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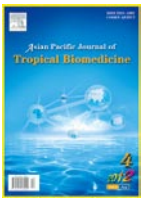

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# Investigation of hypoglycemic, hypolipidemic and antioxidant activities of aqueous extract of *Terminalia paniculata* bark in diabetic rats

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ABSTRACT

**Objective:** To investigate the hypoglycemic, hypolipidemic and antioxidant activities of aqueous extract of *Terminalia paniculata* bark (AETPB) in streptozotocin (STZ)-induced diabetic rats. **Methods:** Acute toxicity was studied in rats after the oral administration of AETPB to determine the dose to assess hypoglycemic activity. In rats, diabetes was induced by injection of STZ (60 mg/kg, i.p.) and diabetes was confirmed 72 h after induction, and then allowed for 14 days to stabilize blood glucose level. In diabetic rats, AETPB was orally given for 28 days and its effect on blood glucose and body weight was determined on a weekly basis. At the end of the experimental day, fasting blood sample was collected to estimate the haemoglobin (Hb), glycosylated haemoglobin (HbA1c), serum creatinine, urea, serum glutamate-pyruvate transaminase (SGPT), serum glutamate-oxaloacetate transaminase (SGOT) and insulin levels. The liver and kidney were collected to determine antioxidants levels in diabetic rats. **Results:** Oral administration of AETPB did not exhibit toxicity and death at a dose of 2000 mg/kg. AETPB treated diabetic rats significantly ($P<0.001$, $P<0.01$ and $P<0.05$) reduced elevated blood glucose, HbA1c, creatinine, urea, SGPT and SGOT levels when compared with diabetic control rats. The body weight, Hb, insulin and total protein levels were significantly ($P<0.001$, $P<0.01$ and $P<0.05$) increased in diabetic rats treated with AETPB compared to diabetic control rats. In diabetic rats, AETPB treatment significantly reversed abnormal status of antioxidants and lipid profile levels towards near normal levels compared to diabetic control rats. **Conclusions:** Present study results confirm that AETPB possesses significant hypoglycemic, hypolipidemic and antioxidant activities in diabetic condition.

## 1. Introduction

Diabetes mellitus is an endocrine metabolic disorder characterized by hyperglycemia, altered lipids, carbohydrates, proteins metabolism and it increases risk of cardiovascular diseases complications[1]. The two forms of diabetes, type 1 and 2, differ in their basic mechanisms of development and in physiologic characteristics such as associations with obesity, age, and insulin. But, both types of the diabetes share the common characteristics of hyperglycemia, microvascular and macrovascular complications. Moreover, the alterations of lipoproteins metabolism are involved to the pathogenesis of the cardiovascular disease in both forms of diabetes in a similar way[2]. Also, diabetes is usually accompanied by increased generation of free radicals or impaired antioxidant defenses. Oxidative stress is also responsible for the development and progression of diabetes and its complications are reported by Maritim *et al*[3]. Diabetes has a considerable impact on the health, life style, life expectancy of patients and its related complications are major healthcare problems. Currently, diabetes is controlled by handful of available drugs such as oral hypoglycemic agents and insulin, but they have their own limitations. Traditionally, many herbal medicines and medicinal plants have been used for the treatment of diabetes as an alternative medicine[4]. Presence of various phytoconstituents in medicinal plants is thought to act on a different series of targets by multiple modes and mechanisms. Hence, plants have the potential

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to impart therapeutic effect in complicated disorders like diabetes and its complications[5]. Screening of medicinal plants is one of the alternative and valid approaches in the drug development process because they contain diverse phytoconstituents which may give new drug leads and may be effective and safe in diabetes. In India, traditionally numbers of plants are used to manage the diabetic conditions and their active principles were isolated but few plants have been scientifically studied.

*Terminalia paniculata* (*T. paniculata*) Roth (Combretaceae) is a large deciduous tree distributed in western and eastern Ghats, in the semi-evergreen and moist deciduous forests of India. The bark is astringent, bitter, cooling and useful in vitiated conditions of kapha and pitta, cough, bronchitis, strangury, diabetes, skin diseases, leprosy condition[6]. In India, it is traditionally used in the treatment of diabetes and up-to-date literature survey revealed that there is no scientific documentation to claim its efficacy in diabetes. Hence, the present investigation was aimed to study the hypoglycemic, hypolipidemic and free radical scavenging properties of the aqueous extract of *T. paniculata* bark (AETPB) in streptozotocin (STZ)-induced diabetic rats. The preliminary phytochemical analysis of AETPB showed the presence of carbohydrate, tannins and phenolic compounds[7].

## 2. Materials and methods

### 2.1. Plant material and extraction

*T. paniculata* Roth. (Combretaceae) bark was collected from Annaimalai hills, Coimbatore, Tamil Nadu, India. The specimen was authenticated at Botanical Survey of India (BSI), Coimbatore (BSI/SRC/5/23/09-10/Tech.-813). The separated barks were shade dried, powdered and 100 g of bark powder was soaked in distilled water for 12 h. On the next day, plant material was boiled for 30 min and filtered. This aqueous extract was concentrated, transferred to air-tight glass container and sealed. The container was stored at (2-8 ℃) until the completion of pharmacological studies and yield of the extract was 11% (w/w).

### 2.2. Experimental animals

Female Wistar rats (150-180 g) were used to assess acute toxicity and male Wistar rats (150-200 g) were used to evaluate anti-diabetic activity. All animals were housed in standard laboratory conditions [temperature (22±2 ℃) and humidity (45±5)% with 12 h day: 12 h night cycle]. The standard laboratory diet was provided to the animals and they were allowed to drink water *ad libitum*. Studies were carried out after the approval of Institutional Animal Ethical Committee in accordance with institutional ethical guidelines for the care of laboratory animals of KMCH College of Pharmacy, Coimbatore, India (approval no. KMCRET/Ph.D/5/09).

### 2.3. Chemicals

The estimation of biochemical parameters was carried out using commercially available kits (Primal Healthcare Limited, Lab Diagnostic Division, Mumbai, India). STZ and other chemicals were procured from Himedia Laboratories, Mumbai, India.

### 2.4. Acute toxicity study

Acute oral toxicity study was performed as per Organization for Economic Cooperation and Development guidelines 423 (acute toxic classic method)[8]. After the oral administration of AETPB (2 000 mg/kg), animals were observed individually at least once during the first 30 min, periodically during the first 24 h, with special attention given during the first 4 h, and daily thereafter, they were observed for a total of 14 days for toxicity determination.

### 2.5. Induction of experimental diabetes in rats

STZ was dissolved in freshly prepared 0.1 M cold citrate buffer (pH 4.5) and administered by intraperitoneal route (60 mg/kg) to the overnight fasted rats[9]. After 6 h of STZ injection, rats were received 5% dextrose solution for the next 24 h to prevent STZ induced fatal hypoglycemia as a result of massive pancreatic insulin release after its administration[10]. Diabetes was confirmed 72 h after induction by measurement of tail vein blood glucose levels using glucose meter (Glucocard™ 01-mini, Arkray Factory, Inc., Japan) by glucose oxidase-peroxidase method using strips. Diabetic rats were kept 14 days under standard laboratory condition for the stabilization of blood glucose levels[9]. After 14 days induction of diabetes, blood glucose was again determined and animals with a blood glucose level greater than 250 mg/dL were selected for the study.

### 2.6. Experimental design for antidiabetic activity

The rats were divided into five groups with six rats in each group. Group 1: normal control rats received propylene glycol (5 mL/kg); group 2: STZ-induced diabetic rats were treated with propylene glycol (5 mL/kg); group 3: STZ-induced diabetic rats were treated with AETPB (100 mg/kg); group 4: STZ-induced diabetic rats were treated with AETPB (200 mg/kg); group 5: STZ-induced diabetic rats were treated with glibenclamide (5 mg/kg)[11]. The vehicle, AETPB and glibenclamide were administered orally to its respective group animals for 28 days. AETPB was dissolved in water and glibenclamide was suspended in propylene glycol just prior to the oral administration of dose throughout the treatment period. The fasting blood glucose level and body weight were estimated every week (0, 7, 14, 21 and 28 day). At the end of the fourth week, vehicle, AETPB and glibenclamide were administered to the overnight fasted animals and after 1 h treatment all animals were anaesthetized with ketamine