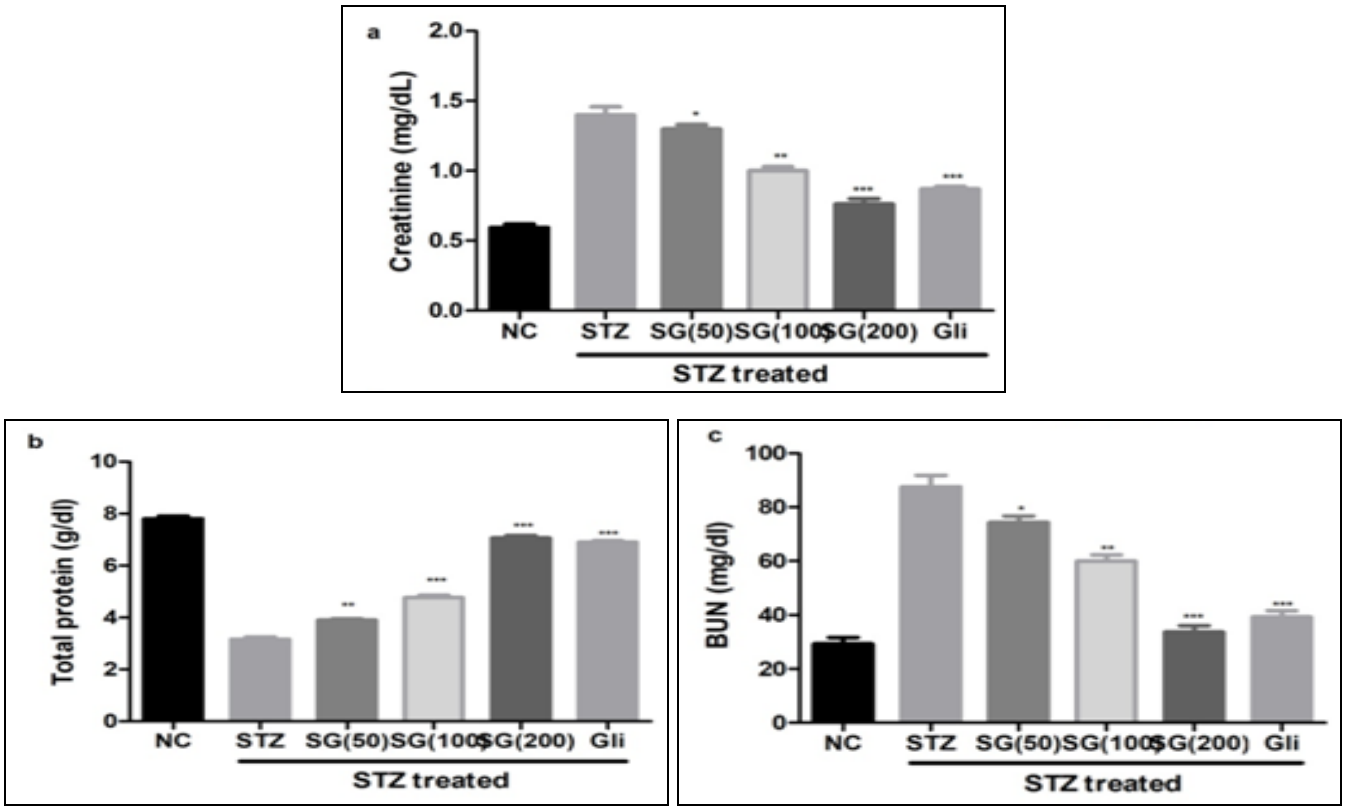

FIG. 8: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE RENAL PARAMETERS OF STZ-INDUCED DIABETIC RATS. A: creatinine, b: total protein and c: BUN as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extremely significant.

Impact on GLUT2 Parameters: Glucose transporter 2 is a transmembrane carrier protein that transports glucose across cell membranes with the aid of proteins. This is looked at in terms of the relative expression of renal and jejunal mRNAs (fold). Similar to GLUT2 transporters, we have

SLGT2 transporters, a type of Sodium-dependent glucose co-transporter, a family of glucose transporters. **Fig. 9** and **10**, GLUT2 levels rose when diabetes was induced in rats. This level was brought down when diabetic rats were treated with sponge gourd peel extract.

All three doses reduced the level of GLUT2, where the maximum effect was observed by 200mg/kg dose along with Glibenclamide. Inducing diabetes in rats leads to inflated GLUT2, as the graph shows. One should also notice the reduction in the risen levels of diabetic rats, post administration of sponge gourd peel extract and standard drug glibenclamide. The results obtained are promising as the level of SGLT 2 is decreased due to the extract.

STZ-induced diabetic rats had greater concentrations of SGLT1 and GLUT2, which were down-regulated by sponge gourd peel extract in a dose-dependent manner, bringing them close to the normal control group. In the Glibenclamide-treated group of rats, similar results were found **Fig. 10.**

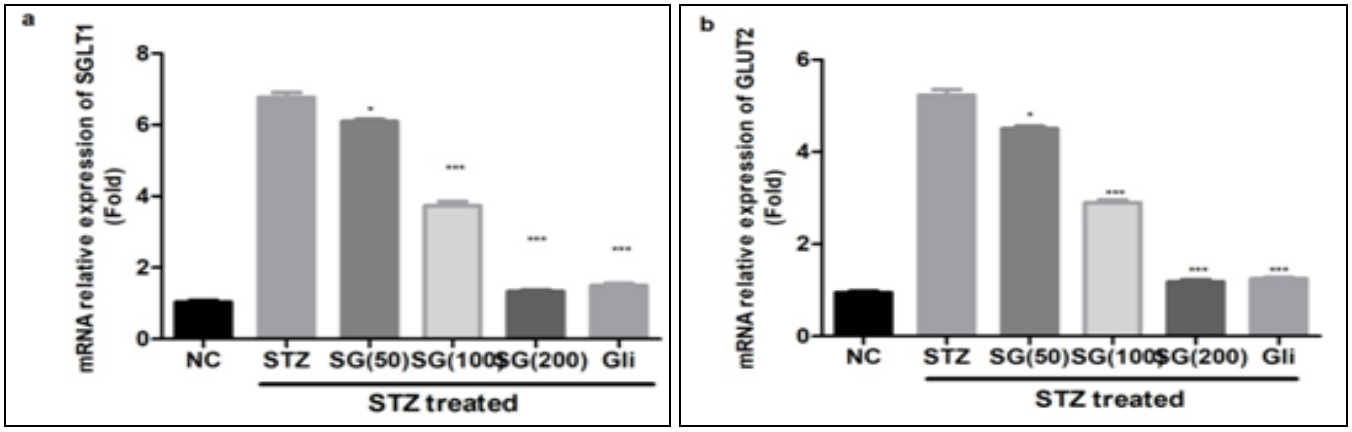

FIG. 9: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE MRNA EXPRESSION (JEJUNUM) OF STZ-INDUCED DIABETIC RATS. a: SGLT1 andb: GLUT2as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extreme significant.

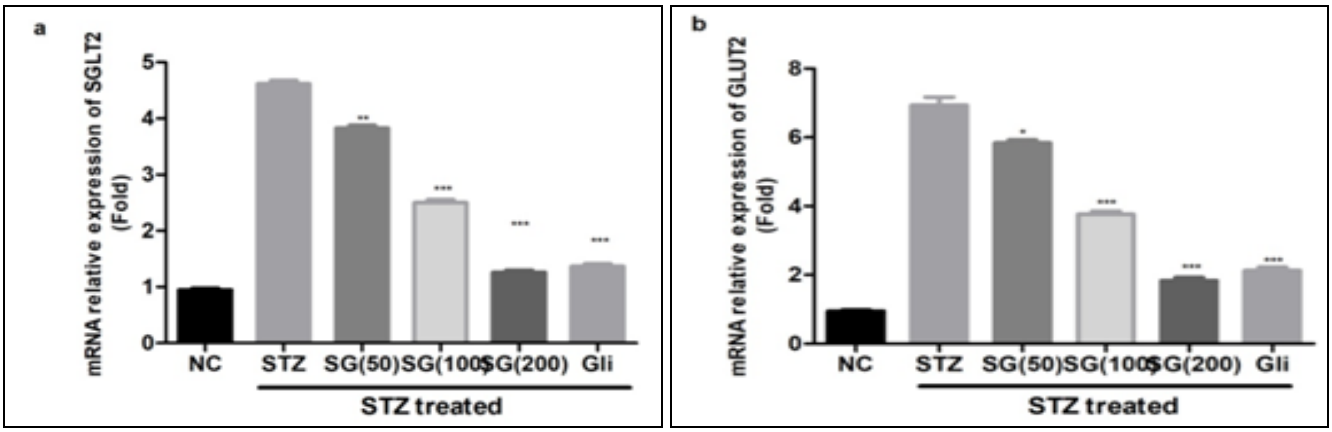

FIG. 10: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE MRNA EXPRESSION (RENAL) OF STZ-INDUCED DIABETIC RATS. A: SGLT1 andb: GLUT2as described in the material and method section. Where *P<0.05 consider as significant, **P<0.01 consider more significant and ***P<0.001 consider as extremely significant.

Effect on Pancreas: The β (beta) cells in the normal control group rats were in a standard state. STZ destroyed the cells and demonstrated the depletion of the Islet of Langerhans. STZ (streptozotocin) induced diabetic group rats displayed a reduction in cell size and necrosis, which was followed by atrophy and fibrosis. The STZ-induced diabetic population rats' histopathology followed a similar pattern. Streptozotocin (STZ)-induced diabetic rats were offered various doses of sponge gourd peel extract and Glibenclamide, resulting in the recovery of necrotic and fibrotic modifications as well as an increase in the proportion of cells **Fig. 11.**

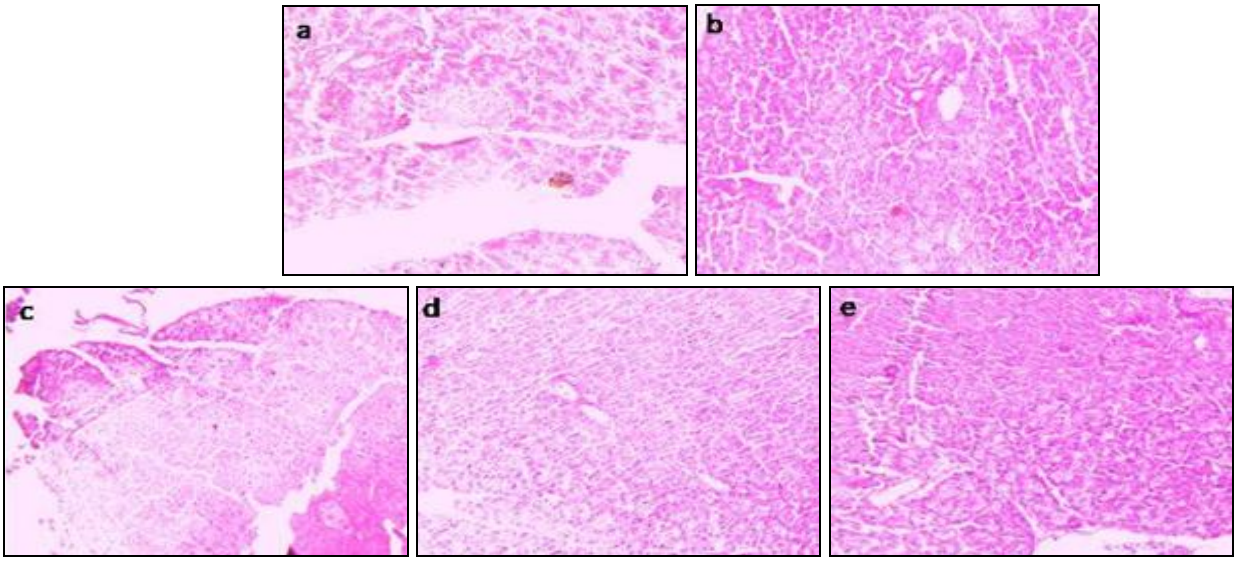

FIG. 11: SHOWED THE EFFECT OF SPONGE GOURD PEEL METHANOLIC EXTRACT ON THE PANCREAS HISTOPATHOLOGY OF STZ INDUCED DIABETIC RATS. A: DM control,b: DM + SG (50 mg/kg), c: DM + SG (100 mg/kg), d: DM + SG (200 mg/kg) and e: DM + Gli.

DISCUSSION: The antidiabetic activity of sponge gourd peel extract is depicted in this report. The hypoglycaemic, antioxidant and antidiabetic function of a methanolic extract of *Luffa cylindrica* peels in diabetic Wistar rats induced by streptozotocin (STZ). Streptozotocin (STZ) is a natural substance alkylating anti-cancer drug that is highly toxic to beta cells in mammals' pancreas (which contain insulin). STZ is a nitrosourea that got its cytotoxic properties from the soil microbe Streptomyces achromogenes [49–51].

Streptozotocin (STZ) works by perforating the β-cells through the glucose transporter and causing the DNA strand of the β-cells to smash, reducing endogenous insulin discharge. The nitrourea portion of STZ causes DNA puncturing. The disintegration of strands of DNA allows for changes in blood sugar and blood glucose. Following the administration of streptozotocin, changes begin to occur (STZ) [52, 53].

Hyperglycemia occurs 2 hours after Streptozotocin (STZ) administration, accompanied by a massive insulin deflation. Hyperglycemia is confirmed after approximately 6 hours caused by elevated insulin levels in the blood. Acute hyperglycemia progresses over time, followed by a decrease in insulin levels. The antidiabetic effect of sponge gourd peel extract is demonstrated in this experiment. After glucose administration, the oral glucose tolerance test is employed to determine changes in carbohydrate metabolism. The potential of a methanolic extract of SG (sponge gourd) peels to reduce blood glucose concentration in an OGTT (oral glucose tolerance test) indicated that rats given different doses of SG extract had better glucose utilization ability. According to the findings, elevated glucose tolerance was caused by insulin release from -cells and elevated glucose transport with multiple concentrations of SG extract treated groups. Due to muscle degradation or loss of organizational proteins, body decrease was noticed n Streptozotocin (STZ)-induced diabetic group rats.

Diabetic rats groups were given separate doses of SG (*Luffa cylindrica*) extract and Glibenclamide, which led to a large increase in body weight compared to diabetic control group rats. Per dose of SG extract and Glibenclamide has been shown to prevent thaw wasting (also referred to as reversal of gluconeogenesis). One dose of SG extract (200 mg/kg) displayed greater body weight recovery compared to the diabetes control rats' group and glibenclamide groups.

Glibenclamide-induced insulin secretion in a pancreatic cell. In diabetic rats induced by streptozotocin (STZ), plasma insulin was reduced [54–56]. Because of an active component in the plant extract that either compels insulin release or shields the completely operational β-cells from further deflation so that they can stay active and produce insulin, different doses of SG extract were given to groups of rats. The SG plant extract protects -cells,

resulting in lower blood glucose levels and reduced glucotoxicity in β-cells. The oral administration of SG extract for 28 days resulted in a significant reduction in blood glucose levels and an increase in plasma insulin levels. The potential mechanism of action of SG extract-treated community animals is that it increases insulin secretion from -cells of the islets of Langerhans in the pancreas [57, 58].

The hypoglycaemic behaviour of SG (*Luffa cylindrica*) extract compared to Glibenclamide gave the impression that their modes of action are likely to be similar. Insulin is a critical drug in the management diabetes mellitus, and several studies have been conducted to find a suitable replacement, secretagogin property, or activators derived from synthetic or natural sources that can be used as a substitute. Plants with high flavonoid content have been shown to have hypoglycemic and antidiabetic properties in a few studies, and our investigations have indicated that SG (*L. cylindrica*) peels extract is rich in flavonoids and phenolic compounds. STZ-induced diabetic rats raise the level of lipid peroxidation as non-primary evidence of originating free radicals (MDA). In STZ-induced diabetic rats, the proportion of lipids increases, resulting in the development of diabetes and accelerated free radical growth. Free radicals play a critical role in the progression of hyperglycemia and the creation of reactive oxygen species (ROS). Uninterrupted, free radical formation triggers tissue abrasion by destroying membranes through unsaturated fatty acid peroxidation; ROS increases lipid peroxidation and alters the antioxidant defence mechanism, and glucose metabolism in biological systems is impaired [59, 60, 61].

Lipid peroxidation eventually results in severe membrane damage and dysfunction. The number of endogenous antioxidant enzymes in pancreatic cells has decreased, posing a risk of free radical toxicological activity. SOD, GPx, and CAT levels were higher in STZ diabetes patients, while MDA levels were lower. Improved H_2O_2 establishment in the pancreas with diabetes elevated the amount of CAT, and increased superoxide development, related to cell malfunction or failure, heightened the amount of SOD. As the amount of SOD is raised without the amount of GPx, the peroxide level in the cells increases, resulting in peroxide overloading. As peroxide interacts with transition metals, it releases the highly toxic radical hydroxyl. Increasing superoxide levels, on the other hand, raises GPx levels, which are directly related/proportional to MDA. Different concentrations of SG (*Luffa cylindrica*) peel extract significantly elevated the concentration of endogenous antioxidants (SOD, CAT and GPx). Also, it protected the membrane from damage by reducing lipid peroxidation compared to diabetic controls. Decreased lipid peroxidation using MDA as an indicator; enhanced antioxidant status is perhaps one-way drug administration suppresses diabetic problems [62–64]. Glycogen is important for intracellular glucose storage. Insulin promotes intracellular glycogen deposition by activating glycogen synthesis and inhibiting glycogen phosphorylase, which is why many tissues have unmediated insulin activities. In Streptozotocin (STZ)-induced diabetes rats, glycogen accumulation in the liver was significantly decreased, directly affecting insulin and resulting in insulin insufficiency [65, 66].

STZ (Streptozotocin)-induced diabetic rats were given several doses of Sponge Gourd (SG) peels extract, raising insulin emission and restoring liver glycogen levels. Due to unrestricted glucose output mostly in blood, which then interacts with blood haemoglobin to produce glycated haemoglobin, the level of glycated haemoglobin (A1c) in streptozotocin (STZ) induced diabetic rats was increased. Streptozotocin (STZ) raised total cholesterol and triglyceride levels in diabetic rats.

The main factors contributing to the onset of diabetes and atherosclerosis (atherosclerotic cardiovascular disease), a secondary complication of diabetes, are hypercholesterolemia and hypertriglyceridemia [54, 67–69]. STZ-induced diabetic rats were given Glibenclamide, and three separate doses of SG (*Luffa cylindrica*) peels extract. Both glibenclamide and SG peels extract were observed to restore normal total cholesterol and triglyceride levels. This could be due to the induction and escalation of insulin secretion, which prevented hormone-sensitive lipase and improved glucose utilization, lowering free fatty acids' mobility from fat depositions. STZ diabetic groups had higher LDL (low-density lipoprotein) and lower HDL (high-density lipoprotein) levels, suggesting a higher coronary risk factor and a reduced

cardiovascular risk factor, respectively. High levels of TC (total cholesterol) and TG (triglycerides) are linked to high levels of LDL, VLDL, and low levels of HDL in diabetics. As a result of the elevated amount of LDL and VLDL accumulated in peripheral tissue due to diabetes, atherosclerosis progresses. Different doses of SG extract were given to the STZ diabetic classes, which resulted in substantial reductions in total cholesterol, triglyceride low-density lipoprotein, VLDL and MDA levels [69–71].

According to the results, different doses of SG were believed to reduce blood lipid abnormalities. The liver is a crucial organ that protects the body from postprandial hyperglycemia. With the aid of hexokinase, the liver transforms glucose to glucose-6-phosphatase and also converts glucose to energy. The volume of glucose-6-phosphatase, which promotes fat transformation to carbohydrates and accumulates in the liver and kidney, was increased in STZ-induced diabetes rat classes. In contrast, the amount of hexokinase, which decreases glucose regeneration and usage, was decreased. Another supplementary result in diabetes is increased fructose-1-6-phosphate levels [69, 72, 73].

CONCLUSION: Finally, we'd like to point out that our studies consistently showed that sponge gourd/ *Luffa cylindrica* peels extract has antidiabetic effectiveness, as it reduces blood glucose levels in the body and the transporters GLUT2 and SGLT1 concentration in hyperglycemic rats. The antioxidant activity of this extract was due to a decline in lipid peroxidation (oxidative degradation of lipids) and elevated amounts of SOD, GPx and CAT. It can be assumed that the methanolic extract of sponge gourd peel has anti-hyperglycaemic activity.

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