Research Article

Antidiabetic Activity of 80% Aqueous Methanolic Bark and Leaf Extract of *Dolichandrone atrovirens*

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ABSTRACT

Diabetes mellitus is still not completely curable by current antidiabetic drugs. Insulin therapy is the only satisfactory approach to diabetes mellitus, even though it has several drawbacks such as insulin resistance, anorexia, brain atrophy and fatty liver in chronic treatment. Treatment of type 2 diabetes mellitus patients with sulfonylureas and biguanides is always associated with side effects. So, herbal drugs are gaining popularity in the treatment of diabetes mellitus. The major merits of herbal medicines seem to be their efficacy, low incidence of side effects, and low cost. The objective of this work is to evaluate the antidiabetic activity of 80% aqueous methanolic bark and leaf extract of *Dolichandrone atrovirens* in streptozotocin (STZ) and nicotinamide induced diabetic male Wistar rats. In this study type, 2 diabetes was induced by intramuscular injection of streptozotocin at a dose 60mg/kg and nicotinamide 120 mg/kg[30]. The animals were divided into four group of 6 animals in each group as follows: group I: normal control; group II: STZ + nicotinamide induced diabetic control; group III: Diabetic rats with leaf extract of *Dolichandrone atrovirens* (200mg/kg); group IV: diabetic rats with methanolic bark extract of *Dolichandrone atrovirens* (200mg/kg). The bark and leaf extract of *Dolichandrone atrovirens*reduce the blood glucose significantly. Aqueous methanolic bark and leaf extract of *Dolichandrone atrovirens*haveprotected the vital organ tissue to reduce the blood glucose in the experimental animals.

Keywords: Dolichandroneatrovirens, STZ, antidiabetic.

INTRODUCTION

Diabetes mellitus is a major health problem worldwide with projected rise prevalence in 2030 is 366 million[1]. This disease is a chronic metabolic disorder of carbohydrate, fat and protein characterized by high levels of glucose in the blood due to the impaired secretion of insulin or insulin insensitivity[2]. Type 1 and type 2 are the two major types of diabetes and type 2 is a most common form of diabetes constituting 90-95% of the diabetic population. Chronic hyperglycemia causes complications linked to diabetes, such as atherosclerosis, peripheral vascular disease, stroke, retinopathy, neuropathy, and nephropathy[3-5]. The management of diabetes mellitus is considered a global problem [6] and currently available therapy for diabetes includes insulin and various oral anti-diabetic agents such as sulfonylureas, thiazolidinedione, biguanide, and α-glucosidase inhibitors etc. These drugs are used to achieve better glycemic control, but these drugs are produced a lot of serious side effect moreover they are not safe in pregnancy[7-10]. So the safer hypoglycemic agents are one of the most important areas of investigation [11, 12]. Hence, antidiabetic drug discovery has shifted its focus to natural plant sources having minimal side effects. Plants have played major source drugs used to treat diabetes all over the world [13, 14]. More than 800 plants have been studied for their ant diabetic potentials[15, 16]. Plants play a major role in the discovery of new antidiabetic agents and this should directly interact with our body chemistry without side effects[17-20]. 21,000 plants are medicinally used in the world which is listed by the world health organization (WHO) and 150 species are used commercially[21, 22]. Around 30% of the diabetes mellitus patients used the complementary and alternative medicine to manage the disease[23]. Many reviews and research articles appear in the journals showed that numerous plants used in the alternatives system of medicine for manage diabetes mellitus and proved scientifically effective[24-27.] We also recently revived the fifty numbers of current trends of medicinal plants having antidiabetic activity[28]. Most of the study frequently implicated the response of antidiabetic activity is due to the plant content glycoside, terpenoids, alkaloids, flavonoids, and carotenoids[29]. The purpose of the present study was to evaluate the antidiabetic activity of leaf and bark extract of *Dolichandrone atrovirens*instreptozotocin and nicotinamide rats. *Dolichandrone atrovirens*isa fairly moderate tree (Family: Bignoniaceae) with white flower, commonly found throughout India. Traditionally, the leaf and bark used for various disorders like arthritis, inflammation, diabetes, rheumatism, liver diseases and this is the first time the current research evaluate the in *vivo* antidiabetic activity of *Dolichandrone atrovirens*.

MATERIALS AND METHODS

Plant Material and Preparation of Extract

The bark and leaves and of *Dolichandrone atrovirens* were collected from Chitheri hills, Salem in August 2017. The plant was authenticated by Dr G.V.S. Murthy, Joint

Director, Botanical Survey of India, Coimbatore, Tamilnadu, India, where a voucher specimen was preserved for further reference. 1.5 kg of shade-dried coarse powders of the plant material was extracted with 80%v/v aqueous methanol by maceration at room temperature for 72 h. After the completion of each extraction, the extracts were filtered, concentrated to dryness in a rotavapor under reduced pressure and controlled temperature (40-50°C). The residues were stored in thevacuumdesiccatorthe residues were then stored ina vacuum desiccator for further use.

Animals

Male Wistar rats weighing (150-160 g) were obtained from Venkateswara enterprises, Bangalore, India. The animals were maintained standard environment condition and fed with standard rat feed and allow drinking water *ad libitum*. The animals are allowed to accommodate the environment for one week before conducting the experiments. The experiment protocols approved by the ethical committee and were in strict accordance with the guidance for the care and use of laboratory animals.

Induction of Diabetes

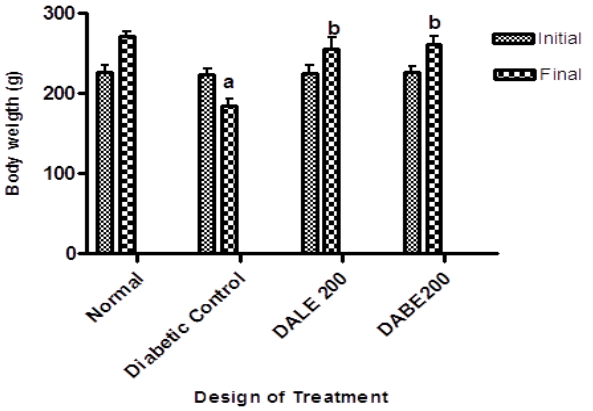
Type 2 diabetes was induced in overnight fasting rats by intramuscular injection of streptozotocin dissolved in 0.1 M citrate buffer, pH 4.5, at a dose of 60mg/kg and nicotinamide dissolved in normal physiological saline and the dose of 120 mg/kg[30]. The animals were allowed to drink the five percentage glucose solution to overcome the drug-induced hypoglycemia and one week later the development of diabetes the fasting glucose greater than 250mg/dl were used for the current study[31].

Experimental Design

The rats were divided into four groups of 6 animal in each group as follows: group I: normal control administered with 0.3% W/V of Carboxymethylcellulose (CMC); group II: STZ + nicotinamide induced diabetic control administered with CMC; group III: Diabetic rats administered with leaf extract of *Dolichandrone atrovirens* (200mg/kg); group IV: diabetic rats administered with methanolic bark extract of *Dolichandrone atrovirens* (200mg/kg).

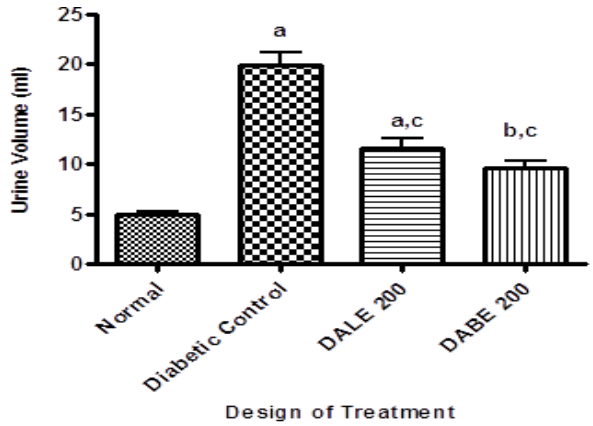
RESULTS

To study the antidiabetic effect of the aqueous methanolic extract of *Dolichandrone atrovirens* leaf extract (DALE) and *Dolichandrone atrovirens* bark extract (DABE) were administered oral route, diabetes was induced in the male Wistar rats by single intraperitoneal injection of streptozotocin and nicotinamide to continue for 60 days. At the end of the experiment 24hours, urine was collected and noted the initial and final body weight (Fig.1) of the various group of animals. The collected urine is used to estimate the urine volume (Fig.2) urine creatinine (Fig.3), urine urea (Fig.4) urine uric acid (Fig.5) urine microalbumin (Fig.6) and the overnight fasted animals blood used to estimate the blood glucose (Fig.7), blood urea (Fig.8), blood uric acid (Fig.9), blood creatinine (Fig.10) and glycosylated hemoglobin (Fig.11). Finally, the animal sacrificed and kidneys were dissected and compare the kidney weight (Fig.12) of various group animals. The Data were statistically analyzed by using one-way ANOVA followed by Tukey-Kramer multiple comparison tests.



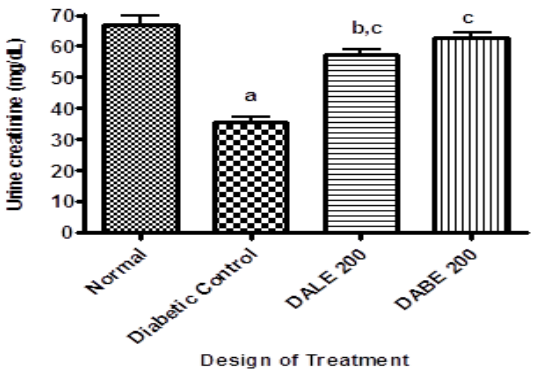
N=6; Mean ± SEM; aP<0.001 vs Normal; bP<0.001 vs Diabetic control

Figure 1: Effect of DALE and DABE on body weight



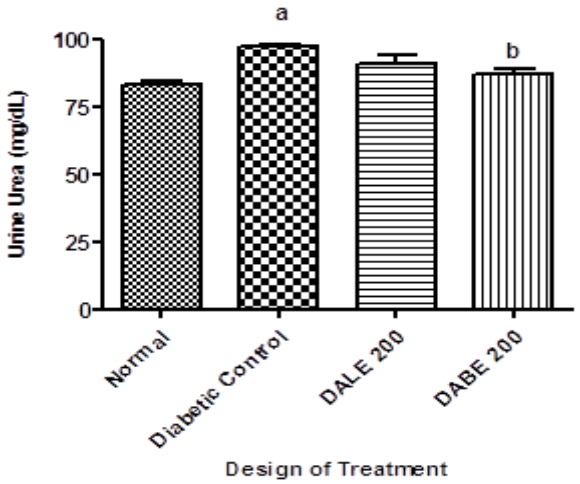
N=6; Mean ± SEM; aP<0.001, bP<0.01 vs Normal; cP<0.001 vs Diabetic control.

Figure 2: Effect of DALE and DABE on urine volume



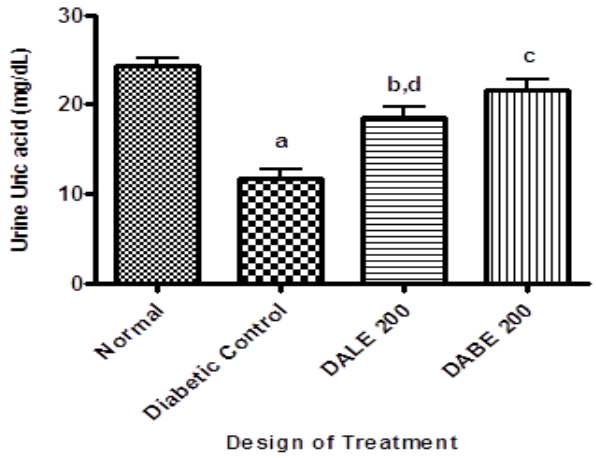
N=6; Mean ± SEM; aP<0.001, bP<0.05 vs Normal; cP<0.001 vs Diabetic control

Figure 3: Effect of DALE and DABE on urine creatinine levels



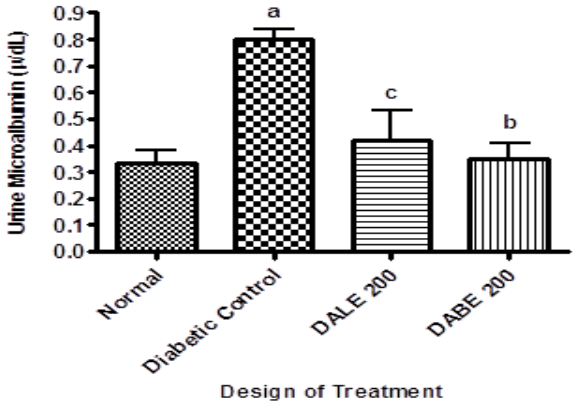
N=6; Mean ± SEM; aP<0.001 vs Normal; bP<0.05 vs Diabetic control

Figure 4: Effect of DALE and DABE on urine urea levels



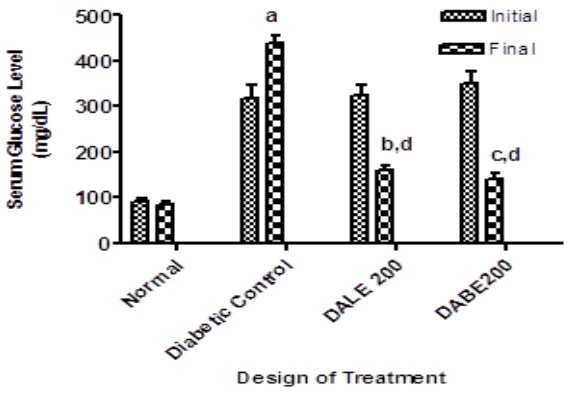
N=6; Mean ± SEM; aP<0.001, bP<0.01 vs Normal; cP<0.001, dP<0.01 vs Diabetic control.

Figure 5: Effect of DALE and DABE on urine uric acid levels



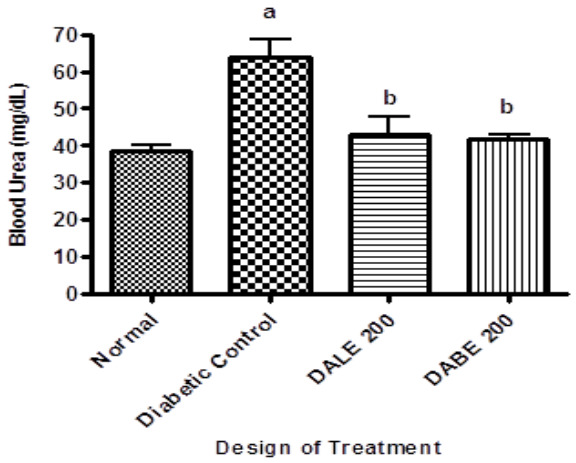
N=6; Mean ± SEM; aP<0.001 vs Normal; bP<0.001, cP<0.01 vs diabetic control

Figure 6: Effect of DALE and DABE on urine microalbumin levels



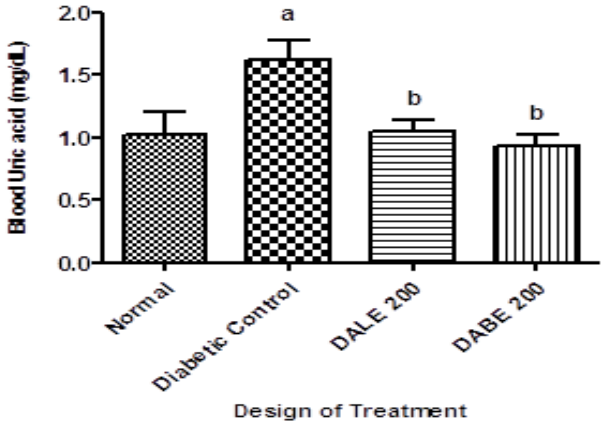
N=6; Mean ± SEM; aP<0.001, bP<0.01, cP<0.05 vs Normal; dP<0.001 vs Diabetic control.

Figure 7: Effect of DALE and DABE on blood glucose levels



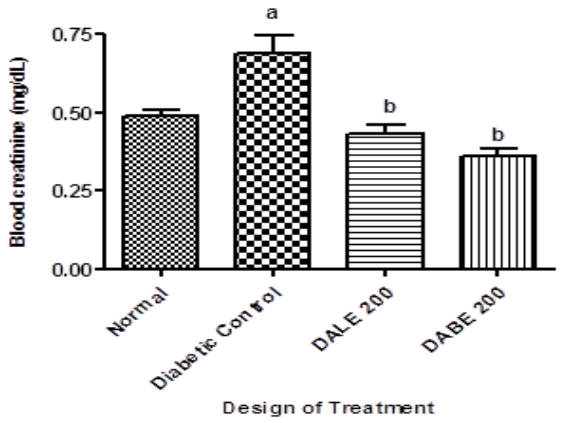
N=6; Mean ± SEM; aP<0.001vs Normal; bP<0.01 vs diabetic control

Figure 8: Effect of DALE and DABE on blood urea levels



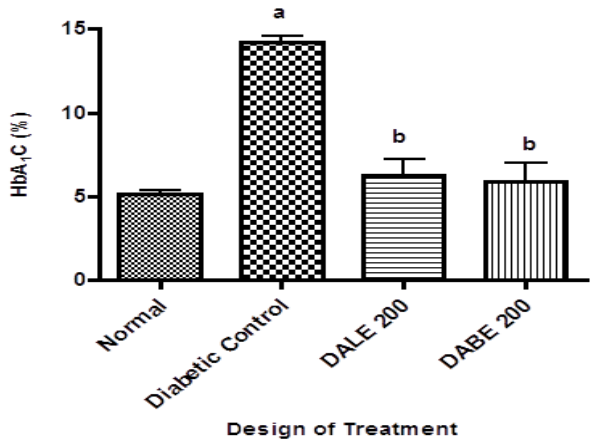
N=6; Mean ± SEM; aP<0.05 vs Normal; bP<0.05 vs diabetic control

Figure 9: Effect of DALE and DABE on blood uric acid levels



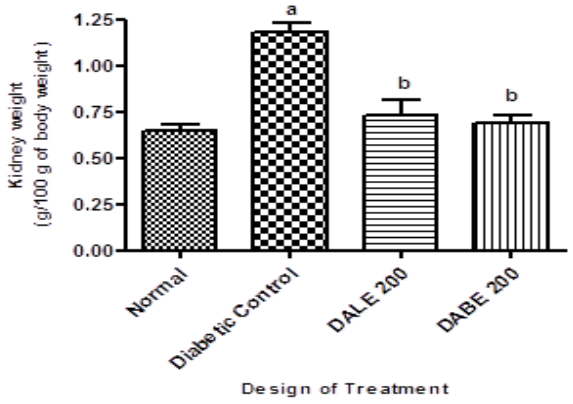
N=6; Mean ± SEM; aP<0.01vs Normal; bP<0.001 vs diabetic control

Figure 10: Effect of DALE and DABE on blood creatinine levels



N=6; Mean ± SEM; aP<0.001 vs Normal; bP<0.001 vs diabetic control

Figure 11: Effect of DALE and DABE on Glycosylated haemoglobin levels



N=6; Mean ± SEM; aP<0.001 vs Normal; bP<0.001 vs Diabetic control

Figure 12: Effect of DALE and DABE on kidney weight (g/100g body weight)

DISCUSSION

Diabetes mellitus is the world's largest endocrine chronic disorder characterized by either insufficient insulin production by pancreatic β-cells or by cellular resistance to insulin and ultimately resulting in increased blood glucose level. Traditional medicine to natural products are used from the long back for the management of diabetes mellitus and that may be better treatments to reduced side effects[32-35]. So the current study evaluates the in the in*vivo* antidiabetic activity of *Dolichandrone atrovirens* bark and leaf extract by using the streptozotocin-induced animal model. It is well documented that STZ destroys the beta cells of the pancreas and causes type 1 diabetes mellitus[36].The current study induced the type 2 diabetes mellitus by using the combination of streptozotocin and nicotinamide in male Wistar rats. The nicotinamide has antioxidant property to protect the cytotoxic action of STZ and cause the minor damage to the pancreatic beta cell to produce type 2 diabetes mellitus[37, 38]. *Dolichandrone atrovirens* already reported to be *in vitro* antidiabetic[39], antioxidant[40,] and anticancer[41]. In our study, the changes in body weight of normal control group and normal rats treated with plant extracts was increased significantly when compared with initial body weight. But the STZ-induced diabetic rats showed a significant decrease in body weight which may be due to deficiency of carbohydrate for the energy metabolism and produced the increased muscle wasting and loss of tissue proteins[42-44].At the same time, the diabetic control group kidney weight was significantly increased when compared to the control group this is due to the development of renal hypertrophy in rats with streptozotocin-induced diabetes [45]. The plant extract treated diabetic group kidney weight were significantly decreased this prove the extract has the protective effect of the kidney. Treatment with aqueous methanolic DALE and DABE showed prevent body weight as compared to diabetic control group indicates its anti-diabetic potential[46, 47].The total urine volume of plant extract treated animal group is significantly lower than the diabetic control. The excess blood glucose in the rates difficult to reabsorb in the kidney and the excess glucose excreted along with fluids drawn from tissues leads to increase the volume of urine[48, 49].Diabetic controlled group creatinine, urea, uric acid and microalbumin significantly increased when compared to normal control group. As seen in the present study the level of non-protein nitrogenous compounds such as creatinine, urea and uric acid which was increased in diabetic rats indicates the dysfunction of kidney[50, 51]. The high concentration of glucose in hyperglycemic state causes severe derangement in protein metabolism those results in the development of negative nitrogen balance to produce elevates urea, uric acid and creatinine level[52,53]. In diabetic rate treated with DALE and DABE showed the significant decrease in the creatinine, urea, uric acid and microalbumin and this clearly shows the renoprotective effect of the extracts. The result of the present study indicates that the 80% aqueous methanol leaf extract of DALE and DABE significantly reduce the blood glucose levels of the STZ and nicotinamide induced diabetic rats with different levels of reduction when compared to the diabetic control rats. The exact mechanism by which the

plant extract lowered the blood glucose level is not yet clear, but the extract significantly protects the loss or degradation of structural proteins, antioxidant activity[39] and significant inhibition with α-glucosidase, α-amylase and glucose-6-phosphatase [40] may be the reason for the antidiabetic activity of the DALE and DABE. The previous studies have shown that *Dolichandrone atrovirens* extracts containing glycoside, phenol, flavonoids, and tannins[54]. It is, therefore, possible that the phytochemicals present in the plant may be responsible for the observedantidiabeticactivity[28]. In conclusion, 80% aqueous methanolic bark and leaf extract of *Dolichandrone atrovirens*has demonstrated significant antidiabetic potentials in this study and may be acting through the restoration of the pancreatic tissues, a decrease in intestinal absorption of glucose, stimulation of the beta cells, and or through its phytochemical content.

CONCLUSION

According to our findings, the *Dolichandrone atrovirens* bark and leaf extracts have proved to possess antidiabetic activity in the combination of streptozotocin and nicotinamide induced diabetic rats. Further research on the molecular mechanism and the isolation of the compound responsible for this effect may lead to new antidiabetogenic agents.

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