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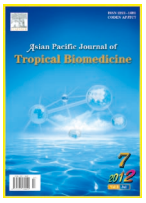

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# Antidiabetic and hypolipidemic activities of *Kigelia pinnata* flowers extract in streptozotocin induced diabetic rats

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ABSTRACT

**Objective:** To evaluate antidiabetic and hypolipidemic activities of *Kigelia pinnata* methanolic flowers extract in streptozotocin (STZ) induced diabetic wistar rat. **Methods:** Rats were made diabetic by a single dose of STZ at 60 mg/kg body weight *i.p.* The blood glucose level was checked before and 72 h after STZ injection to confirm the development of diabetes. The flower extract and glibenclamide were administered orally at the doses of 250 and 500 mg/kg body weight for 21 days. **Results:** Daily oral treatment with the extract and standard drug for 21 days significantly reduced blood glucose, serum cholesterol and triglycerides levels. High density lipoprotein-cholesterol level was found to be improved ($P<0.01$) as compared to diabetic control group. **Conclusions:** It is concluded that *Kigellia pinnata* flowers extract have significant antidiabetic and hypolipidemic effect.

## 1. Introduction

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action or both. Insulin deficiency in turn leads to chronic hyperglycemia with disturbances of carbohydrates, fat and protein metabolism[1]. Globally, the estimated incidence of diabetes and projection for year 2030, as given by International Diabetes Federation is 350 million[2]. Currently available pharmotherapies for the treatment of diabetes mellitus include oral hypoglycemic agents and insulin. However these current drugs do not restore normal glucose homeostasis and they are not free from side effects[3]. In view of the adverse effects associated with the synthetic drugs and as plants are safer, cheaper and much effective, conventional antidiabetic plants can be explored[4]. Over 400 traditional plants have been reported for the treatments of diabetes[5]. Furthermore, after World Health Organization recommended, investigation of hypoglycemic agents from medicinal plants has become more important[6]. Also, diabetes has been treated orally with several medicinal plants or their extracts based on folklore medicine since ancient times.

*Kigelia pinnata* (*K. pinnata*) Jacq. (Family: Bignoniaceae) is known as the cucumber or sausage tree because of the huge fruits (average 0.6 m in length and 4 kg in weight), which hangs from long fibrous stalks. It is distributed all over India but found adundantly in west Bengal. The flowers are found in spring or summer season, hanging ancillary panicles up to 2 m long, corolla of fused petals, irregular bell shaped, 9 -13 cm long two lipped, yellowish on outside and purple on inside. Fruits are oblong, hard, 30-50 cm long, hanging on stalk for several months but not split easily[7,8]. The fruit is used in Africa as therapy for ulcers, syphilis and rheumatism; it has purgative properties. The fruits, pickled in vinegar are used as appetizer, against constipation and to remove kidney stone. Most traditional healers use it to treat a wide range of skin ailments like, fungal infection, boils, psoriasis and eczema. It also has internal application including the treatments in dysentery, ringworm, tapeworm, post- partum haemorrhage, malaria, diabetes, pneumonia and toothache[9,10]. The *Kigelia africana* plant has many medicinal properties due to the presence of numerous secondary metabolites. These compounds include iridoids, flavonoids, naphthoquinones

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and volatile constituent, *etc*. Experimentally the plant has shown antibacterial, antifungal, antineoplastic, analgesic, anti-inflammatory, antimalarial, central nervous system stimulant, anti-protozoal, antidiarrhoeal, and antioxidant properties[10]. The literature survey revealed that there is no experimental evidence of antidiabetic effect of the plant. Therefore, the present work was undertaken to explore the antidiabetic and hypolipidemic potentials of *K. pinnata* methanolic flowers extract (KPFE) of the plant in streptozotocin (STZ) induced diabetic Wistar rat.

## 2. Materials and methods

### 2.1. Plant material

*K. pinnata* flowers were collected during month of October from the campus of Kurukshetra University, Kurukshetra, India and were identified by Dr. BD Vashishta, Department of Botany, Kurukshetra University, Kurukshetra, India. A voucher specimen of the plant is preserved in the herbarium of the Faculty of Pharmaceutical Sciences, Kurukshetra University (No. IPS/KUK/KP/2009).

### 2.2. Chemicals

STZ was purchased from Sigma-Aldrich, India. The STZ solution was prepared by freshly dissolving in citrate buffer (0.01 M, pH 4.5). Total cholesterol, high density lipoprotein (HDL)-cholesterol and triglyceride (TC) standard kits were purchased from Erba Diagnostics Mannheim Gambh, Germany. All reagents used in study were analytical grade.

### 2.3. Extract preparation

The flowers were dried under shade and powdered to coarse particles. The powdered material was defatted with petroleum ether (60-80 ℃) in a Soxhlet extraction apparatus and further the same amount of plant material was extracted with methanol. The extract was dried at 45 ℃ in rotary evaporator to produce a semisolid mass and stored in airtight containers in refrigerator below 10 ℃.

### 2.4. Animals

Wistar rat of either sex, weighing about 150-250 g were used in the study. Animals were maintained under standard environmental conditions, *i.e.* ambient temperature of (22 ± 2) ℃, at 45-55% relative humidity for 12 h, each of dark and light cycle and fed with a standard pellet rats diet obtained from Ashirwad Industries, Chandigarh, India and water was supplied *ad libitum*. All the studies were conducted in accordance with the Animal Ethical Committee of the University.

### 2.5. Induction of diabetes

Rats were made diabetic by a single dose of STZ at 60 mg/kg bw i.p.[11,12]. The blood glucose level was checked before and 72 h after STZ injection to confirm the development of diabetes. The diabetic animals were stabilized for five days and the next day (day 0) experiment was started. Only those animals which showed blood glucose levels >250 mg/dL were separated and used for the study.

### 2.6. Experimental design

All the diabetic animals were randomly divided into five groups with six animals each and treated once a day for 21 days as follows:

Group I (Normal healthy control) was given only vehicle (Tween 80, 1% v/v). Group II served as diabetic control and received only vehicle. Group III as diabetic rats received KPFE at dose of 250 mg/kg bw. Group IV as diabetic rats received KPFE at 500 mg/kg bw. Group V as diabetic rats received glibenclamide (GLB) at 10 mg/kg bw.

Blood glucose was measured with elegance glucometer (CT-X10, Convergent Technologies, Germany) at weekly intervals, *i.e.* 0, 7, 14 and 21 days after daily administration of extract orally.

### 2.7. Lipid profile

On Day 21, blood was collected by retro-orbital puncture under mild ether anesthesia from rats. Total cholesterol and TC were determined by the method of Rifai *et al*[13]. HDL-cholesterol was also evaluated in normal and STZ-induced diabetic rats by autoanalyser (Erba Chem 7, Mannheim, Germany) using Erba diagnostic[14].

### 2.8. Statistical analysis

All the data were expressed as Mean ± SEM. Statistical analysis was carried using Student's *t*-test to analyze the significance between the groups. A value of $P < 0.05$ was considered to be significant.

## 3. Results

### 3.1. Effect on blood glucose level

There was a significant increase in blood glucose level in diabetic rats when compared with normal controls due to injection of STZ. In the study, daily administration of the extract for three weeks led to a dose dependent fall in blood glucose levels. At the end of experiment (the 21st day) blood glucose level was (152.48 ± 2.7) and (138.43 ± 3.5) mg/dL at the doses of 250 and 500 mg/kg of KPFE respectively. The

**Table 1**
Antidiabetic effect of KPFE in STZ-induced diabetic rats (Mean ± SEM).

| Groups/Treatment | Blood glucose level (mg/dL) | | | |
|---|---|---|---|---|
| | Initial day | Day 7 | Day 14 | Day 21 |
| I: Vehicle | 115.27 ± 4.50 | 113.34 ± 3.80 | 112.70 ± 5.20 | 113.82 ± 2.40 |
| II: STZ | 258.41 ± 2.30 | 294.47 ± 5.50 | 348.70 ± 5.30 | 402.00 ± 3.40 |
| III: STZ + KPFE (250 mg/kg) | 288.45 ± 2.30 | 265.50 ± 4.30 | 194.27 ± 3.80* | 152.48 ± 2.70* |
| IV: STZ + KPFE (500 mg/kg) | 298.29 ± 3.50 | 228.67 ± 4.20 | 189.75 ± 4.30* | 138.43 ± 3.50** |
| V: STZ + Std. (10 mg/kg) | 274.27 ± 3.50 | 210.72 ± 4.22* | 125.41 ± 3.40** | 118.53 ± 3.50** |

*$P$<0.05, **$P$ <0.001, When groups III, IV and V compared with diabetic control, *i.e.* group II.

**Table 2**
Effect of extract of KPFE on body weights in diabetic rats (Mean ± SEM).

| Groups/Treatment | Body weight (g) | | | |
|---|---|---|---|---|
| | Initial day | Day 7 | Day 14 | Day 21 |
| I: Vehicle | 215.20 ± 2.30 | 222.43 ± 4.20 | 225.41 ± 3.60 | 228.47 ± 3.20 |
| II: STZ | 225.23 ± 3.40 | 219.42 ± 3.80 | 211.35 ± 2.70 | 208.25 ± 4.30 |
| III: STZ+ KPFE (250 mg/kg) | 233.24 ± 2.70 | 231.34 ± 3.70* | 232.47 ± 3.50 | 232.14 ± 2.80* |
| IV: STZ+ KPFE (500 mg/kg) | 229.43 ± 3.40 | 227.24 ± 2.50 | 227.34 ± 3.50* | 227.73 ± 2.50* |
| V: STZ + GLB (10 mg/kg) | 225.34 ± 2.70 | 227.34 ± 2.30* | 228.78 ± 2.30** | 231.25 ± 1.80** |

*$P$<0.05, **$P$<0.001, When groups III, IV and V compared with diabetic control *i.e.* group II.

**Table 3**
Effect of extract on lipid profile in diabetic rats (Mean ± SEM).

| Groups/Treatment | Total cholesterol (mg/dL) | Triglycerides (mg/dL) | HDL-cholesterol (mg/dL) |
|---|---|---|---|
| I: Vehicle | 87.28 ± 3.80 | 82.42 ± 5.16 | 37.32 ± 2.9 |
| II: STZ | 254.73 ± 7.60 | 150.52 ± 4.71 | 28.23 ± 2.2 |
| III: STZ+ KPFE (250 mg/kg) | 123.54 ± 3.40* | 117.55 ± 4.52* | 36.47 ± 4.7* |
| IV: STZ+ KPFE (500 mg/kg) | 115.27 ± 3.40* | 92.29 ± 4.73 | 41.23 ± 4.9* |
| V: STZ + GLB (10 mg/kg) | 98.72 ± 5.30** | 83.47 ± 4.5* | 45.28 ± 4.8** |

*$P$<0.05, **$P$<0.001, When groups III, IV and V compared with diabetic control *i.e.* group II.

antidiabetic effect of KPFE on the blood glucose levels in diabetic rats is also shown in Table 1.

### *3.2. Effect on body weight*

The body weight of the diabetic controls (group II) significantly decreased compared with the normal controls (group I). During the weekly of observation of the KPFE treated diabetic rats at doses of 250 mg/kg and 500 mg/kg, there were significant ($P$ <0.05) weight gains on day 21 relative to day 0 as shown in Table 2.

### *3.3. Effect on lipid profile*

In the present study the total cholesterol and triglycerides was reduced in by 21 days treatment with KPFE. HDL cholesterol level was significantly improved by treatment of KPFE as compared to diabetic control group (Table 3). The results of present study indicated that the methanolic flowers extract of *K. pinnata* possesses significant hypoglycemic activity. It also maintained the lipid levels and body weight of rats.

## 4. Discussion

STZ is a nitrosourea compound produced by *Streptomyces achromogenes*, which specifically induces DNA strand breakage in β-cells causing diabetes mellitus[15-18]. This leads to insulin deficiency which in turn increases the blood sugar level. In our study the *K. pinnata* flowers extracts decreased the blood glucose level significantly ($P$<0.001) at the dose of 500 mg/kg. The antidiabetic effect was dose dependent. Diabetes is also associated with altered lipid levels. The most commonly observed lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia[19,20] and contribute to coronary artery disease[21]. In diabetic rats there was a significant increase in total cholesterol and triglycerides ($P$<0.05)[22]. In KPFE treated rats, there was a reduction in total cholesterol and triglycerides which showed the hypolipidemic effect of this plant. The hypolipidemic effect may be due to inhibition of fatty acid synthesis[23,24]. In normal metabolism insulin activates the enzyme lipoprotein lipase and hydrolyses triglycerides and the deficiency in insulin results in inactivation of these enzymes thereby causing hypertriglyceridemia[25,26]. The repeated administration of *K. pinnata* extract for a period of 21 days resulted in a significant improvement in lipid parameter levels when compared to the diabetic control. Normal healthy animals were found to be stable in their body weight whereas diabetic animals showed reduction in body weight. The

decrease in weight in diabetes was due to the increased muscle wasting and loss of tissue proteins[27-29]. In the study, the reduction of body weight was diminished by extracts treatment after 21 days of treatment in a dose dependent manner.

From this study, we can conclude that *K. pinnata* flowers extract have significant antidiabetic effects. The extract also showed improvement in lipid profile and body weight. Further studies are required to identify the active constituents.

## Conflict of interest statement

We declare that we have no conflict of interest.

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