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Assessment Of The Anti-Diabetic Activicty Of Schefflera Stellata Leaves Ethanolic Extract On Streptozotocin-Induced Diabetes In Wistar Rats

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels, affecting millions of people worldwide. This study aimed to evaluate the potential anti-diabetic activity of Schefflera stellata leaves ethanolic extract in a streptozotocin (STZ)-induced diabetic Wistar rat model. Wistar rats were induced with diabetes using STZ and subsequently treated with Schefflera stellata leaves ethanolic extract. Various biochemical parameters such as fasting blood glucose levels, serum insulin levels, lipid profile, and antioxidant enzyme activities were assessed. Additionally, histopathological examination of pancreatic tissues was performed to evaluate the impact of the extract on structural alterations. The results revealed a significant reduction in fasting blood glucose levels in rats treated with Schefflera stellata extract compared to the untreated diabetic group. Moreover, the extract exhibited a positive influence on serum insulin levels, lipid profile, and antioxidant enzyme activities, suggesting its potential in ameliorating diabetes-induced metabolic dysregulation. Histopathological analysis of pancreatic tissues indicated a preservation of islet architecture in the extract-treated group, highlighting the protective effects of Schefflera stellata against STZ-induced pancreatic damage.

Keywords: ***Schefflera stellata, Ethanolic extract , Anti-diabetic activity, Wistar rats, Fasting blood glucose***

INTRODUCTION:

Herbs are making a comeback, and the herbal 'renaissance' is taking place all over the world. Herbal goods now represent safety in contrast to synthetics, which were once thought to be harmful to both humans and nature. Although herbs had long been valued for their medicinal, flavorful, and aromatic properties, synthetic products of the modern era temporarily overshadowed their significance. However, the naïve reliance on synthetics has ended, and people are returning to naturals in search of safety and security. More than three-quarters of the world's population relies mostly on plants and plant extracts for healthcare. More than 30% of all plant species have at some point been utilized medicinally. It is estimated that world market for plant derived drugs may account for about Rs.2,00,000 crore [1]. It has been estimated that in developed countries like United

States, plant drugs constitute as much as 25% of the total drugs, while in fast developing countries such as China, India and Bangladesh, the contribution is as much as 80%. Thus, the economic importance of medicinal plants is much more to countries such as India, Bangladesh than to rest of the world.

Diabetes mellitus is a type of hyperglycemia that can result from insufficient insulin production or insulin resistance. Type 2 diabetes mellitus (T2D), also referred to as adult-onset diabetes, is primarily caused by resistance to insulin and insufficient synthesis of the hormone by the pancreatic ß-cells [2]. Obesity or overweight, physical inactivity, a family history of the condition, high blood pressure, or cholesterol are risk factors for diabetes [3]. One of the biggest problems with public health that could spread worldwide is this [4]. By 2025, there will be 300 million more people affected by the chronic metabolic disorder globally, which currently affects 150 million people [5].

Insulin and synthetic oral anti-diabetic drugs used to treat diabetes complications have a number of side effects and don't treat the problems on their own [6]. Various diabetes issues are treated using traditional medicinal herbs. Numerous herbal remedies and minerals for the treatment of diabetes mellitus have been described in earlier traditional literature. Herbal medicines are less likely to have side effects and are safer than manufactured drugs. Researching the hypoglycemic potential of medicinal plants is essential to giving humanity a safer substitute for pharmaceutical drugs. This study's main goal was to find out if an ethanolic extract of Schefflera arboricola leaves could lower blood sugar levels in rats that had been given alloxan to induce diabetes.

DIABETES MELLITUS

Type 1 Diabetes mellitus

The degeneration of insulin-producing beta cells in the pancreas results in a shortage of insulin, which is the cause of type 1 diabetes. The immune system of the body targets and kills beta cells in type 1 diabetes, an autoimmune condition. By recognizing and eliminating bacteria, viruses, and other potentially dangerous foreign substances, the immune system typically keeps the body safe from infection. However, the immune system targets the body's own cells in autoimmune illnesses. Though the disease's symptoms typically appear quickly, beta cell death in type 1 diabetes can occur over several years [7]. Although it can manifest at any age, type 1 diabetes usually affects children and young people.

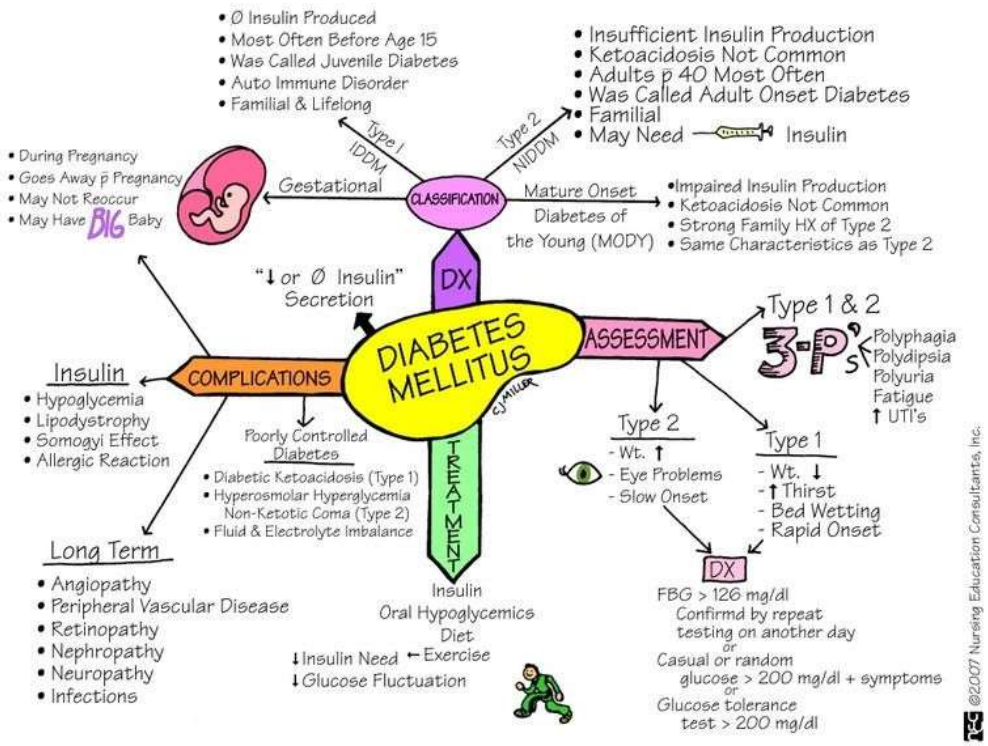

Figure 1: Overview of Diabetes Mellitus

Type 2 Diabetes mellitus

The most prevalent type of diabetes, type 2, is brought on by a number of variables, including insulin resistance, a disorder in which the body's fat, muscle, and liver cells are unable to utilise insulin as intended. When the

body can no longer make enough insulin to make up for its decreased ability to use insulin, type 2 diabetes develops [8]. Type 2 diabetes symptoms can appear gradually and subtly; some patients with the disease go years without receiving a diagnosis. People who are overweight or obese and in their middle age or older are more likely to develop type 2 diabetes.

Once uncommon in children, the illness is now more prevalent in overweight and obese children and teenagers. Researchers believe that the most likely causes of type 2 diabetes are environmental factors and genetic predisposition. Diabetes can be brought on by a number of factors, including genetic predisposition, obesity and physical inactivity, insulin resistance, abnormal liver glucose production, metabolic syndrome, and beta cell dysfunction [9,10].

MATERIALS & METHODS

Identification, authentication and Collection of Plant material: The whole plant of Schefflera stellata used for the present study was obtained from Nandivaram, Guduvancherry, Chennai, Tamil Nadu, India.

Authentication of plant: The plant material was identified and authenticated by Dr. A. Balasubramanian, Botanatist, ABS Botanical Garden, Ammapet, Salem-636 003, Tamilnadu. [AUT/JKKMMRF/260].

Sample Extraction: The sample was washed with distilled water to remove any adherent particles, shade dried and powdered. 25g of each sample was weighed and extracted with 300ml of ethanol by continuous hot percolation with the help of soxhlet apparatus for 10hrs of time. On completion the extract was filtered and concentrated using rotary evaporator under reduced pressure and controlled temperature of 500C – 600 C. The concentrates were stored in the refrigerator for further use.

Percentage yield: The percentage yield of Ethanolic extract was 8.84 % w/v and it was preserved in refrigeration for further use.

Chemicals : All the Chemicals used in the study were of analytical grade. The following chemicals were used for the experimental study.

Table1: Name of the chemicals and their source

S.No	Materials	Sources
1.	Absolute alcohol	S.d.fine chemicals Ltd, Mumbai
2.	Chloroform	S.d.fine chemicals Ltd, Mumbai
3.	Copper sulphate	Qualigens fine chemicals, Mumbai
4.	Creatinine kit	Span diagnosis Ltd, Bangalore
5.	DNS (3,5-dinitrosalicylic acid)	Sigma chemical Co., USA
6.	Ethanol	S.d.fine chemicals Ltd, Mumbai
7.	Glucose test strips	One touch Horizon test strips
8.	HDL kit	Span diagnosis Ltd, Bangalore
9.	Hydrochloric acid	Qualigens fine chemicals, Mumbai
10.	Hydrogen peroxide solution	Qualigens fine chemicals, Mumbai
11.	Sodium hydrogen carbonate	S.d.fine chemicals Ltd, Mumbai
12.	LDL kit	Span diagnosis Ltd, Bangalore
13.	Petroleum ether	Sigma chemical Co., USA
14.	p-nitrophenyl glucopyranoside	S.d.fine chemicals Ltd, Mumbai
15.	Pyrogallol	S.d.fine chemicals Ltd, Mumbai
16.	SGOT kit	Span diagnosis Ltd, Bangalore
17.	SGPT kit	Span diagnosis Ltd, Bangalore
18.	Sodium hydroxide	Qualigens fine chemicals, Mumbai
19.	Total protein kit	Span diagnosis Ltd, Bangalore
20.	Total cholesterol kit	Span diagnosis Ltd, Bangalore
21.	Triglycerides kit	Span diagnosis Ltd, Bangalore
22.	Urea kit	Span diagnosis Ltd, Bangalore
23.	VLDL kit	Span diagnosis Ltd, Bangalore

Experimental Design:

For this investigation, adult male Wistar rats weighing 180–230 g were utilized. The JKKMMRFs' animal home, Annai JKK Sampoorani Ammal College of Pharmacy, Komarapalayam, Namakkal-638183, is where the inbred animals were obtained. Five of them were kept in each cage in typical laboratory settings, with a 12-

hour light/dark cycle and an ambient temperature of 22±20 C. The animals were given ordinary pellet meal and unlimited water after spending a week getting used to the lab environment. The IAEC of CPCSEA granted clearance for the ethical committee. (IAEC/number:)

PHYTOCHEMICAL ANALYSIS [11]

Test For Tannins: 1ml of sample was taken, to that few drops of 0.1 % ferric chloride was added and observed for brownish green or blue black coloration.

Test For Saponins: 1 ml of sample was taken, to that 2 ml of water was added .The suspension was shaken in a graduated cylinder for 15 minutes. A layer of foam indicates the presence of saponins.

Test For Flavonoids: 1 ml of sample was taken; to that few drops of Sodium hydroxide solution was added. Formation of intense yellow colour, which becomes colourless on further addition of diluted hydrochloric acid, indicated the presence of flavanoid.

Test For Alkaloids: 1 ml of sample was taken, to that few drops of dragandoff reagent was added. Prominent yellow precipitates indicate the test as positive.

Test For Protein: 1 ml of sample was taken, to that few drops of Millon's reagent was added. A white precipitate indicates the presence of Protein.

Test For Steroids: 1 ml of sample was taken, to that two drops of concentrated sulphuric acid was added and observed for brown colour.

Test Fof Anthraquinones: 1 ml of sample was taken, to that aqueous ammonia was added and observed for change in colour. Pink, red, or violet colour in aqueous layer indicates the presence of anthraquinoness.

Test For Phenol: 1 ml of sample was taken, to that 3 ml of 10% lead acetate solution is added a bulky white precipitate indicates the presence of phenolic compounds.

The animals were divided into 5 groups each constituting 6 rats. Group I were normal rats received water, Group II were STZ (55 mg/kg b.w., i.p) induced diabetic rats which acts as diabetic control group. Group III STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with Glibenclamide 5mg/kg b.w/p.o Group IV STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with EESS 200mg/kg b.w/ p.o Group V STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with EESS 400mg/kg b w/p.o for 21 days58.

Table 2: Diabetic Control group of animals

Group (n=6)	Treatment	Dose
I	Normal Saline 0.9 %	1 ml/kg p.o.
II	Disease control (Sterptozozin)	55 mg/kg b.w., i.p
III	STD – group 1 (Sterptozozin 55 mg/kg + Glibenclamide)	5mg/kg b.w/p.o
IV	Test – group 1 (Sterptozozin 55 mg/kg + EESS leaves extact)	200 mg/kg, p.o
V	Test – group 2 (Sterptozozin 55 mg/kg + EESS leaves extact)	400 mg/kg, p.o

Fasting blood glucose levels was measured before the administration of extracts. The blood glucose levels were checked on 0th, 7th, 14th, and 21st day of the treatment period. Blood was collected from snipping of the rat tail. Blood glucose levels were measured by using the glucose oxidase peroxidase reactive strips and a glucometer (One touch glucometer).

RESULT & DISCUSSION:

The result of preliminary phytochemical analysis of Ethanolic extract of Schefflera stellata (Geartn.) (EESS) showed presence of various phytochemical constituents such as, flavonoids, alkaloids, tannins, proteins, steroids and phenol with absence of saponins and anthroquinones. The results were shown in (Table-3)

Table- 3. Phytochemical screening of EESS

The Phytochemical studies of the sample TEST	Sample [(+) Present , (-) Absent]
TANNINS	+
SAPONINS	-
FLAVONOIDS	+
ALKALOIDS	+
PROTEINS	+
STEROIDS	+
ANTHROQUINONES	-
PHENOL	+

Thin Layer Chromatography (TLC)

The ethanolic extract of Schefflera stellata (Geartn.) was subjected for TLC by using various solvent systems. On the basis of trial and error method, the following solvent system showed 2 to 4 different spots with different Rf values on development. The results are tabulated in Table No: 4

Solvent system	No. of spots	Colour of spots	Detecting agent	Rf value
Toluene : Ethyl acetate (5:5)	2	Green Green	Iodine chamber	0.71 0.89
Ethyl acetate : Methanol (3:7)	1	Brown	Iodine chamber	0.89
Ethyl acetate : Methanol (4:2)	4	Brown Brown Brown Brown	p-toluene sulphuric acid	0.41 0.56 0.75 0.95
Toluene : Chloroform Acetone (4:2.5:3.5)	1	Green	p-toluene sulphuric acid	0.72
Benzene : Ethyl acetate (7.5:2.5)	2	Brown Brown	Iodine chamber	0.58 0.71
Benzene : Ethyl acetate : Diethyl amine (7:2:1)	3	Brown Brown Brown	Iodine chamber	0.30 0.66 0.76

The TLC study was carried out and reported as per the procedure57. From the TLC study of the ethanol extract of Schefflera stellata (Geartn.) Showed the presence of four spots as the maximum number of spots with solvent system Ethyl acetate : Methanol (4:2) using p-toluenesulphuric acid as detecting agent. The Rf values of the spots were calculated and found to be 0.41, 0.56, 0.75 and 0.95 respectively.

Effect of EESS on body weight of STZ induced diabetic rats

It was found that the body weight was decreased significantly ($p<0.001$) when the comparison was made between group I with group II, group III, group IV and group V. -The bodyweight in group II was compared with group III, group IV and group V were increased significantly ($p<0.001$). The results were shown in (Table-4) (Histogram-1)

Table-4. Effect of EESS on body weight of STZ induced diabetic rats

Group	Body weight (gm)			
	Day – 0	Day – 7	Day – 14	Day – 21
I	185.2±1.930	184.2±2.271	194.5±0.7548	202.3±1.173
II	182.2±4.010	151.5±1.482 a***	134.5±1.988 a***	125.7±0.892 a***
III	182.34±2.186	171.2±2.012 a***b***	172.5±1.222 a***b***	180.0±1.780 a***b***
IV	182.12±3.615	161.7±2.236 ns a***b	162.8±0.9458 a***b***	167.2±0.938 a***b***
V	184.8±3.137	167.3±1.914 a***b***	169.8±0.9098 a***b***	173.8±1.337 a***b***

Comparisons were made between the following:
a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.
Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

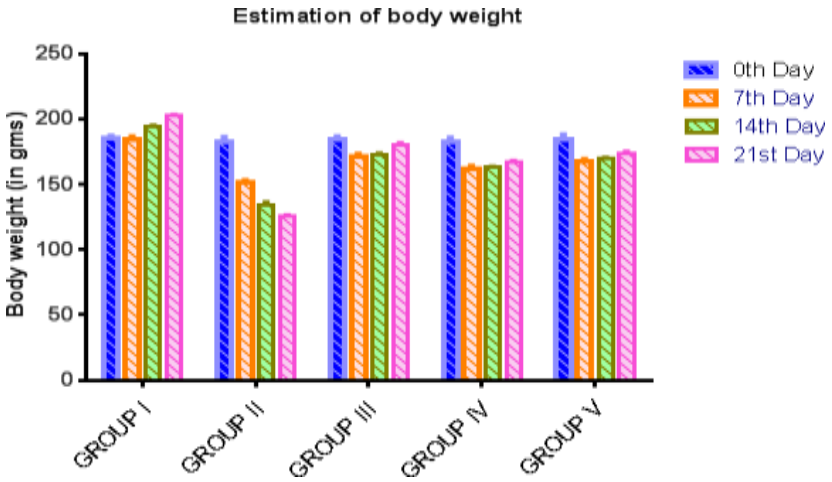

Figure 2 :Effect of EESS on body weight

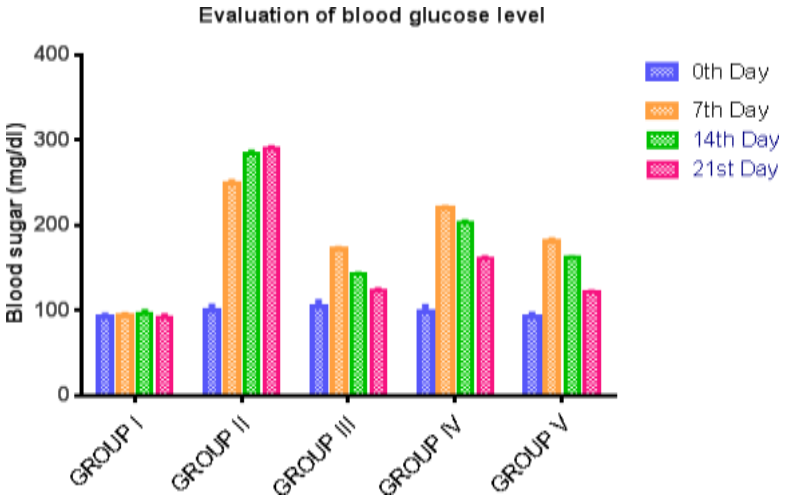

Figure 3 :Effect of EESS on blood glucose

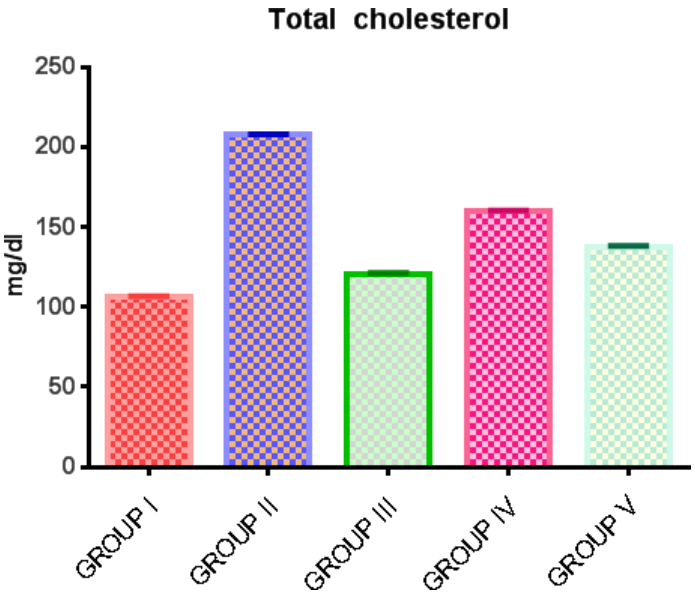

Figure 4: Effect of EESS on Total cholestrol

The ethanolic extract from whole plant of Schefflera stellata (Geartn.) were subjected to preliminary phytochemical analysis which shown presence of flavonoids, alkaloids, tannins, proteins, steroids and phenol with absence of saponins and anthroquinones. The TLC study was carried out and summarized in Table No.2. From the TLC study of the ethanol extract of Schefflera stellata (Geartn.) the presence of four spots were observed as maximum number of spots with Ethyl acetate : Methanol (4:2) using ptoluenesulphuric acid as detecting agent. The Rf values of the spots were calculated and found to be 0.41, 0.56, 0.75 and 0.95 respectively.

Acute oral toxicity studies of EESS did not produce any mortality or signs of toxicity at the dose of 2000 mg/kg b.w/p.o, in experimental rats. The plants' anti-hyperglycemic helps stem from their ability to restore pancreatic tissue function by increasing insulin secretion, inhibiting intestinal glucose absorption, or facilitating metabolites in insulin-dependent activities. Consequently, treatment with herbal medications has an effect on preserving the b cells and regulating out variations in glucose levels.72 The present study evalulation of anti-diabetic activity of whole plant of Schefflera stellata (Geartn.) STZ induced diabetic rats.

Experimental induction of hyperglycemia with STZ is associated with the characteristic loss of body weight which is due to loss or degradation of structural proteins it leads to increased muscle wasting and due to loss of tissue protein, as the structural proteins are known to contribute to body weight. Diabetic rats treated with glibenclamide and EESS showed increased body weight when compared to untreated diabetic animals. It may be due to increased insulin secretion and glycemic control of EESS.

Reduced glucose transport or absorption from the gut, extra pancreatic action, most likely through stimulation of glucose utilization in peripheral tissues, an increase in glycogenic or glycolytic enzyme activities in peripheral tissues, and a decrease in the secretion of counter-regulatory hormones such as glucagon and growth hormones are all possible mechanisms for suppressing blood glucose levels. Glibenclamide inhibits ATP-sensitive KATP channels in the plasma membrane, increasing insulin production from pancreatic β cells and decreasing blood glucose level73. Blood glucose level decreased significantly in glibenclamide and EESS treated diabetic rats and the histopathology of pancreas showed normal islets in pancreas with normal anatomy compared with normal rats which may be due to the anti-diabetic activity.

Hyperglycaemia is accompanied with dyslipidemia under normal circumstances; insulin activates the enzyme lipoprotein lipase, which hydrolyses triglycerides. However, in diabetic state lipoprotein lipase is not activated due to insulin deficiency, resulting in hyper triglyceridemia, and insulin deficiency is also associated with hyper cholesterolemia due to metabolic abnormalities. The dyslipidemia is characterized by increase in TC, LDL, VLDL, TG and fall in HDL which is observed in STZ induced diabetic rats74. The diabetic rats treated with glibenclamide and EESS showed reduced severity of dyslipidemia with decrease in TC, LDL, VLDL, TG and increase in HDL.

Both SGOT and SGPT enzyme levels get elevated during liver damage which is more in diabetic rats75. The diabetic rats treated with glibenclamide and EESS reduced the SGOT and SGPT level. The liver histopathology of STZ induced diabetic rats showed centrilobular necrosis accompanied by fatty changes and ballooning degeneration in the hepatocytes treatment with EESS reversed in diabetic rats treated with glibenclamide and EESS which indicates that the liver damage is reduced in EESS treated group. The diabetic hyperglycaemia induces elevation of the serum levels of creatinine which are significant markers of renal dysfunction, The treatment of EESS in rats showed marked decrease in serum creatinine levels in diabetic animals.

CONCLUSION:

Blood glucose levels, the estimation of Schefflera stellata's lipid profile activity, and the noticeable decrease in SGOT, SGPT, and creatinine in serum all support the plant's anti-diabetic properties. Schefflera stellata also appears to have a protective effect on the pancreas, as diabetes is known to cause liver damage. Therefore, it can be said that in streptozotocin-induced diabetic rats, Schefflera stellata exhibited strong antidiabetic effects. Schefflera stellata's effectiveness was similar to Glibenclamide's. With particular reference to phytochemicals, more research was required to clarify the mechanism of action behind Schefflera stellata's anti-diabetic efficacy.

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CONFLICT OF INTEREST:

The author has no conflict of interest.

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CONTRIBUTIONS:

1) DR. K. SUMATHI *- Contributed for the conceptual work in schemes of research work.
2) PRIYANKA. V - Contributed for the laboratory works in research and literature works.
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