

**How to Cite:**

Nepal, A. ., Chakraborty, M., Jana, S., & Haldar, P. K. (2022). Anti - diabetic activity of *aeschynanthus sikkimensis (clarke) stapf.* extract in streptozotocin induced hyperglycemic rats. *International Journal of Health Sciences*, 6(S1), 9919–9933.  
<https://doi.org/10.53730/ijhs.v6nS1.7355>

## **Anti - diabetic activity of *aeschynanthus sikkimensis (clarke) stapf.* extract in streptozotocin induced hyperglycemic rats**

**Abhimanyu Nepal**

Department of Pharmaceutical Technology, Jadavpur University, Kolkata-700032, West Bengal, India

**Mainak Chakraborty**

Department of Pharmaceutical Technology, NSHM Knowledge Campus Kolkata Group of Institutions, 124, B.L Saha Road, Kolkata-700053, India

**Sandipan Jana**

Department of Pharmaceutical Technology, Jadavpur University, Kolkata-700032, West Bengal, India

**Pallab Kanti Haldar**

Department of Pharmaceutical Technology, Jadavpur University, Kolkata-700032, West Bengal, India

Corresponding author email: [pallab\\_haldar@rediffmail.com](mailto:pallab_haldar@rediffmail.com)

**Abstract---**Objective: The research was design to conduct anti-diabetic activity of methanol extract of *Aeschynanthus sikkimensis (Clarke) Stapf.* in streptozotocin induce hyperglycemic rats. Material and method: Streptozotocin 35mg/kg body weight was injected intraperitoneal to produce hyperglycemia rats which were pretreated with a high fat diet.72 hours after introduction of STZ, the hyperglycemic rats received MEAS at dose 200 and 400 mg/kg body weight for 28 days. Reference drug used was Glibenclamide (0.5 mg/kg, orally). During the 28 days treatment fasting blood glucose level were determined on every 7<sup>th</sup> day. Serum and hepato renal biochemical parameters were estimated. Result: MEAS at the dose of 200 and 400mg/kg outstandingly (P <0.05) and dosage dependently reduce blood glucose levels towards normal as differentiate to STZ control group Serum and hepato renal biochemical parameter were altogether (P<0.05) restore towards the typical levels in MEAS sedated rats as differentiated to STZ control group. Conclusion: It may be concluded that the whole plant extract of *Aeschynanthus sikkimensis (Clarke)*

*Stapf* which belong to the family Gesneriaceae showed encouraging hypoglycemic action in STZ induced diabetic rats.

**Keywords**--Streptozotocin (STZ), *Aeschynanthus sikkimensis* (Clarke) *Stapf.*, phytol, glibenclamide.

## Introduction

The foremost costly blessing nature has given to human are herbal plant. Secondary products combination is taxonomically distinct in an isolated plant species, making plant unique to its medicinal action. The phyto chemical presents in plant extricate choose out the bio chemical pathways making it a more secure pharmaceutical. With expanding side impact of the manufactured drugs, the plant based herbal drugs are getting to be more promising. Most recently, studies on phytochemical constituents of medicinal plant and its pharmacological activities have gain generous notice (Rajeswari et al., 2013).

Diabetes mellitus is a metabolic disorder identified by a loss of glucose homeostasis, with unsettling influences in digestion system of carbohydrate, fat and protein coming about in absconds of affront emission, affront activity, or both (Imam 2021). It is one of the most challenging global epidemics of the twenty first century. Universally in 2017 diabetes caused four million deaths, making it among top ten cause of death in grown-ups. According to the International diabetes federation it was approximated that 425 million individuals with diabetes worldwide in 2017(Saeedi et al., 2019) and by 2035 it will rise to 592 million (Joshi 2015). In India 62 million people are currently affected by diabetes. The highest absolute number in any countries. Respectively by 2030, the estimated number will rise to 101.2 million. The existing burden of this disease is rapidly raised in the Indian middle class, coupled with sedentary lifestyles and a shift in dietary pattern (Mitra 2019).

Right now, there are number of compelling western medicine accessible for the treatment of diabetes but still it's higher taken a toll and side impact may be an enormous challenge for its administration. Utilize of herbal pharmaceutical for the protective treatment of diabetes has been within the history of a few thousand a long time within the Indian and Chinese culture (Wang et al., 2013). Plant and its products are being used as traditional medicine for primary health by 90% of the population in developing countries, as stated by World Health Organization (WHO). Among 21,000 plants listed by WHO having medicinal property 2500 species are found in India. It's reported that 800 plants show ant diabetic potential (Rizvi et al., 2013).

*Aeschynanthus sikkimensis* (Clarke) *Stapf.* is an epiphytic under shrub in the Gesneriaceae family that grows in Himalaya at an altitude of 5000-7000ft above sea level in north east India, Nepal and Bhutan. Rootstock leaves and flowers are widely used traditionally for fever, throat pain and tonsillitis (Rai et al., 2010). A detailed literature review shows that there was no scientific report to give credence to the ethnomedicinal usage of this plant therefore, in the light of its use in traditional medicine, an effort has been made to explore anti diabetic activities of

methanol extract of *Aeschynanthus sikkimensis* (Clarke) Stapf. (Gesneriaceae) on streptozotocin induced diabetic wistar rats.

## **Materials and Methods**

### **Plant material**

*Aeschynanthus sikkimensis* (Clarke) Stapf. whole plant was procured on May, 2016 from the hill region of Sikkim, India. The genuineness of the plant species was identified by referring the deposited specimen by Botanical Survey of India, Gangtok, Sikkim. The specimen voucher number is SHRC- 5/02/2012-Tech 88. The whole plant was washed properly and with occasional shifting it was shade-dried at room temperature (24–26 °C). The dried plant was powdered mechanically into coarse powder. It was then stored in an airtight container for further use.

### **Drugs and chemicals**

The chemicals, solvents and drugs used to conduct this experiment were of analytical grade. Streptozotocin, thiobarbituric acid, phenazoniummethosulfate, 5, 5'- dithiobis-2-nitrobenzoic acid, nicotinamide adenine dinucleotide and reduced glutathione (GSH) were obtained from Sisco Research Laboratory, Mumbai. Trichloroacetic acid from Merck Ltd., Mumbai, India. Potassium dichromate and glacial acetic acid from Ranbaxy, India; and glibenclamide from Hoechst, India.

### **Preparation of extract**

The maceration of powdered plant material (200 g) using methanol (450ml) was done at room temperature (24–26°C) for 4 days with occasional shaking, followed by 3 days of re-maceration. After filtration, under reduced pressure in a rotary evaporator (Buchi R-210) the filtrate was evaporated at 30 °C. The extract was dried and weighed. The yield was 15g. The concentrated extract was maintained in a refrigerator for further use.

### **Experimental animals**

Healthy male wistar albino rats (180±20gm) with no prior drug treatment were procured from registered breeder (Chakraborty and Co., Kolkata). Before the study commenced the animals were adapted to laboratory hygienic condition for seven days. The animals were held on to 25°C±2°C and at 40% - 45% relative humidity with 12hours day and night cycles. The animals were fed with commercial pellet diet (Hindustan Unilever, Mumbai, India) and water *ad Libitum*. The animals study procedure expressed were evaluated and accepted by the university animal ethical committee, Jadavpur University (367001/C/CPCSEA).

### **Acute toxicity**

The acute toxicity was evaluated as per the described method (OECD 2008). The animals treated with extract were observed for 14 days for mortality and general behavior. No toxic effect or death was observed by the end of the study. The test sample was valued safe up to the dose of 2000mg/kg.

### **Induction of diabetes with high-fat diet and streptozotocin**

Male rats were fed with high-fat diet comprising 22% fat, 48% carbohydrate and 20% protein in blend with standard laboratory chow consisting of 5% fat, 53% carbohydrate and 23% protein for 8 weeks. After the period of dietary manipulation, rats were injected intraperitoneally (i.p) with low dose of STZ (35 mg/kg). Then the animals had free access to water and standard food (Ghorbanzadeh *et al.*, 2016). One week after the injection of streptozotocin the fasting blood glucose levels were appraised and the animals exhibiting fasting blood glucose level of  $170 \pm 30$  mg/dl were considered to be type 2 diabetic (T2D) rats and included for the further experiments (Bhattacharjee *et al.*, 2016).

### **Oral glucose tolerance test**

Normal overnight fasted rats were used for oral glucose tolerance test. Three groups of six rats were caged. Group I received distilled water (5ml/kg. b.w., p.o.) and served as normal control. Group II and Group III received MEAS at dose of 200 and 400 mg/kg respectively. Glucose (2gm/kg b.w.) was given orally after these treatments. The single touch glucometer (Accu-Chek, Roche Diagnostics, USA) was used to check the blood glucose levels at 0, 30, 60 and 120 minutes after oral glucose administration (Halder *et al.*, 2010).

### **Experimental design**

On the 8<sup>th</sup> days after STZ injection, the FBG levels of overnight- fasted rats were evaluated, and the animals showing FBG levels of  $170 \pm 30$  mg/dl were considered to be T2DM rats and incorporate for the experiments. The rats were split up into five groups (n=6) and receive following treatment for 28days.

Group I: Normal non-diabetic control, which receive normal Saline (0.5 ml/kg orally by oral gavages) daily.

Group II: Diabetic (STZ) control rats were administered high fat diets + normal Saline (0.5 ml/kg orally by oral gavages) daily.

Group III: Diabetic rats, which received MEAS (200 mg/kg body weight) + high fat diets orally daily.

Group IV: diabetic rats, which received MEAS (400 mg/kg body weight) + high fat diets orally daily.

Group V: diabetic rats, which received reference drugs glibenclamide (0.5 mg/kg b.w.) + high fat diets orally daily.

### **Estimation of fasting blood glucose level**

The rats were divided into five groups (n=6). Except group I, which served as normal control, all other groups were comprised of diabetic rats. Group II served as diabetic (HFD-STZ) control. Group III and IV received MEAS (200 and 400 mg/kg body weight respectively) and group V received reference drug daily for 28 days (Biswas *et al.*, 2011). Fasting blood glucose was measured on days 0, 7, 14, 21 and 28 using a one-touch glucometer (Accu-Chek).

### Determination of serum biochemical parameters

The blood was collected from overnight fasted rats by cardiac puncture from each group, after twenty-four hours of last dose administered. The collected blood was used to estimate total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, glycosylated hemoglobin (HbA1c), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and total protein were estimated using commercially obtainable reagent kits (ERBA Diagnostics, Andheri (E), Mumbai 400072, India, and Span Diagnostics Ltd., Surat, Gujarat 394230, India) (Das *et al.*, 2011).

### Estimation of liver and kidney biochemical parameter

Animals were sacrificed, liver and kidneys were collected and homogenized separately in 10 ml of phosphate buffer (20 mM, pH: 7.4) and centrifuged at 12,000 rpm for 30 min at 4°C. The collected supernatants were used for estimation of lipid peroxidation (LPO), GSH, superoxide dismutase (SOD), and catalase (CAT) (Haldar *et al.*, 2010 and Das *et al.*, 2011).

### Statistical Analysis

The results were analyzed for scientific importance by one-way analysis of variance, followed by post hoc Dunnett's test using Graph Pad Prism 5.0 software (Graph Pad Software Inc, La Jolla, CA, USA).  $P < 0.05$  was observed as scientific importance. Three individual measurements were done and the data given as mean  $\pm$  standard error of mean.

### Results

MEAS when administered showed no harmful effect or death at the dose of 2000 mg/kg, b.w., p.o. for acute toxicity studies. Normal rats were used to study oral blood glucose tolerance test. Increased in blood glucose level was observed for first 30 minute. It nearly returned to normal at 120 minutes, gradually decreasing at 30 and 60 minutes which are shown in Table 1.

Table 1  
Effect of MEAS on Oral blood glucose tolerance test

Groups	0 Minutes	30 Minutes	60 Minutes	120Minutes
Normal Control	80.32 $\pm$ 1.016	129.45 $\pm$ 1.881	121 $\pm$ 1.046	111 $\pm$ 2.281
MEAS 200	76.45 $\pm$ 2.122	132.78 $\pm$ 1.725	129.29 $\pm$ 1.804*	122.67 $\pm$ 3.478
MEAS 400	86.33 $\pm$ 1.035*	139.45 $\pm$ 2.338*	117.56 $\pm$ 1.114*	114.23 $\pm$ 3.326
Glibenclamide	79.55 $\pm$ 0.773	135.34 $\pm$ 1.562*	119.57 $\pm$ 1.139*	112.59 $\pm$ 2.123

Values are represented as mean  $\pm$  SEM, where n = 6. \* $P < 0.05$  when compared to normal control.

As compared to the normal group fasting blood glucose level was elevated significantly ( $P < 0.05$ ) in STZ-induced diabetic rats. Fasting blood glucose level was reduced significantly ( $P < 0.05$ ) toward normal after administration of MEAS at dose

200 and 400 mg/kg in diabetic rats as compared to that of diabetic control group (Table 2).

Table 2  
Effect of MEAS on Fasting Blood Glucose (mg/dl)

Groups	Day 0	Day 7	Day 14	Day 21	Day 28
Normal Control (5ml/kg)	73±1.352	79±2.883	81±2.108	80±1.641	79±2.793
HFD and STZ Control (35mg/kg)	273±1.232 <sup>a</sup>	284±3.887 <sup>a</sup>	296±2.725 <sup>a</sup>	310±3.357 <sup>a</sup>	331±2.845 <sup>a</sup>
STZ + 200mg/kg MEAS	277±1.238	268±2.044 <sup>b*</sup>	260±2.496 <sup>b*</sup>	251±1.333 <sup>b</sup>	221±1.994 <sup>b</sup>
STZ + 400mg/kg MEAS	280±1.285 <sup>b*</sup>	262±2.509	252±1.687 <sup>b*</sup>	153±1.965 <sup>b</sup>	147±1.939 <sup>b</sup>
STZ + 0.5 mg/kg Glibenclamide	276±1.621	260±1.887	251±1.875 <sup>b*</sup>	143±1.764 <sup>b</sup>	141±2.201 <sup>b</sup>

<sup>a</sup>Normal control group versus diabetic control group, <sup>b\*</sup>All treated group versus diabetic control group on corresponding day,  $P < 0.05$ . Each volume expressed as mean  $\pm$  SEM (n=6).

As compared to STZ control animals reduced HbA1c was found in MEAS treated animals (Table 3).

Table 3  
Effect of MEAS on HbA1c

Groups	HbA1c (%)
Normal	6.3±0.1542
STZ control (diabetic)	8.9±0.2082**
Diabetic + MEAS (200 mg/kg)	8.1±0.3380**
Diabetic + MEAS (400 mg/kg)	7.6±0.1455**
Diabetic + glibenclamide (0.5 mg/kg)	7.3±0.2338**

Values are represented as mean  $\pm$  SEM (n=6). \*\* $P < 0.05$  when compared to normal control

MEAS showed a significant ( $P < 0.05$ ) lowering of serum biochemical parameter like SGPT, SGOT and ALP as compared to the STZ control group. In tested group level of total protein increases when compared to the STZ control Figure 1.

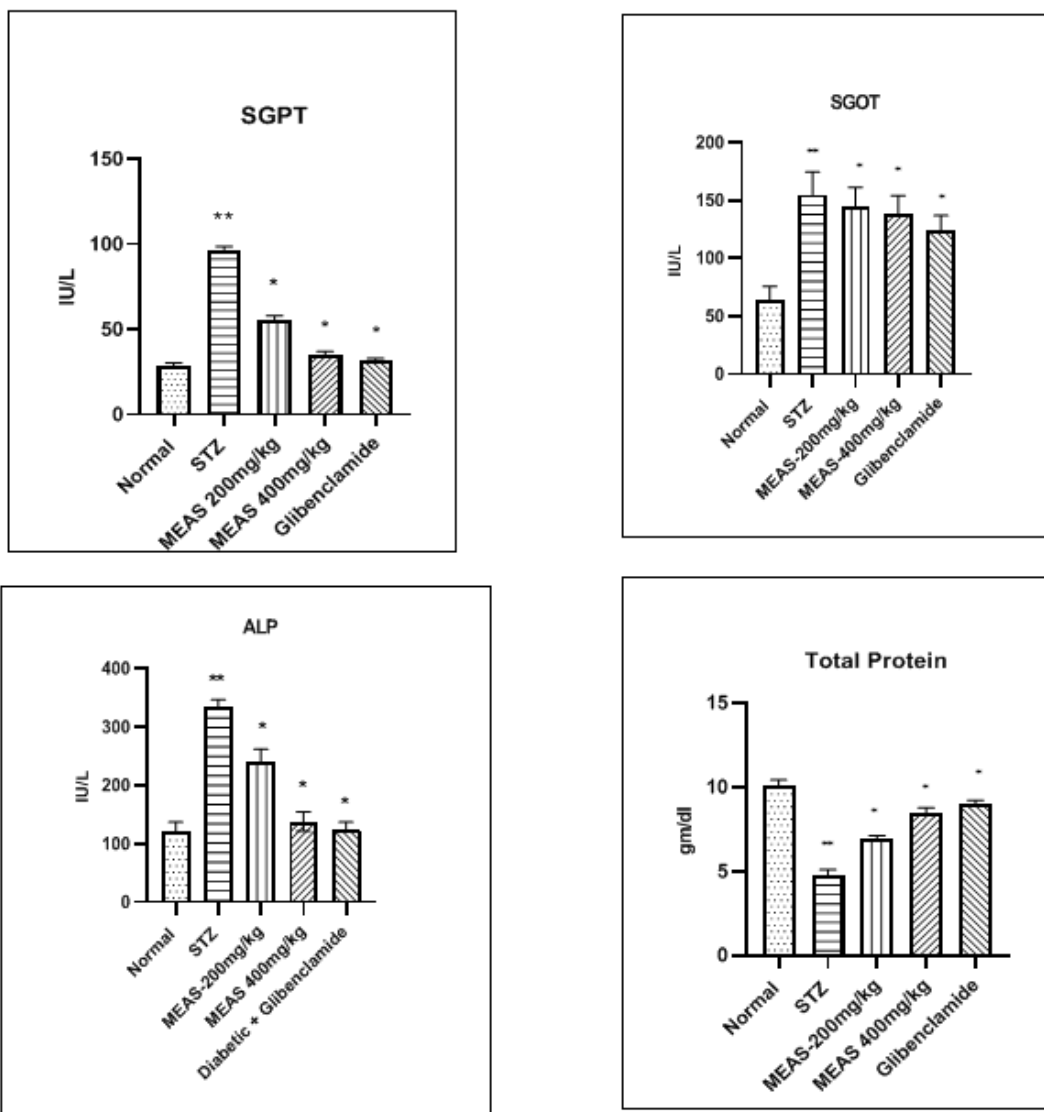


Figure 1: Effect of MEAS on Serum Biochemical Parameters. Each value is expressed as mean  $\pm$  standard error of mean ( $n = 6$ ). Where \*\*  $p < 0.0001$  when compared to normal and \*  $< 0.0001$  When compared to diabetic control.

When compared to the diabetic control group, the treatment group with the dose of 200 and 400mg/kg significantly ( $P < 0.05$ ) reduced the total cholesterol and triglyceride level, whereas there was significantly ( $P < 0.05$ ) increase of HDL cholesterol (Figure 2).

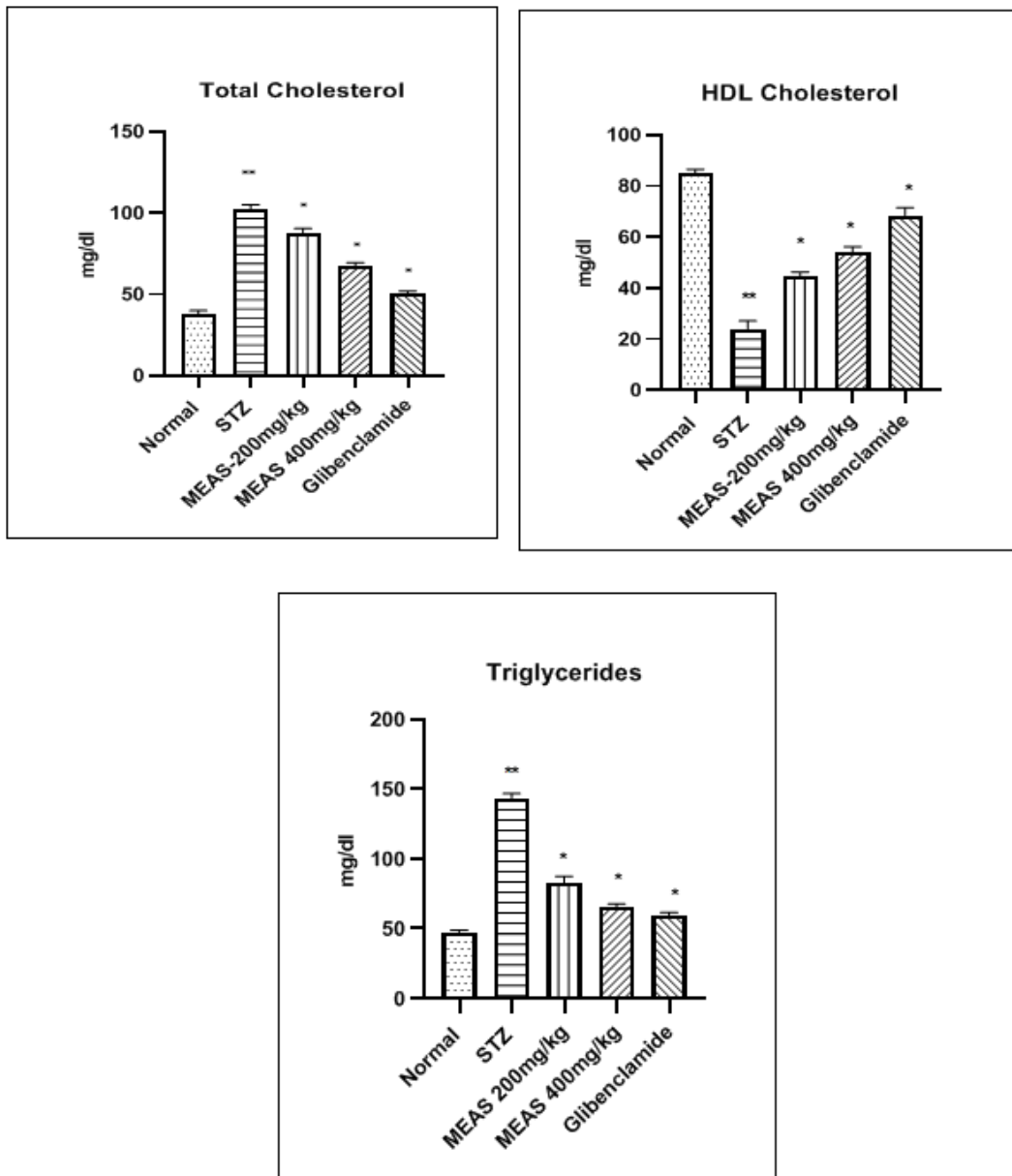


Figure 2: Serum Lipid Profile. Effect of MEAS on Total Cholesterol, HDL Cholesterol and Triglyceride. Each value is expressed as Mean  $\pm$  SEM where  $n=6$ . \*\*  $p < 0.05$  when compared to normal and \*  $p < 0.0001$  when compared to diabetic control. In liver and kidney tissue antioxidant studies, LPO level decreased ( $P < 0.05$ ) and SOD, GSH, and CAT level increased ( $P < 0.05$ ) in treated animals [Figure 3].

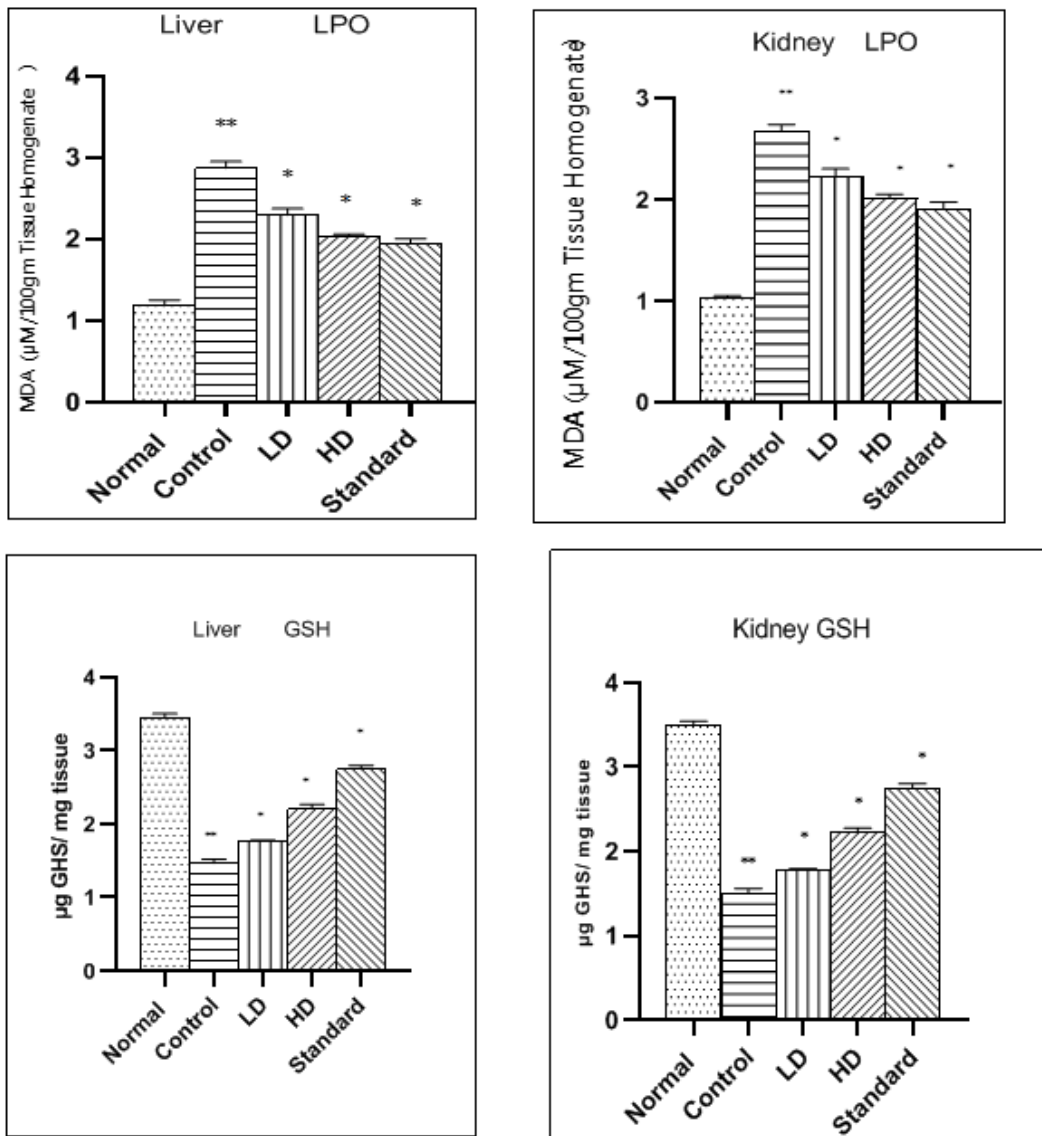


Figure 3: Liver and Kidney Antioxidant Parameter. Effect of MEAS on LPO and GSH. Each value is expressed as Mean  $\pm$  SEM where n= 6. \*\* p < 0.05 when compared to normal and \* p < 0.0001 when compared to diabetic control.

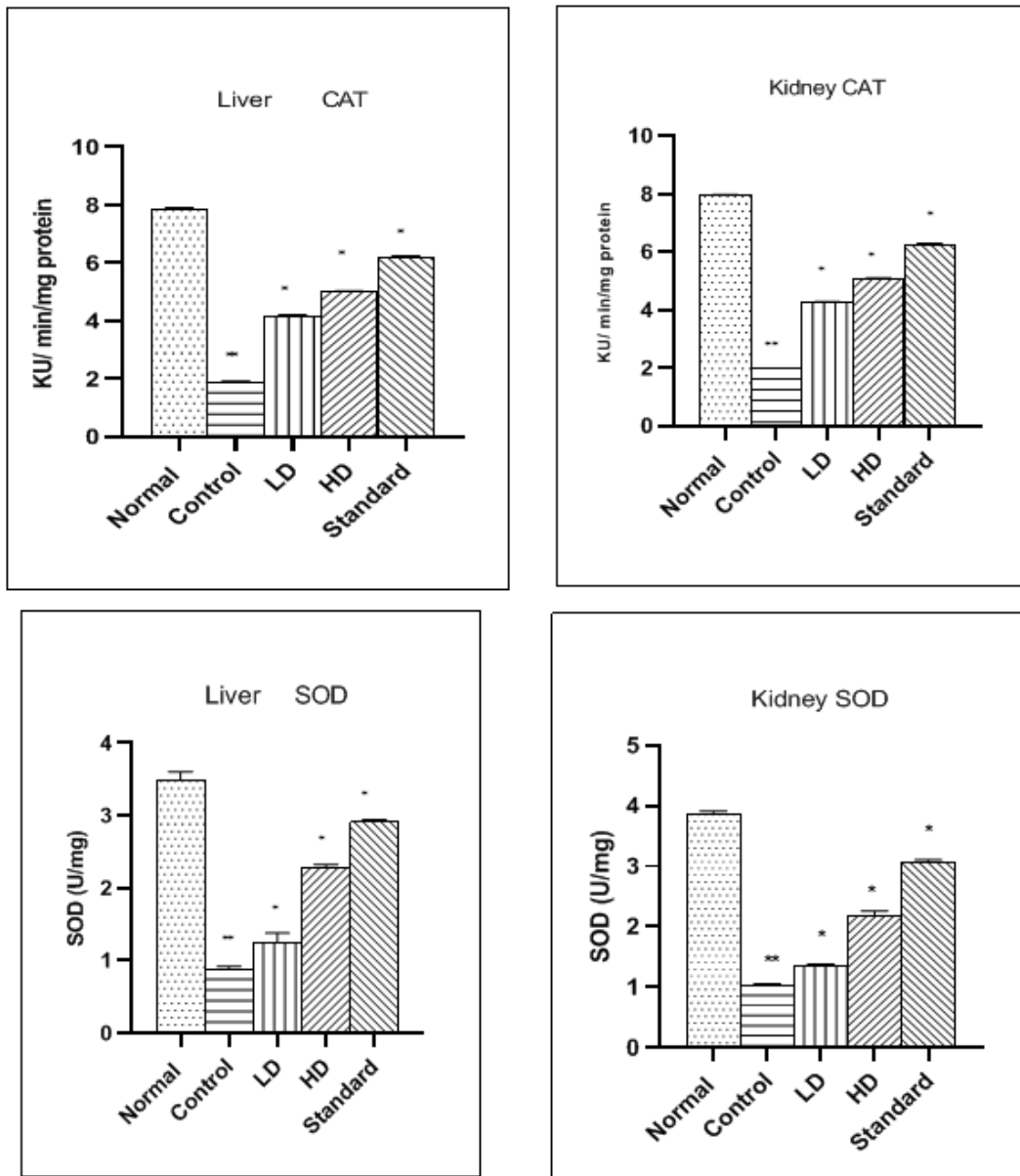


Figure 4: Liver and Kidney Antioxidant Parameter. Effect of MEAS on CAT and SOD. Each value is expressed as Mean  $\pm$  SEM where  $n=6$ . \*\*  $p < 0.05$  when compared to normal and \*  $p < 0.0001$  when compared to diabetic control.

## Discussion

The present study was focus to investigate the anti diabetic activity of whole plant extract of *Aeschynanthus sikkimensis* (Clarke) Stapf which belong to the family Gesneriaceae in STZ (35mg/kg) induced diabetic rats. The results of the study disclosed that MEAS at the dose of 200 mg/kg and 400 mg/kg undoubtedly

regularize elevated blood glucose level and bring back serum, liver and kidney biochemical parameter towards the normal level.

The HFD-STZ induced diabetic rat is one of the animal models of human non-insulin dependent diabetes mellitus (NIDDM) or type 2 diabetes mellitus. As in human T2DM, diet has a great influence on the development of diabetes as well as hypertension, hyperlipidaemia and eventually nephropathy in experimental model (Chakraborty *et al.*, 2018).

According to many previous studies data, insulin resistance developed in rat feed with high fat diet. Pancreatic  $\beta$  cell functioning get critically damage with injection of high dose STZ leading to stop in insulin secretion resembling T1DM. Gradual impairment of insulin secretion has been reported in high fat low dose STZ administered animals, which is similar to the natural progression of T2DM in human. Therefore, in the current study a high fat low dose STZ was adopted to develop type 2 diabetes in rats (Qian *et al.*, 2015).

OGTT data revealed that the MEAS at dose of 200 and 400mg/kg successfully avoid serum glucose level increase without causing hypoglycemia as efficiently as the reference drug glibenclamide. Intestinal glucose transporter reduction can be corroborated from the result (Panda *et al.*, 2016).

Increased formation of HbA1C might lead to lowering of total hemoglobin. Administration of MEAS decreased the level of HbA1C. On the 8<sup>th</sup> days of STZ induction, hyperglycaemic was observed. The fasting blood glucose levels started reducing in high fat low dose of STZ induced diabetic rats in the dose dependent manner after 7, 14, 12 days and after 28 days the concentration of glucose in the blood was near to normal level. The antihyperglycemic effect of MEAS at the dose of 200 mg/kg and 400 mg/kg was found to be similar to the effect exercise by the reference drug glibenclamide at a dose of 0.5 mg/kg.

In the pathogenesis of diabetes mellitus lipids has an important role. Rise in total cholesterol in blood is a familiar factor related to uncontrolled diabetes mellitus and may contribute to coronary artery disease (Arvind *et al.*, 2002). In the present investigation, the elevated serum lipids profile was improved by MEAS at the dose of 200mg/kg and 400mg/kg towards normal in diabetic rats. Treatment of diabetic rats with MEAS at a dose of 200 and 400mg/kg showed considerable reduction in hepatic lipid accumulation. Lipase functions as a lipolytic enzyme that hydrolyzes triglyceride and phospholipids in circulating plasma lipoproteins. Reduction of fat absorption by the inhibition of pancreatic lipase is known to be beneficial for the regulation of obesity and related metabolic disorders (Bhandaria *et al.*, 2013).

Hepatocellular necrosis in diabetic rats is responsible for increase in the plasma AST, ALT, ALP activities and it also led to decrease of total proteins. The degree of liver damage in STZ induced diabetic rats can be evaluated by AST and ALT (Al-Musa *et al.*, 2014). All the above mentioned hepatic biochemical parameter was brought back towards the normal levels in a dose dependent manner after 28days treatment with MEAS. These results indicate the plant is having a good protective effect on liver.

Diabetes is a chronic metabolic disease associated with hyperglycemia and oxidative stress which generally cause several tissue damage and subsequently degenerative complication in many organs such as liver, kidney etc. (Jemai *et al.*, 2015).

Autoxidation of glucose, protein glycation, lipid peroxidation, and low activities of antioxidant enzymes cause elevated levels of oxidative stress in diabetic animals (Giugliano *et al.*, 1996). Tissue damage related to lipid peroxide has been observed that in the development of both Type 1 and Type 2 diabetes mellitus. In biological system due to impaired insulin secretion lipid peroxidation get evoked. With increase in TBARS formation in liver and kidney of diabetic rats prove the excessive formation of free radicals leading to activation of lipid per oxidative system. In this study, administration of MEAS 200 and 400 mg/kg inhibit MDA production. This show MEAS has an anti lipid per oxidative potential.

The most important scavenging enzymes SOD and CAT play protective role in deleterious effect in cells. Activation of SOD and CAT to near normal level in diabetic rats was observed after administration of MEAS at dose of 200 and 400mg/kg, showing that the extract exhibit free radical scavenging activity.

Endogenous non enzymatic antioxidant system glutathione plays an important role. Primarily acting as a reducing agent, it detoxifies hydrogen peroxide with the help of enzyme glutathione peroxidase (Biswas *et al.*, 2011). The exhausted GSH may be due to reduction in GSH synthesis or degradation of GSH by oxidative stress in HFD and STZ- induced hyperglycemic animals but after treatment with MEAS increased the GSH level in both liver and kidney tissues

GC-MS analysis of methanol extract of *Aeschynanthus sikkimensis* (Clarke) Stapf confess the presence of pyridine, tetradecane, 2,4-Di-tert-butylphenol, hexadecane, Tridecanoic acid, 12-methyl-, methyl ester, octadecane, 13-methyltetradec-9-enoic acid methyl ester, neophytadiene, 2-Pentadecanone - 6,10,14-trimethyl, 9,12-Octadecadienoic acid (Z,Z)-, hexadecanoic acid, methyl ester, n-Hexadecanoic acid, eicosane, hexadecanoic acid, 14-methyl-, methyl ester, palmitic Acid, TMS derivative, methyl 10-trans,12-cis-octadecadienoate, 13-Octadecenoic acid, methyl ester, 11,13-Dimethyl-12-tetradecen-1-ol acetate, phytol, methyl stearate and oleic acid (Nepal *et al.*, 2021).

An acyclic diterpene alcohol molecule and a precursor of synthetic vitamin E and K1, Phytol was first obtained by chlorophyll hydrolysis. It has been reported that the phytol has been involved in control of diabetes (Verma *et al.*, 2018 and Heim *et al.*, 2002). In the management of insulin resistance and metabolic disorders that include diabetes and/or obesity phytol play a potential role, through activating RXR via its metabolite, and regulating other factors that imply in metabolic disorders (Elmazar *et al.*, 2013).

Oleic acid has been reported to ameliorate the diabetic symptoms of type II diabetic mice characterized by inflammation by insulin production and recovery the inhibitory insulin effect of TNF alpha (Vassiliou *et al.*, 2009). Oleic acid also activates the signaling pathways promoting triglyceride storage and insulin generation (Nemecz *et al.*, 2019). Blood glucose level and pancreatic beta cell

function in T2DM can be improved by various anti-inflammatory agents as demonstrated in various preclinical and clinical studies (Gothai *et al.*, 2016). Thus, the notable antidiabetic effect of the extract may be due to the presence of eicosane, phytol, oleic acid and a phenolic compound (2, 4-Di-tert-butylphenol) in methanol extract of *Aeschynanthus sikkimensis* (Clarke) Stapf or their synergistic properties.

## Conclusion

The present study distinctly indicate that the use of MEAS shows notable reduction in blood glucose level. A clear indication of improvement in the antioxidant defense system in liver and kidney and normalization of serum biochemical profile including lipid content as compared to diabetic rats. However, further examination of secondary metabolites responsible for antidiabetic property and antioxidant effect should be undertaken to confirm the compound which is responsible for these activities.

## Conflict of Interest Statement

We declare that we have no conflict of interest.

## Acknowledgements

The authors acknowledge the support extended by Department of Pharmaceutical Technology, Faculty of Engineering and Technology, Jadavpur University, Kolkata, India and Department of Pharmaceutical Technology, NSHM Knowledge Campus, Kolkata - Group of Institutions for providing necessary infrastructure and financial support.

## Reference

1. Al-Musa, H., AL-Hashem, F. (2014). Hypoglycemic, hepato-renal and antioxidant potential effects of *Chamomile recutita* flowers ethanolic extract in streptozotocin - diabetic rats. *Am J PharmacolToxicol.* 9, 1-12.
2. Arvind, K., Pradeep. R., Deepa, R., Mohan, V. (2002). Diabetes and coronary artery diseases. *Indian J Med Res.* 116, 39-44.
3. Bhandaria, U., Chaudharia, H.S., Khannab, G., Najmia, A.K. (2013). Antidiabetic effects of *Embelia ribes* extract in high fat diet and low dose streptozotocin-induced type 2 diabetic rats. *Frontiers in life science.* 7(34), 186-196.
4. Bhattacharjee, N., Khanra, R., Dua, T.K., Das, S., De, B., Zia-Ul-Haq, M., Feo V.D., Dewanjee, S. (2016). *Sansevieria roxburghiana* Schult. & Schult. F. (Family: Asparagaceae) Attenuates Type 2 Diabetes and its associated cardiomyopathy. *PLoS ONE.* 11(11), e0167131.
5. Biswas, M., Kar, B., Bhattacharya, S., Kumar, R.B.S., Ghosh, A.K., Haldar, P.K. (2011). Antihyperglycemic activity and antioxidant role of *Terminalia arjuna* leaf in streptozotocin-induced diabetic rats. *Pharm Biol.* 49(4), 335-340.
6. Chakraborty, M., Bala, S., Bhattacharya, S., Haldar, P.K. (2018). Hypoglycemic effect of ethyl acetate fraction of methanol extract from *Campylandra aurantiaca* rhizome in high-fat-diet and low-dose streptozotocin-induced diabetic rats. *Pharmacognosy Magazine.* 14, S539-545.

7. Das, S., Bhattacharya, S., Prasanna, A., Suresh Kumar, R.B., Pramanik, G., Haldar, P.K. (2011). Preclinical evaluation of antihyperglycemic activity of *Clerodendron infortunatum* leaf against streptozotocin-induced diabetic rats. *Diabetes Ther.* 2, 92-100.
8. Elmazar, M.M., El-Abhar, H.S., Schaalan, M.F., Farag, N.A. (2013). Phytol/Phytanic acid and insulin resistance: Potential role of phytanic acid proven by docking simulation and modulation of biochemical alterations. *PLoS ONE.* 8(1), 1-13.
9. Ghorbanzadeh, V., Mohammadi, M., Mohaddes, G., Dariushnejad, H., Chodari, L., Mohammadi, S. (2016). Protective effect of crocin and voluntary exercise against oxidative stress in the heart of high-fat-diet-induced type 2 diabetic rats. *Physiology International.* 103(4), 459-468.
10. Giugliano, D., Ceriello, A., Paolisso, G. (1996). Oxidative stress and diabetic vascular complications. *Diabetes Care.* 19(3), 257-267.
11. Gothai, S., Ganesan, P., Park, S.Y., Fakurazi, S., Choi, D.K., Arulselvan, P. (2016). Natural Phyto-Bioactive Compounds for the Treatment of Type 2 Diabetes: Inflammation as a Target. *Nutrients.* 8(461), 1-28.
12. Haldar, P.K., Kar, B., Bhattacharya, S., Bala, A., Kumar, R.B.S. (2010). Antidiabetic activity and modulation of antioxidant status by *sansevieria roxburghiana* rhizome in streptozotocin-induced diabetic rats. *Diabetol Croat.* 39(4), 115-123.
13. Heim, M., Johnson, J., Boess, F., Bendik, I., Weber, P., Hunziker, W., Flühmann, B. (2002). Phytanic acid, a natural peroxisome proliferator-activated receptor agonist, regulates glucose metabolism in rat primary hepatocyte. *The FASEB Journal.* 16(1), 1-17.
14. Imam, K. (2021). Clinical features, diagnostic criteria and pathogenesis of diabetes mellitus. *Journal of Advances in Experimental Medicine and Biology.* 771, 340-355.
15. Jemai, H., Sayadi, S. (2015). Heart Histopathology and Oxidative features in diabetic rats and protective effects of Oleuropein. *J Biosci.* 6, 383-389.
16. Joshi, S.R. (2015). Diabetes care in India. *Annals of global health.* 81(6), 830-838.
17. Mitra, S. (2019). Diabetes Research, Prevalence, and Intervention in India. *European Journal of Environment and Public Health.* 3(1): 01-05.
18. Nemezc, M., Constantin, A., Dumitrescu, M., Alexandru, N., Filippi, A., Tanko, G., Georgescu, A. (2019). The distinct effects of Palmitic and Oleic Acid on pancreatic beta cell function: The elucidation of associated mechanisms and effector molecules. *Frontiers in Pharmacology.* 9, 1-16.
19. Nepal, A., Chakraborty, M., Sarma, D., Haldar, P.K. (2021). Phyto-chemical characterization of *Aeschynanthus sikkimensis* (Clarke) Stapf. (Gesneriaceae) using GC-MS. *International Journal of Pharmaceutical Research.* 13(3), 597-602.
20. OECD. (2008). Guidelines for the testing of chemicals/section 4: Health effects test No. 425: Acute oral toxicity: up-and-down procedure. Paris: Organisation for economic co-operation and development publishing.
21. Panda, S., Chakraborty, M., Majumder, P., Mazumder, S., Das, S., Haldar, P.K. (2016). Antidiabetic, antioxidant and anti-hyperlipidaemic activity of *cucumis callosus* in streptozotocin-induced diabetic rats. *IJPSR.* 7(5), 1978-1984.

22. Qian, C., Zhu, C., Yu, W., Jiang, X., Zhang, F. (2015). high-Fat Diet/Low-Dose Streptozotocin-induced type 2 diabetes in rats impacts osteogenesis and Wnt signaling in bone marrow stromal cells. *PLoS One*. 10(8), e0136390.
23. Rai, P.K., Lalramnghinglova, H. (2010). Lesser known ethnomedicinal plants of Mizoram, North East India: An Indo-Burma hotspot region. *Journal of Medicinal Plants Research*. 4(13), 1301-1307.
24. Rajeswari, G., Murugan, M., Mohan, V.R. (2013). GC-MS analysis of bioactive components of *Hugoniamystax L. bark* (Linaceae). *Journal of pharmaceutical and biomedical sciences*. 29(29), 818-824.
25. Rizvi, S.I., Mishra, N. (2013). Traditional Indian Medicines Used for the Management of Diabetes Mellitus. *Journal of diabetes research*. 2013, 1-11.
26. Saeedi, P., Petersohn, I., Salpea, P., Malanda, B et.al. (2019). Global and regional diabetes prevalence estimates from 2019 and projection for 2030 and 2045: results from the international diabetes federation Diabetes atlas 9<sup>th</sup> edition. *Diabetes research and clinical practice*. 157, 1-10.
27. Vassiliou, E.K., Gonzalez, A., Garcia, C., Tadros, J.H., Chakraborty, G., Toney, J.H. (2009). Oleic acid and peanut oil high in oleic acid reverse the inhibitory effect of insulin production of the inflammatory cytokine TNF- $\alpha$  both *in vitro* and *in vivo* systems. *Lipids in Health and Disease*. 8(25), 1-10.
28. Verma, J., Arora, D., Singh, A. (2018). Evaluation of anti-hyperglycemic potential of the ethanolic leaf extract of *Quisqualisindica*. *Biosci. Biotech. Res. Comm*. 11(2), 324-334.
29. Wang, Z., Wang, J., Chan, P. (2013). Treating Type 2 Diabetes Mellitus with Traditional Chinese and Indian Medicinal Herbs. *Evidence-based complementary and alternative medicine*. 2013, 1-17.