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Anti hyperglycemic and antihyperlipidemic activity of aerial parts of *Aerva lanata* Linn Juss in streptozotocin induced diabetic rats

Rajesh R[1*], Chitra K[2], Padmaa M Paarakh[1]

[1] *The Oxford College of Pharmacy, Hongasandra, Bangalore- 560 068, Karnataka, India.*
[2] *Faculty of Pharmacy, Sri Ramachandra University, Porur, Chennai- 600 116, Tamil Nadu, India*

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ABSTRACT

Objective: To evaluate the effect of methanol extract (MEAL) and aqueous extract (AEAL) of the aerial parts of *Aerva lanata* Linn Juss (*A. lanata*) in streptozotocin induced diabetic rat. **Methods:** The streptozotocin induced diabetic rats were orally treated with vehicle (Normal saline), glibenclamide (0.5 mg/kg), MEAL (200 and 400 mg/kg) and AEAL (200 and 400 mg/ kg) to the respective treatment groups. The blood glucose level, lipid profile, body weight on 0 day, 1 week and 2 week and biochemical parameters on 2 week of treatment were measured and are compared to the diabetic control rats. **Results:** MEAL, AEAL and glibenclamide were found to significantly ($P<0.01$ and $P<0.05$) reduce the blood glucose level, lipid profile, increase body weight and reduce serum glutamate- oxaloacetate transaminase (SGOT), serum glutamate- pyruvate transaminase (SGPT), creatinine, alkaline phosphatase (ALP), blood urea nitrogen (BUN) and total bilirubin to significant level. The antidiabetic effect was sustained from 1 week onwards till the end of the study. **Conclusions:** It has been concluded that MEAL and AEAL in addition to the antidiabetic activity, also possess antihyperlipidemic and the normal value of the hepatic biochemical parameters reveals the safety profile of the extract on liver function in the streptozotocin induced diabetic model.

1. Introduction

India is a rich source of medicinal plants and a number of plant extracts have been used in various systems of medicines such as Ayurveda, Siddha and Unani etc to cure various diseases. Only a few of them have been scientifically explored. Plant derived natural products such as flavanoids, terpenoids, alkaloids etc have received considerable attention in recent years due to their diverse pharmacological properties including cytotoxic and cancer chemo preventive effects [1]. Herbal medicine is based on the premise that plants contain natural substances that can promote health and alleviate illness. In recent times, focus on plant research has increased throughout the world and the immense potential of medicinal plants used in various traditional systems has been established scientifically. Screening plants with such ethno medical uses is believed to increase the odds in discovering new medicines. Diabetes mellitus is a metabolic disorder characterized by disturbances in carbohydrate, protein and lipid metabolism and by complications like micro vascular (retinopathy, neuropathy and nephropathy) and macro vascular (heart attack, stroke and peripheral vascular disease) complications [2]. A world wide survey has reported that diabetes mellitus affects nearly 10% of the population. It has been predicted that the prevalence of diabetes in adults will increase from 135 million in 1995 to 350 million in 2030 as given by International Diabetes Federation [3]. Currently available synthetic antidiabetic agents produce serious side effects like hypoglycemic coma and hepatorenal disturbances [4, 5]. Patients are therefore using herbal medicines which have fewer side effects and have the potential to impart therapeutic effect in complicated disorders like diabetes and its complication [6]. Following the WHO's recommendation for research on the beneficial uses of medicinal plants in the treatment of diabetes mellitus, investigations on hypoglycemic agents derived from medicinal plants have also gained momentum. Antidiabetic agents from medicinal plants could serve as a good source for drug design and much attention has been fixed on formulation of herbal medicine [7]. *Aerva lanata* Linn Juss (Family: Amaranthaceae) (*A. lanata*) is an important source of chemicals of immense medicinal and pharmaceutical importance. The plant is distributed throughout Tropical India as a common weed in fields

*Corresponding author: Rajesh R, Dept of Pharmaceutical Chemistry, The Oxford College of Pharmacy, No 6/9, 1 Cross Begur road, Hongasandra, Bangalore- 560068, Karnataka, India.
Tel: +91 9448516903
Fax: +91-80-30219829
E-mail: rajeshsrn@gmail.com

and wasteland and is also found to be grown in Arabia, Tropical Africa, Sri Lanka, Philippines and Java [8]. The *A. lanata* Linn Juss is useful for curing anthelmintic [9] and urolithiasis[10]. The *A. lanata* has been reported to possess anti-inflammatory [11], diuretic [12] and nephroprotective actions in rats [13]. The whole plant of *A. lanata* showed significant antimicrobial activities [14]. Alcoholic extracts of *A. lanata* has shown significant antidiabetic activity in rats[15]. The partially TLC purified fraction of petroleum ether extract was proved to be cytotoxic [16]. Hepatoprotective activity was studied on the aqueous alcoholic extracts of leaf and root [17]. Anticancer activity of aerial parts of *A. lanata* Linn Juss ex Schult against Dalton's ascitic Lymphoma was studied [18]. *A. lanata* Linn are reported to be used in diabetes in folklore and traditional medicine [19] and based on the above perspective, an effort was made to ascertain the possible role of MEAL and AEAL in Streptozotocin-induced diabetes mellitus in vivo.

2. Materials and methods

2.1. Collection and authentication of plant

Fresh aerial parts of the plant *A. lanata* Linn Juss were collected from Tirunelveli district in Tamil Nadu, India during the month of November and it is identified and authenticated by Dr. Shiddamallayya N, Asst. Director in charge from Regional Research Institute (AY.), Bangalore and Voucher specimens (RRCBI- 5588) was deposited in the Institute for future reference. The aerial parts of *A. lanata* Linn Juss were dried in the shade and it is milled into coarse powder by a mechanical grinder and it is stored in closed vessel for further use.

2.2. Plant crude extracts

The air dried coarse powder of the aerial parts of *A. lanata* was extracted successively with organic solvents of increasing polarity like petroleum ether, chloroform, acetone, methanol using soxhlet's apparatus and water by maceration for 7 days. Each time before extracting with next solvent, the marc was dried in the air and it is then repacked in the apparatus. After each extraction was completed, the extracts were cooled at room temperature, filtered and concentrated under reduced pressure in the rotator evaporator; it is then dried and kept in the desiccators. The extracts of aerial parts of *A. lanata* were subjected to qualitative test for the identification of various active constituents.

2.3. Chemicals and reagents

Streptozotocin (Sigma chemical co., U.S.A), glibenclamide (micro labs, India), glucose, triglyceride and total cholesterol estimation kit (Accurex Biomedical pvt Ltd, India). Other chemicals and reagents used for the study were of analytical grade and procured from approved organizations.

2.4. Preliminary phytochemical screening

MEAL and AEAL was screened for the presence of various phytoconstituents [20, 21].

2.5. Experimental animals

Male Sprague Dawley (150-180 g) rats were used for the present study. The animals were maintained under standard environmental conditions and were fed with standard pellet diet and water *ad libitum*. The experimental protocol was approved by the Institutional animal ethics committee, Approval no IAEC- XII/ SRU/80/ 2008. CPCSEA guidelines were adhered during the maintenance and experiment.

2.6. Acute toxicity studies

Acute oral toxicity study of MEAL and AEAL was studied in healthy rats (n=3) according to the guidelines set by Organisation for Economic Cooperation and development (OECD) guidelines [22]. Starting dose was selected to be 2 000 mg/kg b.w. and finally a dose of 4 000 mg/kg b.w. was evaluated for toxicity. The animals were observed continuously for 24 h for mortality.

2.7. Evaluation of anti diabetic activity

2.7.1. Treatment protocol

The animals were divided into seven groups of six animals each as follows:

Group I- Vehicle control, Normal saline (0.9% w/v NaCl); Group II- Diabetic control; Group III- Diabetic standard treated, 0.5 mg/kg of glibenclamide, *p.o.* (micro labs); Group IV- Diabetes MEAL 200 mg/ kg, *p.o.*; Group V- Diabetes MEAL 400 mg/ kg, *p.o.*; Group VI- Diabetes AEAL 200 mg/ kg, p.o.; Group VII- Diabetes AEAL 400 mg/ kg, *p.o.*.

Diabetes was induced in all groups except normal control by a single intraperitoneal injection of 60 mg/ kg of Streptozotocin (STZ) dissolved in a freshly prepared 0.1 M citrate buffer (pH 4.5). The animals in the vehicle control (Group I) received normal saline orally (0.9% w/v NaCl). The rats with blood glucose levels above 250 mg/dL were considered as diabetic and used in this study [23]. After 72 h, the blood was withdrawn by retro orbital puncture under light ether anaesthesia and the blood glucose level was estimated. Serum was separated by centrifugation at 3 000 rpm for about 5 minutes. The clear straw coloured serum was collected and stored at 4 ^{0}C for the measurement of marker enzymes level to assess the liver functions. Blood glucose levels and body weight were measured on day 0, 7 and 14 of the study. Finally on day 14, blood was collected to perform various biochemical parameters [24].

2.7.2. Estimation of plasma glucose and lipid profile

Every week, following overnight fasting (16 h fasting with free access to water), the blood samples were withdrawn from the animals by retro orbital puncture under light ether anaesthesia. The plasma glucose estimation was done based on enzymatic method using glucose oxidase/ peroxidase (GOD/POD) method using a standard kit obtained from Accurex Biomedical pvt Ltd, India. Serum glucose levels are expressed in mg/ dL. The serum triglycerides (TG), total cholesterol (TC) levels and various biochemical parameters were also estimated.

2.7.3. Effect on body weight