ANTI DIABETIC AND HYPOLIPIDEMIC SCREENING OF CELTIS PHILIPPENSIS EXTRACTS INSTREPTOZOTOCIN INDUCED DIABETIC RATS

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Abstract

Diabetes Mellitus is a metabolic disease that happens either due to insufficient insulin secretion (a hormone that regulates blood glucose), or deficiency in insulin action thus leading to raised blood glucose levels. Celtis philippensis to the Ulmaceae family. It is colloquial as Vellai Thovarai, Kalluviri, Pinari and Kodalimuruki. It is a large deciduous tree distributed in most of India at an altitude of 1400 m. It is distributed in evergreen forests. Roots Celtis philippensis astringent. The phytochemical analysis of the drug and, the evaluation using streptozotocin induced diabetes, were performed. In the case of streptozotocin induced diabetes the results revealed that the vital organs such as kidney, pancreas, heart, small intestine and liver were not severely affected during treating with extract. The outcome was found to be more significant in lowering the level of blood glucose related to a controlled diabetic, and there was no significant variation between treated groups during the 14 days of study showed the disruption of the isletina circular shape; restraining membranes among the adjacent acinar tissue and the islet is dissolved.

Keywords: Diabetes mellitus, Streptozotocin, Blood Glucose, Celtis philippensis

INTRODUCTION

Diabetes is one of the most common deadliest diseases usual in the world next to coronary artery disease, cancer and HIV/AIDS. The intensification in population, aging, steady urbanization, growth in obesity and physical inactivity are the features that are accountable for the occurrence of diabetes (1), Affording to current estimates, about 438 million people (7.8%) of the world population (particularly in adults), it is predictable to have diabetes by 2030 (2). The emerging republics including India will dominate the world with the rise in the occurrence of diabetes.

Type 1 Diabetes Mellitus (T1DM) is one of the greatest severe procedures of diabetes considered by the dysfunction of the pancreatic beta-cells. It is also named as “juvenile” diabetes since it typically happens in children and adults. In this form of diabetes, the pancreas is demolished by its own body’s immune system. The immune system identifies the insulin creating cells as non-self and destroys it. Therefore, diabetes is referred as “autoimmune” disease. Type II Diabetes Mellitus (T2DM) is considered by raised blood glucose and changed metabolism of lipids when there is insufficient insulin secretion in response to varying degrees of over-nutrition, inoperativeness and insulin resistance (3). Gestational Diabetes Mellitus (GDM) happens owing to inappropriate purpose of the pancreas to overcome the diabetogenic situation of pregnant women. The influences that administrate insulin fight through pregnancy are: secretion of insulinase formed by the placenta which in turn enables insulin metabolism, lactogen secretion formed by the placenta affecting fatty acid and glucose metabolism and modification in development hormones and cortisol secretion which is an insulin opponent.

Celtis philippensis belongs to the Ulmaceae family. It is colloquial as Vellai Thovarai, Kalluviri, Pinari and Kodalimuruki. It is a large deciduous tree distributed in most of India at an altitude of 1400 m. It is distributed in evergreen forests. Roots Celtis philippensis astringent. They are used as a treatment for diarrhoea. Sap leaf is used for parasitic infection.

MATERIAL AND METHODS COLLECTION AND AUTHENTICATION OF PLANT

The entire plant of Celtis philippensis Blanco was collected from cultivated lands of semi-evergreen forests plains grows upto 1200m. Commonly seen in the Tropical Africa to Madagascar, India, Sri Lanka, Myanmar, Thailand, Indo-China and Malaysia to Northern Australia. The composed material was authenticated by Dr. K. Madhava Chetty, Plant taxonomist, (IAAT:357)

EXTRACTION OF THE PLANT

Extractions using solvent and distilled water are the common method of choice for the isolation and extraction of various phytochemicals from plants. The polarity and the nature of the solvent influence the yield and activity of the extract. Five hundred gm of dried and powdered plant material was extracted with 1000 mL of hexane for 2 hat slow heat (40°C-45°C). The extract was then sieved using a muslin cloth and centrifuged at 5000 rpm for 15 minutes. The upper layer was composed and subjected to evaporation and a crude extract was acquired. The fraction yield of crude extract was calculated and stored at 4°C for additional use for analysis. The dried reasonable powder of the leaves of the Celtis philippensis plant was also subjected to consecutive solvent extraction using soxhlet.The dried leaf material (500g) of Celtis philippensis Blanco was extracted with hexane, chloroform, ethyl acetate, ethanol and chloroform:water consecutively. Each extract was filtered and concentrated using rotary flash vacuum evaporator (4) and the dried extract was stored at 4°C for further use.

STREPTOZOTOCIN-INDUCED DIABETIC MODEL

In investigational animals, diabetes was induced by intraperitoneal (i.p.) injection of nicotinamide (230 mg/kg) 15 min before streptozotocin (65 mg/kg i.p) administration. The streptozotocin (STZ) was freshly prepared by dissolving in 0.1 M citrate buffer, pH 4.5, and nicotinamide was prepared in normal saline. The blood glucose level was observed at 48 h interval and diabetes was confirmed when fasting blood glucose level had reached above 250 mg/dl. As STZ is capable of inducing fatal hypoglycaemia as a result of massive pancreatic insulin release, STZ-treated rats were provided with 10% glucose solution after 3 h for the next 24 h to prevent fatal hypoglycaemia (5). Diverse dosages of the extract were designated on the basis of acute toxicity study.

RESULTS

EFFECTS OF CELTIS PHILIPPENSIS EXTRACT OF BODY WEIGHT BY STREPTOZOTOCIN INDUCEDHYPERGLYCAEMICRATS

The impact plant tested extract on principal organ weights relative to weight square measure shown in Table 1, it shows the body weight of the normal and treated groups significantly differ

from diabetic control on the 14th day. The treated group's animal body weight maintained throughout the experiment compared to diabetic control. The results unconcealed that the important organs like liver, kidney, heart, exocrine gland and little viscus weren't adversely affected throughout the treatment by extract.

Table 1. Effect of various extracts of leaves of Celtis philippensis on body weight by Streptozotocin induced hyperglycaemic rats

Groups	Treatment	Body weight in gm	
		0th day	14th day
I	Normal control	180.25±3.52	203.33±5.42[a]
II	Diabetic control	174.65±2.98	149.27+4.56[b]
III	Glibenclamide (5mg/kg)	170±4.64	195.59±5.27**[a]
IV	CECP 200 mg/kg	175.82±4.31	187.5±5.94**[a]
V	EAECP 200 mg/kg	184.54±2.54	198.21±3.58**[a]
VI	EECP 200 mg/kg	172.32±3.84	184.73±4.42**[a]
VII	AECP 200 mg/kg	180.78±2.47	200.45±4.19**[a]

The values are mean ±SEM, n=6, **p<0.01when treated groups compared with diabetic control, a, indicates there is no significant variation between treated groups and normal control. b, indicates there is a significant variation between diabetic control and normal control

EFFECTS OF CELTIS PHILIPPENSIS EXTRACTS ON BLOOD GLUCOSE LEVEL 0 TO 14TH DAY

The standard (Glibenclamide 5mg/kg) and different solvent extracts (200 mg/kg) treated groups, the peak values of blood sugar significantly decreased to Glibenclamide (5mg/kg)-120, CECP 200 mg/kg -195.56,EAECP 200 mg/kg-138.37,EECP 200 mg/kg -164.53 and AECP 200 mg/kg -152.38mg/dl simultaneously on the 14th day (Table2). Thus, the result was found to be more significant ($p<0.01$) in lowering blood glucose level compared to diabetic control. There was no significant variation between treated groups during the 14 days of study.

Table 2: Effect of various extracts of dried leaves o f*celtis philippensis* on blood glucose level by Streptozotocin induced hyperglycemic rats.

Groups	Treatment	Blood glucose level in mg/dl				
		0th day	3st day	6th day	9th day	14th day
I	Normal control	91.24±6.833[a]	83.35±9.32[a]	86.91±7.28[a]	99.58±7.39[a]	85.64±9.79[a]
II	Diabetic control	285.15±8.41[b]	342.16±10.9[b]	384.33±9.35[b]	401.66±5.38[b]	425.16±9.51[b]
III	Glibenclamide (5mg/kg)	298.28±6.01[c]	251.88±8.32**[c]	215.0±9.02**[c]	161.7±5.88**[c]	120.0±5.39**[a]
IV	CECP 200 mg/kg	280.66±4.26[c]	291.58±6.82**[c]	273.0.±9.93**[c]	235.0±8.68**[c]	195.56±7.09**[c]
V	EAECP 200 mg/kg	308.56±7.25[c]	264.52±9.75**[c]	237.86±5.46**[c]	187.24±6.48**[c]	138.37±8.17**[a]
VI	EECP 200 mg/kg	290.58± 5.54[c]	273.57±5.28**[c]	258.34±6.75**[c]	219.76±5.72**[c]	164.53±4.71**[a]
VII	AECP 200 mg/kg	280.91±7.89[c]	266.25±4.67**[c]	237.45±5.23**[c]	205.90±5.87**[c]	152.38±4.28**[a]

The values are mean±SEM, n=6 , **p<0.01 when treated groups compared with diabetic control, [a], indicates there is no significant variation between treated groups and normal control. [b], indicates there is a significant variation between diabetic control and normal control.[c] , Indicates there is significant variation between treated group and normal control.

EFFECTS OF CELTIS PHILIPPENSIS EXTRACTS ON BIOCHEMICAL PARAMETERS

Table2 shows extracts has significantly reversed the diabetes-induced hyperlipidemia Compared to diabetic control. A significant reduction of total cholesterol level, normal control-124, diabetic control-276, Glibenclamide-128, CECP 200 mg/kg-192, EAECP 200 mg/kg-132, EECP 200 mg/kg-139 and AECP 200 mg/kg-159).In TGL level normal control-152, diabetic control-226, Glibenclamide-156, CECP 200mg/kg-174, EAECP 200mg/kg-164, EECP 200mg/kg-162 and AECP 200 mg/kg-168).In HDL level normal control-63, diabetic control-25, Glibenclamide-68,

CECP 200mg/kg-32, EAECP 200mg/kg-59, EECP 200mg/kg-60 and AECP 200 mg/kg-52. In LDL level normal control-81, diabetic control-170, Glibenclamide-72, CECP 200mg/kg-86, EAECP 200mg/kg-74, EECP 200mg/kg-78 and AECP 200 mg/kg-79.In VLDL level normal control-24, diabetic control-48, Glibenclamide-22, CECP 200mg/kg-33, EAECP 200mg/kg-27, EECP 200mg/kg-26 and AECP 200 mg/kg-27in extract treated was significant to diabetic group. However HDL level increased with extract and GLB group respectively when compare to diabetic control. The results show there is no significant variation between treated groups and normal control group.

Table: Effect of various extracts of dried leaves of*celtis philippensis*on biochemical parameters by Streptozotocin induced hyperglycemicrats.

Groups	Treatment	TC mg/dl	TGL mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl
I	Normal control	124.66±2.02[a]	152.6±5.9[a]	63.66±2.51[a]	81.5±4.63[a]	24.83±1.034[a]
II	Diabetic control	276.16±3.52[b]	226.83±6.01[b]	25.3±3.2[b]	170±8.58[b]	48.66±3.56[b]
III	Glibenclamide	128.16±3.60**[a]	156.83±7.51**[a]	68.6±1.15**[a]	72.51±4.16**[a]	22.83±2.66**[a]
IV	CECP 200 mg/kg	192±3.53**[a]	174.16±8.21**[a]	32.83±4.8**[a]	86.12±6.11**[a]	33.59±6.5**[a]
V	EAECP 200 mg/kg	132.24±4.57**[a]	164.16±6.24**[a]	59.87±4.25**[a]	74.85±3.71**[a]	27.34±3.58**[a]
VI	EECP 200 mg/kg	139.82±2.54**[a]	162.32±6.31**[a]	60.59±2.46**[a]	78.15±6.93**[a]	26.76±3.96**[a]
VII	AECP 200 mg/kg	159.47±3.28**[a]	168.93±7.68**[a]	52.84±5.27**[a]	79.62±5.49**[a]	27.64±5.24**[a]

The values are mean±SEM, n=6 , **p<0.01 when treated groups compared with diabetic control, [a], indicates there is no significant variation between treated groups and normal control. [b], indicates there is a significant variation between diabetic control and normal control.

HISTOPATHOLOGY OF THE PANCREAS IN STZ INDUCED MODEL NORMAL CONTROL:

Histopathology of pancreas STZ induced model shows in normal control the islets are normal. The architecture is preserved. The acini are lined by round to oval cells with moderate cytoplasm and small round to oval nuclei shown in figure-1A.

DIABETIC CONTROL: Histopathology of pancreas STZ induced model of diabetic control shows pancreas with engorged and congested blood vessels. The islets show patchy necrosis. The acini are lined by round to oval cells with moderate cytoplasm and small round to oval nuclei. There is mild inflammation composed of lymphocytes shown in Figure-1B.

GLIBENCLAMIDE 5 mg/kg: Histopathology of pancreas STZ induced model of Glibenclamide 5 mg/kg the islets show depletion of cells. There is a mild infinite of lymphocytes at some foci. The acini are lined by round to oval cells with moderate cytoplasm and small round to oval nuclei shown in Figure 1C

CHLOROFORM EXTRACTS 200 mg/kg: Histopathology of pancreas STZ induced model of Chloroform extracts 200 mg/kg the islets showed a different morphology,i.e.,the circular shape of the islet is disrupted, limiting membranes between the islet and the surrounding acinar tissue is dissolved shown in figure-1D.

ETHYL ACETATE EXTRACTS 200 mg/kg: Histopathology of pancreas STZ induced model of Ethyl acetate extracts 200 mg/kg shows the architecture is partially affected. The islets are normal. The acinar normal. There is a mild and diffuse infiltrate of lymphocytes within the stroma shown in figure-1E.

ETHANOL EXTRACTS 200 mg/kg: Histopathology of pancreas STZ induced model of Ethanol extracts 200 mg/kg shows the architecture is normal. The islets show depletion of the acinar cells. The acinar cells show moderate cytoplasm and round to oval nuclei. There is no evidence of inflammation shown in figure-1F.

AQUEOUS EXTRACT 200 mg/kg: Histopathology of pancreas STZ induced model of aqueous extract 200 mg/kg shows pancreas with normal architecture. The islets are composed of normal acini. The acini are lined by round to oval cells with moderate cytoplasm and small round to oval nuclei. There is an infiltrate of lymphocytes and a few plasma cells within the stroma shown in figure-1G.

Fig. 1 Histopathology of pancreas (STZ induced model) A) Normal control, B) Diabetic control, C) Glibenclamide 5 mg/kg, D) Chloroform extracts 200 mg/kg, E) Ethyl acetate extracts 200 mg/kg, F) Ethanol extracts 200 mg/kg, G) Aqueous extract 200 mg/kg

Figure 1 A : Normal Control (STZ)

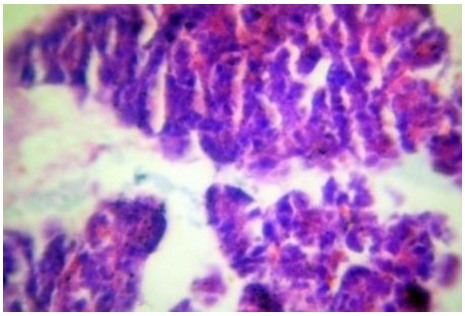


Figure 1 B: Diabetic Control (STZ)

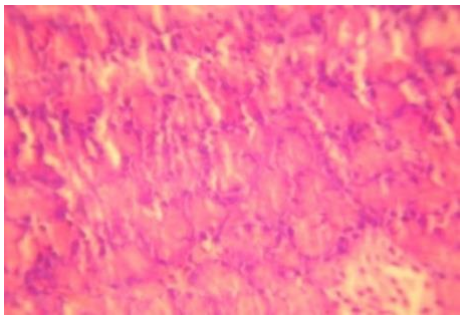


Figure 1 C: Glibenclamide 5mg/kg (STZ)

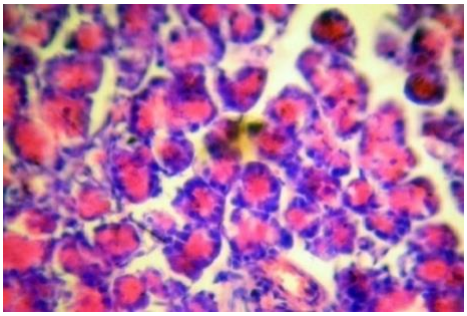


Figure 1 D: CECP 200 mg/kg (STZ)

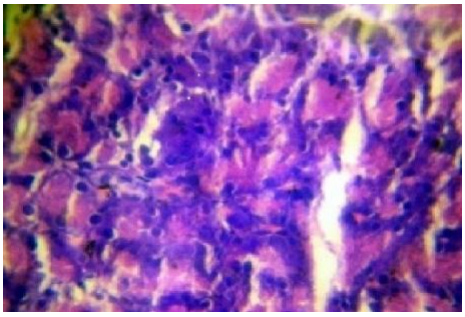


Figure 1 E: EAECP 200mg/kg (STZ)

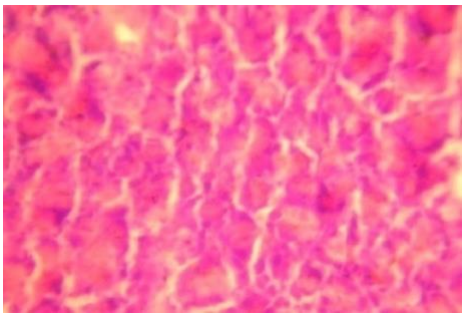


Figure 1 F: EECP 200mg/kg (STZ)

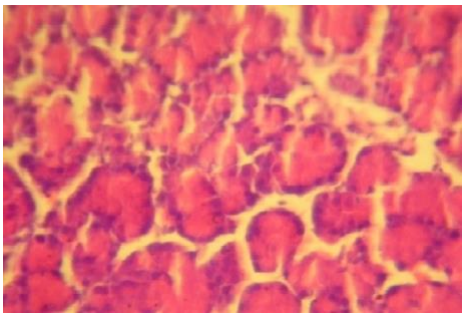
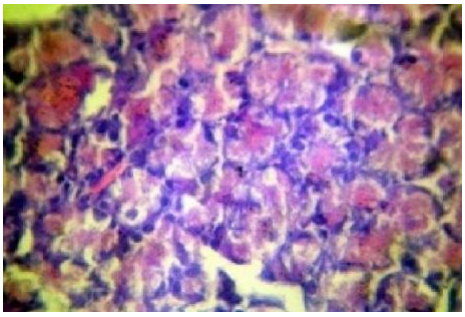


Figure 1 G: AECP 200mg/kg (STZ)



DISCUSSION

In the present study, most of the biologically active compounds such as flavonoids, alkaloids, glycosides, steroids, phenols, saponins, terpenoids, cardiac glycosides,and tannins were found to be present in the ethanolic extracts of Celtis philippensis leaves. The medicinal properties of C. philippensisleaf extracts may be due to the presence of phytochemicals mentioned above. Studies on the efficiency of medicinal plants concerning the control of infectious diseases are more essential to know their therapeutic value in pharmaceutical arenas (6).

For instance, flavonoids have been referred to as nature's biological response modifiers, because of their inherent ability to modify the body's reaction to allergies and virus and they showed their anti-allergic, anti-inflammatory, anti-microbial and anti-cancer activities (7,8). Plant steroids square measure known to be vital for his or her cardiotonic activities and additionally possess insecticidal and antimicrobial properties. They are also used in nutrition, herbal medicine,and cosmetics.Tannins were reported to exhibit antiviral, antibacterial and anti-tumor activities. It was also reported that certain tannins were able to inhibit HIV replication selectively and was also used as a diuretic (9). Saponin is used as mild detergents and in intracellular histochemical staining. It is also used to allow antibody access in intracellular proteins. In medication, it's utilized in symptom, hyperglycaemia, inhibitor, anticancer, medicament, weight loss, etc. It is also known to have antifungal properties(10).

Tannins arephenolic compounds that act as principal antioxidants or free radical scavengers. Since these phenolic compounds were originated to be present in the extracts, it might be accountable for the potent antioxidant capacity of C. philippensis. These phytochemicals of medicinal plants have primarily reported for their medicinal value, which can be valuable for the therapeutic index. For instance, saponins proved hypotensive and cardio-depressant properties (11), which are helpful for the treatment of congestive heart failure and cardiac myopathy (12). The occurrence of saponins in ethanol extracts of leaves of C. philippensis might play a role in the cardioprotective potential. Alkaloids and tannins have the potential of hypoglycemic and anti-inflammatory activities (13).

CONCLUSION

Moreover, the terpenoids have also been revealed to decrease blood sugar level in animal studies.

Also, the steroids and triterpenoids demonstrated the analgesic properties and central nervous system activities. Hence the preliminary phytochemical investigation is obliging to find chemical ingredients in the plant that may help with their quantitative evaluation and also in locating the source of pharmacologically active principle.

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