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Hepatoprotective activity of ethanol extract of *Mimosa* pudica leaves in type 2 diabetic rats

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Abstract

Mimosa pudica Linn is a traditional plant with high medicinal value used for the treatment of numerous diseases. The parts of the plant such as leaves, roots and whole plant used for the treatment of diabetes mellitus. The hepatoprotective activity of ethanol extract of *Mimosa pudica* leaves extract was studied in high fat diet (HFD) and streptozotocin (STZ)-induced type 2 diabetes mellitus. The rats were divided into five groups of six animals each. Type 2 diabetes mellitus was induced by feeding high fat diet for two weeks followed by intraperitoneal injection of streptozotocin (35 mg/kg bwt). The diabetic rats were administered *Mimosa pudica* leaves extract (300mg/kg bwt) daily for 30 days. The results showed the significant increase of glucose, AST, ALT, ALP and LDH whereas the insulin and total protein level were decreased in STZ induced diabetic rats. The treatment of *Mimosa pudica* leaves extract showed hepatoprotective activity by significantly restored the activity of liver markers.

Keywords: Type 2 diabetes, Mimosa pudica, streptozotocin, hepatoprotective activity, liver markers

Introduction

Diabetes mellitus, a major metabolic disease which is characterized by elevated blood glucose level. The increased concentration of glucose which causes various complications on heart, liver and kidney because of deficiency of insulin. The prevalence of diabetes was raised worldwide, since 61.3 million people reported with type 2 diabetes mellitus in 2011 and it is expected to raise 101.2 million by 2030 ^[1, 2]. Diabetic people in India was increasing year by year due to the high incidence of obesity ^[3].

Liver is an important organ for glucose homeostasis. In diabetes mellitus condition, the damage of liver is correlated with formation of free radicals through glucose oxidation, non-enzymatic glycation of protein, decrease in antioxidant defense mechanism, increased activity of polyol pathway, and cytokine production leads to oxidative stress which plays a major role in etiology of diabetes and its complications ^[4]. Chronic hyperglycemia is a major reason for oxidative stress which leads to pathological changes in liver cell. The liver marker enzymes are increased in diabetes mellitus condition due to liver damage ^[5].

Nowadays the attention has been continued for searching new antidiabetic herbal drug is an important interesting field to find new drug without any adverse effect. Accumulated data or literature revealed the hypoglycemic activity of different plant species ^[6]. The presence of secondary metabolite in plant extract which is responsible for the hypoglycemic and hepatoprotective activity ^[7]. The heptoprotective activity of some of plants such as been reported in the previous studies.

Mimosa pudica Linn is a sensitive plant belongs to family of mimosea. In English it is named as sensitive or humble plant, in tamil thottal sinungi, in hindi lajwanti, in urdu chui-mui. The plant is located throughout in India ^[8]. According to previous research of *Mimosa pudica* shown their antimicrobial, anti-inflammatory, anticonvulsant, antioxidants, anti-hepatotoxicity and antidiabetic activity. The phytochemical studies of *Mimosa pudica* leaf extract showed the presence of active compound such as flavonoids, glycosides, terpinoids, alkaloids, phenol and tannin in the previous study ^[9]. The underlying mechanism of antidiabetic and antioxidants activity of *Mimosa pudica* is totally the presence the phytoconstituents ^[10].

Materials and Methods

Preparation of plant extract

Mimosa pudica Linn leaves were collected from Kanchipuram district, Tamil Nadu, India. The plant was authenticated by taxonomist at the department of botany, plant anatomy research

institute, Tambaram, Chennai, Tamil Nadu, India. The *Mimosa pudica* leaves were dried at room temperature, powdered and stored at 5 °C until needed. A 100 g of the powder was defatted with 500 ml of petroleum ether (60–80 °C) overnight, and it was then extracted with 500 ml of 95% ethanol by soxhalation. Ethanol was evaporated in a rotary evaporator at 40–50 °C under reduced pressure. The yield of the plant extract was 3.8% (w/w).

Induction of type 2 diabetes

Type 2 diabetes was induced by high fat diet and low dose of streptozotocin. The normal control rats were fed with normal pellet diet and experimental group were fed with a high fat diet for 2 weeks. After two weeks of high fat diet, the animals were fasted overnight and injected with low dose of streptozotocin (35 mg/kg body weight in 0.1 M citrate buffer pH 4.5) ^[11]. The animal had free access to food and water after the injection. Both diabetic induced rats and normal rats continued on their diet for the duration of the study. After 12 hrs fast, glucose level was measured in all experimental rats. Rats having 250 mg/dl of fasting blood sugar were considered as diabetic and used for the experiment.

Experimental animals

The rats are divided into five groups of six animals each. Group I: Normal control rats receiving olive oil as a vehicle; Group II: HFD+STZ induced diabetic control rats; Group III: HFD+STZ diabetic rats treated with ethanol extract of Mimosa pudica leaves at dosage 300mg/kg of bwt for 30 days; Group IV: HFD+STZ diabetic rats treated with standard drug metformin at dosage of 200 mg/kg of bwt for 30 days; Group V: Control rats were treated with ethanol extract of Mimosa pudica leaves at dosage of 300 mg/kg of bwt for 30 days. After 30 days of treatment, the animals were fasted overnight, anesthetized and sacrificed by cervical decapitation. The blood was collected with and without anticoagulant for plasma and serum separation, respectively. The samples are used for biochemical estimation.

Estimation of plasma Glucose

Glucose was estimated by the method of Trinder (1969) using reagent kit ^[12]. Glucose is oxidized in the presence of enzyme glucose oxidase to produce D-Gluconic acid and H_2O_2 . H_2O_2 in the presence of enzyme peroxidase oxidizes phenol which combines with 4-aminoantipyrine to produce colored quinoneimine dye. The intensity of the color developed is proportional to the glucose concentration in the sample. Units are expressed as mg/dl.

Insulin

Plasma insulin level was assayed by Solid-phase enzyme-

linked immunosorbent assay (ELISA). Units are expressed as $\mu U/ml.$

Estimation of liver markers

The liver markers were assayed in serum sample. Total protein and albumin was estimated by method of biuret ^[13]. AST and ALT were assessed by method of Reitman and Frankel, (1957) ^[14]. ALP activity was estimated by King and Armstrong, (1934) ^[15]. LDH activity was measured by King (1965) ^[16].

Statistical Analysis

The data were statistically evaluated with SPSS 21.0 software. Hypothesis testing methods included one way analysis of variance (ANOVA) followed by least significant difference (LSD) test. p-value of less than 0.05 was considered to indicate statistical significance. All the results were expressed as the mean \pm SD for six animals in each group.

Results and Discussion

Fig. 1 showed the concentration of glucose and insulin in type 2 diabetic wistar rats. In STZ treated group, the concentration of glucose significantly increased (p<0.05) with concomitant decrease of insulin when compared to control rats. Upon exposure of STZ to wistar rats causes the destruction of beta cell of pancreas during experimental diabetes, as a result the glucose concentration is increased due to decreased level of insulin ^[17]. Insulin is a hormone, to regulate the glucose homeostasis. In diabetic condition the regulation is affected which attribute to hyperglycemia. The same results have been reported in the earliest study.

The *Mimosa pudica* leaf extracts treatment significantly reduced the concentration of glucose by means of improved insulin activity. The normalization of both glucose and insulin is accompanied by the antioxidants nature of this plant. The antioxidants property of *Mimosa pudica* leaves extracts have been reported in previous experiments. The presence of high content of flavonoids and phenolic compound of *Mimosa pudica* leaf extract which altered the above mentioned parameters ^[18].

A significant decrease (p<0.05) of serum total protein, albumin and globulin level of high fat fed and STZ induced diabetic wistar rats shown in table 1. The same liver marker decreased in the previous experiments in which they are reported the antidiabetic and antioxidant effect of methanol extract of Artanema sesamoides in Streptatozocin-induced diabetic rats ^[19]. The decreased concentration of protein in diabetes condition is possibly the increased catabolism of protein. However, the hormone insulin which increases the synthesis of protein in normal condition while due to its deficiency in diabetic state leads to micro proteinuria ^[20].



Fig 1: Effect of ethanol extract of *Mimosa pudica* leaves on, blood glucose and insulin level in HFD and low dose of STZ induced- type 2 diabetic rats. Group I: Control, Group II: HFD+STZ-Induced diabetic rats, Group III: Diabetes +*Mimosa Pudica*, Group IV: Diabetes+
Metformin, Group V: *Mimosa Pudica* Alone. Each bar represents mean ±SEM for 6 animals. a: Control Vs Diabetic control, b: DC Vs. DC+Mp and DC+Metformin. c: *Mimosa pudica* Vs Other groups. a, b and c denotes Statistical significance at **p*<0.05.

The administration of *Mimosa pudica* leaf extract and metformin which significantly increases (p<0.05) the protein, albumin and globulin level because of the improved activity of insulin in treated wistar rats, which in turn promote the protein synthesis in the present study. Same effect have been demonstrated in the previous study of *Mimosa pudica* leaf extract ^[21]. The result of current study shown the protective nature of *Mimosa pudica* against STZ induced hepatotoxicity in type 2 diabetes.

The activity of AST, ALT, ALP and LDH of HFD and STZ induced diabetic rats were shown in Table 2. The level of

liver marker enzymes such as aspartate transaminase, alanine transaminase, alkaline phosphatase and lactate dehydrogenase was significantly increased (p<0.05) in blood of diabetic rats when compared to control rats. The raised level of marker enzymes in diabetic condition indicates the hepatic damage which is caused by streptozotocin. The hepatic cell which release the intracellular enzymes in circulation during diabetes mellitus condition [²²]. In the earlier study, Ghanbari *et al.* have been reported the elevation of serum alanine transaminase and aspartate transaminase enzymes in streptozotocin induced diabetic rats [²³].

Table 1: Effect of ethanol extract of *Mimosa pudica* leaves on total protein, albumin and globulin of control and experimental rats.

Parameters	Group-I	Group II	Group III	Group IV	Group V
Total protein(gram/dl)	8.05±0.2	4.23±0.61 ^a	7.65±0.17 ^{ab}	7.5±0.14 ^{ab}	8.25±0.10
Albumin(gram/dl)	5.06 ± 0.30	3.18 ± 0.70^{a}	4.56 ± 0.10^{ab}	4.80 ± 0.71^{ab}	5.3 ± 0.11
Globulin(gram/dl)	3.7 ± 0.74	2.68± 0.12 ^a	3.13±05 ^{ab}	3.40 ± 0.1^{ab}	3.64 ± 0.61

Group I: Control, Group II: HFD+STZ-Induced diabetic rats, Group III: Diabetes +*Mimosa Pudica*, Group IV: Diabetes+ Metformin, Group V: *Mimosa Pudica* Alone. Each bar represents mean ±SEM for 6 animals. a: Control Vs Diabetic control, b: DC Vs. DC+Mp and DC+Metformin. c: *Mimosa pudica* Vs Other groups. a and b denotes Statistical significance at *p < 0.05.

Table 2: Effect of ethanol extract of Mimosa pudica leaves on AST, ALT, ALP and LDH of control and experimental rats.

Parameters	Group-I	Group II	Group III	Group IV	Group V
AST	13.71 ± 0.16	21.72 ± 3.3^{a}	15.06 ± 0.64^{ab}	16.4 ± 1.4^{ab}	14.1 ± 0.52
ALT	31.62 ±2.2	50.69±3.8 ^a	35.82 ± 1.7^{ab}	42.86 ± 0.87^{ab}	29.33±1.97
ALP	6.17 ± 0.29	24.3±0.69 ^a	9.34±0.45 ^{ab}	15.8 ± 0.4^{ab}	6.21 ± 0.28
LDH	0.88±0.19	4.2±0.69 ^a	1.22±0.27 ^{ab}	3.1±0.39 ^{ab}	0.79±0.61

Unit: AST, ALT and LDH- μ moles of pyruvate liberated/mg of protion/min. ALP-mg p-nitrophenol/mg protein. Group I: Control, Group II: HFD+STZ-Induced diabetic rats, Group III: Diabetes +*Mimosa Pudica*, Group IV: Diabetes+ Metformin, Group V: *Mimosa Pudica* Alone. Each bar represents mean ±SEM for 6 animals. a: Control Vs Diabetic control, b: DC Vs. DC+Mp and DC+Metformin. c: *Mimosa pudica* Vs Other groups. a and b denotes Statistical significance at **p*<0.05.

The *Mimosa pudica* treatment restored the level of hepatic marker enzymes to near normal when compared to diabetic rats. The result of the present study shown, the *Mimosa pudica* leaves extracts which ameliorated liver damage in diabetic rats which is likely due to antioxidant activity.

Conclusion

The *Mimosa pudica* leaf extract ameliorated hepatic cell against HFD and STZ-induced hepatotoxicity in type 2 diabetes mellitus as evidenced from the improved levels of serum glucose, insulin, and total protein, AST, ALT, ALP and LDH. Therefore the antioxidant property of *Mimosa pudica* leaves extracts might have contributed the hypoglycemic and heptoprotective activity.

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