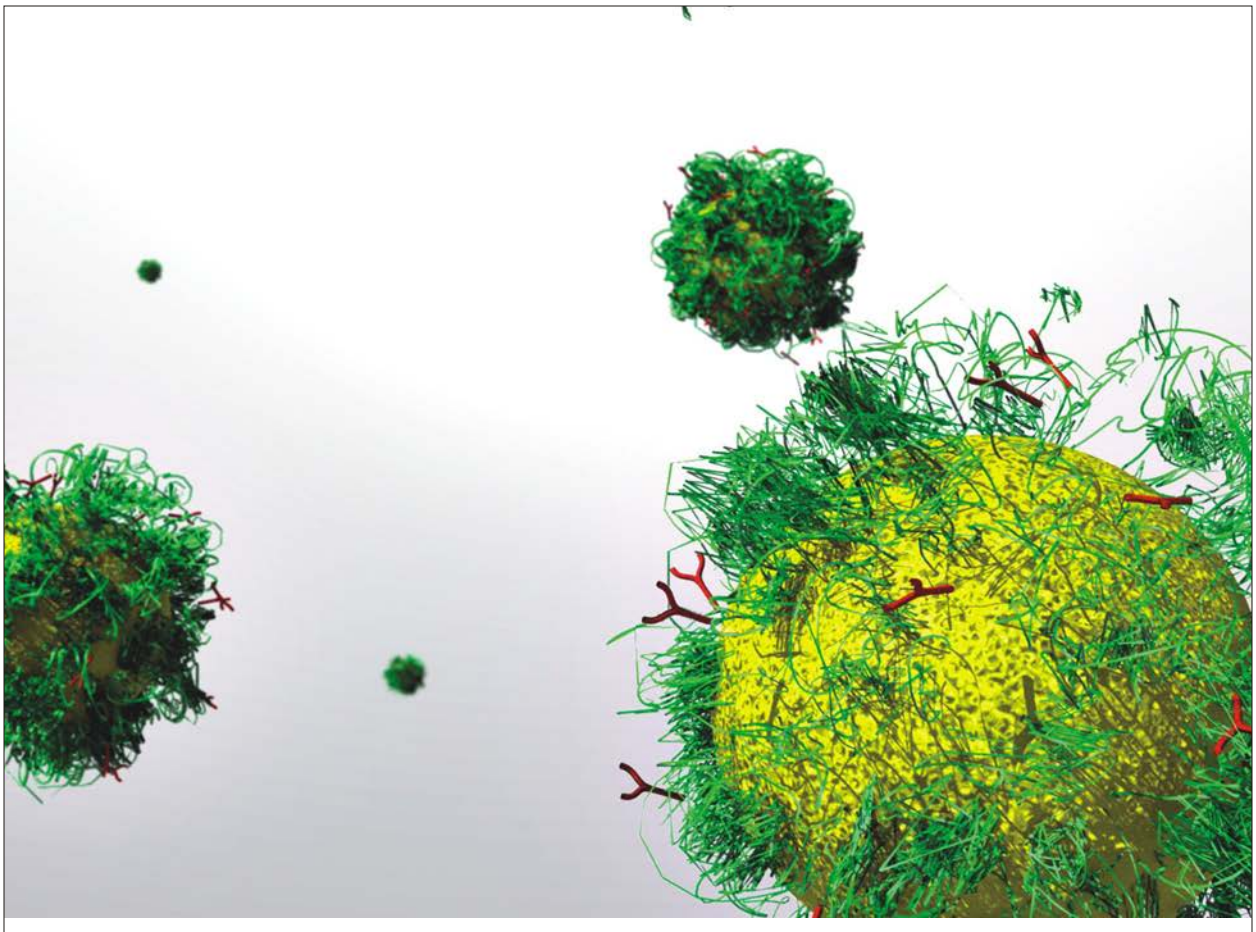

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Hypoglycemic, Hypolipidemic and Anti-free Radical Effects of Ethyl Acetate Extract of *Bridelia micrantha* (Hochst) Baill. (Euphorbiaceae) Leaves in Streptozotocin-induced Diabetic Wistar Rats

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ASBTRACT

The crude ethyl acetate extract of *Bridelia micrantha* leaves was tolerated orally in Wistar rats up to 2000 mg kg^{-1} without overt clinical manifestations. The extract demonstrated a high hypoglycemic potency in streptozotocin-induced diabetic rats. The effect of 300 and 600 mg kg^{-1} of the extract was most significant ($p<0.01$) and comparable to that of glibenclamide, the reference anti-diabetic agent at day 21 of treatment but in contrast to the untreated, control. In the *in vivo* antioxidant studies, the test doses (150, 300 and 600 mg kg^{-1}) of the extract also exhibited equipotency with glibenclamide in preserving endogenous serum catalase and reduced glutathione. The extract remarkably suppressed lipid peroxidation and lowered total serum triglyceride as well as total serum cholesterol at 300 and 600 mg kg^{-1} relative to the control. *Bridelia micrantha* leaves could be a source of potent anti-diabetic, hypolipidemic and antioxidant compounds.

Key words: *Bridelia micrantha*, ethyl acetate, antidiabetic rats, *in vivo*, antioxidant, streptozotocin

INTRODUCTION

The trend in diabetes mellitus has almost assumed a global pandemic proportion without regard for sex, age, race or geographic location (Rewers *et al*., 1988). Diabetes mellitus is considered as a terminal disease not only due to challenges in its treatment but also the involvement of complications traversing diverse body organs. The disease is a major cause of serious health deterioration, incessant fatigue, debilities and diseases of the cerebrovascular system, renal failure, blindness, neurological complications and premature death (Jayatilake *et al*., 1993; Harris *et al*., 1987). Basically, diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia (fasting plasma glucose >7.0 mmol L^{-1}, or plasma glucose >11.1 mmol L^{-1} 2 h after a meal) caused by insulin deficiency and often combined with insulin resistance (Rang *et al*., 2003). Two forms of diabetes mellitus: Type 1 and 2 have been identified. Type 1 diabetes mellitus is primarily due to

the autoimmune-mediated and idiopathic destruction of pancreatic β-cells of the islets of Langerhans, resulting in absolute insulin deficiency (Alberti and Zimmet, 1998). People with type I diabetes mellitus must rely on exogenous insulin to prevent the development of ketoacidosis for survival. Type 2 diabetes mellitus on the other hand, is characterized by relative insulin deficiency due to defects in insulin secretion and a failure of normal insulin levels to stimulate glucose uptake by tissue cells (Lillioja *et al.*, 1993). People with Type 2 diabetes mellitus are not dependent on exogenous insulin. Genetic defects of beta-cell function, genetic defects in insulin action, diseases of the exocrine pancreas, endocrinopathies, drug or chemical-induced assault and autoimmune-mediated syndromes are some of the specific predisposition to diabetes mellitus (Alberti and Zimmet, 1998). In concise terms, excessive production with reduced utilization of glucose by tissues is the basic cause of diabetes (Chattopadhyay, 1993). However, the incidence of Type I diabetes mellitus is low relative to Type 2 which accounts for more than 90% of the diabetic cases globally (Alberti and Zimmet, 1998). Treatment regimes include administration of insulin, oral anti-hyperglycemic agents and inhibitors of α-glycosidase enzyme but sometimes, alternative therapies including plant products are employed (Sabo *et al.*, 1999) in the absence of a novel antidiabetic drug.

Bridelia micrantha (Euphorbiaceae) synonymously called Candelabria micrantha Hochst is highly acclaimed for high efficacy in the treatment of diabetes by traditional medicine healers in Nsukka community of Enugu State, Nigeria. The plant is known with various common names: Bridelia, coast gold leaf in English, umshonge in Zulu, mitserie in Afrikaans, mushiwe in Tongan, ogaofia in Ibo and asha, ida odan in Yoruba language (www.worldagroforestry.org). Decoction of the bark, leaves and roots of the plant is locally used to treat bruises, boils, ulcers, burns, dislocations, eye sore and as cough remedy (Ainslie, 1937; Smith, 1966). Extracts from the leaves and stem bark of B. micrantha reportedly possess significant antibacterial activity against beta-lactam-resistant Gram-negative bacilli as well as beta-lactam-resistant Gram-positive cocci (Abo and Ashidi, 1999; Gangoue-Pieboji *et al.*, 2009).

In an effort to explore for a more effective hypoglycemic agent, the present study seeks to evaluate the effects of the crude ethyl acetate extract of *B. micrantha* leaves in streptozotocin-induced diabetic Wistar rats as a preliminary step towards isolation of the bioactive principle.

MATERIALS AND METHODS

Chemicals, reagents, drugs and equipment: Freshly prepared solutions, analytical grade chemicals and reagents were used in the experiments. Ethyl acetate purchased from Sigma Aldrich, Germany; Streptozotocin, glibenclamide (Sigma-Aldrich, USA), Accu-chek Advantage II auto-analyser (Roche, Germany), spectrophotometer (Spectrumlab, USA), rotary evaporator (Rotavapor R 210, Büchi, Switzerland), Soxhlet extractor (Büchi, Switzerland), serum triglycerides kit (Cayman's Chemical Company, USA), Total cholesterol kit obtained from Crest Biosystems, India; Tween 20, electronic weighing balance (Furi, India), test tubes, beakers, measuring cylinders and intragastric lavage were used for the study.

Plant collection and identification: Fresh leaves of *B. micrantha* were collected from Obukpa village, Nsukka Local Government Area of Enugu State, Nigeria in April, 2013. The plant leaves were authenticated by Mr A.O. Ozioko, a taxonomist with Bioresources Development and Conservation Programme (BDCP), Aku road, Nsukka, Enugu State, Nigeria.

Preparation and extraction of plant material: The fresh leaves of *B. micrantha* were dried under mild sunlight and then reduced to coarse particles with mortar and pestle before been pulverized into fine particles using a laboratory hammer mill. The plant material was exhaustively extracted with ethyl acetate using a Soxhlet extractor at 40°C for 48 h. The extract was filtered and concentrated *in vacuo* using a vacuum rotary evaporator. The concentration and percentage yield were determined and the extract was stored in a refrigerator at 4°C until when used.

Experimental animals: Matured inbred Wistar rats of both sexes weighing between 80-190 g were purchased from the Laboratory Animal unit of the Department of Biochemistry, University of Calabar, Nigeria. The rats were kept in the same room with a temperature varying between 28 and 30°C; lighting period was between 15 and 17 h daily. The rats were kept in stainless steel wire mesh cages which separated them from their faeces to prevent coprophagy. They were supplied clean drinking water and fed standard commercial feed (Grower mash pellets, Vital feed®, Nigeria). The animals were allowed two weeks to acclimatize prior to commencement of the experiments. The laboratory animals were used in accordance with laboratory practice regulation and the principle of laboratory animal care as documented by Zimmermann (1983).

Acute toxicity studies: Acute toxicity studies were conducted using the method described by Lorke (1983). Twenty-five (25) matured Wistar rats of both sexes were marked with 10% picric acid, weighed and randomly separated into 5 groups (A-E) of 5 rats each. Groups A-D were given varying oral doses (200, 400, 800 and 2000 mg kg^{-1}) of the leaf extract of *B. micrantha*, respectively while group E (5th group) received an equivalent volume (10 mL kg^{-1}) of distilled water. All treatments were given orally by gastric intubation. The rats were observed for signs suggestive of toxicity within 72 h. The animals that survived were further monitored for two weeks for toxic effects. The test was terminated after two weeks and all the animals were humanely sacrificed and postmortem examinations carried out on them.

Evaluation of anti-diabetic activity of the ethyl acetate extract of *B. micrantha* leaves: All rats were fasted for 12 h before the administration of Streptozotocin (STZ). Freshly prepared STZ dissolved in 0.1 M citrate buffer and pH 4.5 was given by a single intraperitoneal injection at a dose of 50 mg kg^{-1}. Control rats were injected with citrate buffer only. After 3 days post challenge with STZ, blood glucose levels were measured. Animals with blood glucose level above 9 mmol L^{-1} were considered diabetic and were selected randomly into five groups comprising of five animals each. Group 1, II and III were treated daily with the extract of *B. micrantha* solublised in 10% Tween 20 at doses of 150, 300 and 600 mg kg^{-1}, respectively. Group IV was treated daily with a reference drug, glibenclamide (2 mg kg^{-1}) while group V was treated with 10% Tween 20 only. At Day 0, 7, 14 and 21 of treatment, blood samples were collected from the rat tail vein under mild anesthesia. The fasting blood sugar level was measured using the Accu-chek Advantage II glucometer. The percentage reductions in fasting blood glucose level in experimental animals were calculated using the formula given below:

$$\text{Decrease in blood glucose level (\%)} = \frac{\text{Before treatment-After treatment}}{\text{Before treatment}} \times 100$$

Blood was collected from the rats on day 14 of the treatment for the antioxidant and biochemical assays.

Serum lipid biochemical assays of the crude ethyl acetate extract of *B. micrantha* leaves

Serum triglycerides (TG) assay: Determination of serum triglycerides was carried out with Cayman's Triglyceride assay kit (Cayman's chemical Company, USA). The samples and reagents were freshly prepared as specified and serial dilutions of triglyceride standard diluent were made accordingly. Serum sample from each animal in the groups was prepared on day 21 of treatment. Triglyceride standard diluent was used as the blank. Ten microliter of triglyceride standard was added with pipette into designated wells on a plate and this was followed by the addition of equal volume (10 µL) of serum sample from individual rats into separate wells. The set up was done in duplicates. The reaction was initiated by adding 150 µL of diluted enzyme buffer solution to each well. The micro titre plate was carefully shaken for 5 sec to achieve proper mixing before it was covered with the plate cover. The plate was incubated at room temperature for 15 min before absorbance was read at 540 nm using a plate reader. The concentration of triglycerides in the samples was determined from the linear regression of the standard curve by substituting corrected absorbance value for each sample into the equation:

$$\text{Triglyceride (mg dL}^{-1}) = \frac{\text{Corrected absorbance-(y-intercept)}}{\text{Slope}}$$

Determination of total serum cholesterol: Total serum cholesterol was assayed with total cholesterol kit obtained from Crest Biosystems, India. Cholesterol esterase hydrolyses esterified cholesterols to free cholesterol. The free cholesterol is oxidized to form hydrogen peroxide which further reacts with phenol and 4-aminoantipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of cholesterol present in the sample. The absorbance of the Standard (Abs.S) and Test samples (Abs.T) against the Reagent blank was read at 505 nm. Distilled water was used as zero setting in the spectrophotometer. The concentration of cholesterol in the samples was determined from the equation:

$$\text{Cholesterol (in mg dL}^{-1}) = \frac{\text{Abs.T} \times 200}{\text{Abs.S}}$$

***In vivo* antioxidant activities of the crude extract of *B. micrantha* leaves**

Assay of serum catalase (CAT) activity: Catalase activity was measured according to the method of Aebi (1984). A given volume (0.1 mL) of the serum was pipetted into cuvette containing 1.9 mL of 50 mM phosphate buffer of pH 7.0. Reaction was started by the addition of 1.0 mL of freshly prepared 30% (v/v) hydrogen peroxide (H_2O_2). The rate of decomposition of H_2O_2 was measured spectrophotometrically from changes in absorbance at 240 nm. The enzyme activity was expressed as units mL^{-1} protein.

Assay of reduced glutathione (GSH) concentration: Reduced glutathione concentration was determined by the method of Ellman (1959). A volume (1.0 mL) of serum was treated with 0.5 mL of Ellman's reagent (19.8 mg of 5, 5-dithiobis-2-nitrobenzoic acid (DTNB) in 100 mL of 0.1% sodium nitrate) and 3.0 mL of phosphate buffer (0.2 M, pH 8.0). Then 0.4 mL of distilled water was added. The mixture was thoroughly mixed; absorbance was read at 412 nm and expressed as units mL^{-1}.

Estimation of lipid peroxidation (malondialdehyde): Lipid peroxidation in the plasma was estimated colorimetrically as thiobarbituric acid reactive substances (TBARS) using the method of Buege and Aust (1978). A principle component of TBARS is malondialdehyde (MDA), a product of lipid peroxidation. In brief, 0.1 mL of tissue homogenate (Tris-HCl buffer, pH 7.5) was treated with 2 mL (1:1:1 ratio) of TBA-TCA-HCl reagent (thiobarbituric acid 0.37%, 0.25 N HCl and 15% TCA). The mixture was placed in water bath for 15 min; it was then allowed to cool. The absorbance of clear supernatant was measured against reference blank at 535 nm. Concentration was expressed as nmol mL^{-1}. This method is based on the principle that acetic acid detaches the lipid and protein of a tissue, thiobarbituric acid reacting with lipid peroxide, hydrogen peroxide and oxygen-labile double bond to form the colour adducts with maximal absorbance at 530 nm.

Statistical analysis: All data were expressed as Mean±SEM. Data were analyzed using one-way analysis of variance (ANOVA) and Duncan Multiple range *post hoc* test. Differences at $p<0.05$ were considered significant.

RESULTS

Description of the extract: The ethyl acetate leaf extract of *B. micrantha* was dark brown in colour. The total solid recovered from the extraction was 135.3 g.

Acute toxicity study of the leaf extract of *B. micrantha* in rats: No death was recorded in the rats treated orally within 72 h even at the highest test dose of 2000 mg kg^{-1} body mass of the extract. However, treatment with 2000 mg kg^{-1} of the extract induced transient dullness which disappeared 8 min after administration of the extract. At post mortem, there was no observable gross lesion in the liver, gastro-intestinal tract, spleen, heart and kidneys of the experimental rats.

Anti-diabetic activity of *B. micrantha* leaf extract: There was a remarkable reduction in the fasting blood glucose level of diabetic rats due to treatment with various doses of the crude ethyl acetate extract of *B. micrantha* leaves. The extract at a dose of 150 mg kg^{-1} was able to induce a significant ($p<0.05$) decrease in the glucose level of diabetic rats at day 21 of the treatment but higher doses (300 and 600 mg kg^{-1}) of the extract produced a similar effect earlier, right from day 7 of the treatment. Furthermore, at day 21 of the treatment, 300 and 600 mg kg^{-1} of the extract and glibenclamide (the reference drug) induced a corresponding and highly significant ($p<0.01$) reduction in the fasting sugar level of diabetic rats. At day 21, 300 mg kg^{-1} of the extract produced a fasting blood glucose value of 5.74±0.17 mmol L^{-1} relative to 4.56±0.64 mmol L^{-1} with 600 mg kg^{-1} of the extract, 3.18±0.27 mmol L^{-1} with glibenclamide and 24.12±1.39 mmol L^{-1} for the untreated, control rats (Table 1). The hypoglycemic effects of 300 and 600 mg kg^{-1} of the extract at day 21 were comparable to that of glibenclamide (the reference anti-diabetic agent).

***In vivo* antioxidant activities and serum lipid biochemical assays with *B. micrantha* leaf extract:** The serum concentration of catalase and GSH were significantly ($p<0.05$) higher in rats treated with glibenclamide and the various doses (150, 300 and 600 mg kg^{-1}) of the extract in contrast to the values in untreated, negative control rats. There was however, no significant ($p>0.05$) difference in CAT and GSH levels of rats treated with glibenclamide and the varying doses of extract. *Bridelia micrantha* leaf extract induced significant ($p<0.05$) reduction in MDA values of 4.45±0.72 and 2.73±1.33 mmol mL^{-1} at 300 and 600 mg kg^{-1}, respectively when compared with

Table1: Effects of ethyl acetate extract of *Bridelia micrantha* leaves on fasting blood glucose of streptozotocin-induced diabetic rats

	Mean fasting blood glucose level (mmol L^{-1})					
Day	Normal (non-diabetic control)	10% Tween 20 (Negative control)	150 mg kg^{-1} extract	300 mg kg^{-1} extract	600 mg kg^{-1} extract	Glibenclamide 2 mg kg^{-1}
Before induction	5.04±0.21	5.82±0.34	5.46±0.27	5.63±0.42	4.70± 0.71	5.35±0.60
After induction	5.45±2.90	24.82±2.97	27.88±2.26	17.40±2.55	20.50±1.80	21.36±1.85
7	5.30±0.14	22.62±1.63	15.92±3.65	8.68±0.88*	8.96±1.03*	4.78±0.55**
14	5.10±0.09	23.48±1.58	12.26±3.40	6.56±0.59*	7.98±1.26*	3.60±0.35**
21	5.16±0.24	24.12±1.39	7.00±1.77*	5.74±0.17**	4.56±0.64**	3.18±0.27**

*,**Significant decreases at $p<0.05$ and $p<0.01$, respectively, compared to negative control. Values are Mean±SEM. n = 5 in each group

Table 2: *In vivo* effects of the ethyl acetate extract of *Bridelia micrantha* leaves on oxidative stress and serum lipid biochemical parameters in streptozotocin-induced diabetic rats

Treatment (mg kg^{-1})	Serum CAT (U mL^{-1})	Serum GSH (U mL^{-1})	Serum MDA (mmol mL^{-1})	Serum TG (mg dL^{-1})	Total serum cholesterol (mg dL^{-1})
150 extract	0.61±0.21*	8.19±0.41*	6.02±1.03	70.47±2.60^{+}	112.31±1.48
300 extract	0.63±0.04*	9.49±0.45*	4.45±0.72^{+}	58.33±2.15^{+}	95.81±2.43^{+}
600 extract	0.69±0.03*	13.14±0.41*	2.73±1.33^{+}	51.45±3.01^{++}	77.20±2.51^{+}
Glibenclamide	0.77±0.06*	14.61±0.59*	3.00±1.14^{+}	50.32±2.76^{++}	78.35±3.55^{+}
Negative control	0.40±0.04	4.04±0.38	6.92±0.82	109.42±2.71	122.83±3.03

*Significant decreases at $p<0.05$ compared to negative control. $^{+,++}$ Significant decreases compared to negative control at $p<0.05$ and $p<0.01$, respectively, values are Mean±SEM n = 5 in each group

the value of 6.92±0. 82 mmol mL^{-1} for the negative, control rats. All the test doses (150, 300 and 600 mg kg^{-1}) of the extract and glibenclamide significantly ($p<0.05$) reduced total serum triglyceride in the experimental animals relative to the value in negative control but the extract was only significantly ($p<0.05$) effective at 300 and 600 mg kg^{-1} in decreasing the concentration of total serum cholesterol (Table 2). The suppressive effects of the extract on MDA, serum triglycerides and total serum cholesterol in the studied animals were found to be dose dependent.

DISCUSSION

The crude extract did not cause mortality in the experimental rats even at the highest oral dose of 2000 mg kg^{-1}, an indication that the extract was less toxic at the test dose by this route. This was further supported by the absence of gross lesions in post mortem examinations. Diverse plants have proven anti-diabetic effects in the ability to prevent degenerative and metabolic effects in STZ-induced diabetic animal models (Soleimani *et al.*, 2007). The crude ethyl acetate extract of *B. micrantha* leaves was effective in reducing fasting blood glucose level of diabetic rats with profound potency at 300 and 600 mg kg^{-1} within the duration of the study. The hypoglycemic effects of the extract at both high doses were comparable to that of glibenclamide, a reference anti-diabetic agent at day 21. From Table 1, the mean blood glucose value of rats treated with 300 mg kg^{-1} of the extract = 5.74±0.17 mmol L^{-1}; 600 mg kg^{-1} of the extract = 4.56±0.64 mmol L^{-1}; 2 mg kg^{-1} of glibenclamide = 3.18±0.27 mmol L^{-1} and in negative control rats, the value = 24.12±1.39 mmol L^{-1}). The blood sugar levels corresponding to the high doses (300 and 600 mg kg^{-1}) of the crude extract-treated rats were observed to have exhibited equipotency with 2 mg kg^{-1} of glibenclamide. The hypoglycemic effects of the extract at high dose is significant and at the same time, logical because glibenclamide is a pure compound but the extract is crude and a mixture of different contaminants. Hence, a high dose is required to achieve therapeutic concentration.

Streptozotocin(1-methyl-1-nitroso-3-[(2S,3R,4R,5S,6R)-2,4,5-trihydroxy-6-(hydroxymethyl) oxan-3-yl]urea), STZ is an antibiotic produced by *Streptomyces achromogenes* and it induces both type 1 and type 2 diabetes mellitus in adult rats (Matteucci and Giampietro, 2008). The blockade in the removal of O-GlcNAc from intracellular proteins by O-GlcNAcase accounts for the diabetogenic toxicity of STZ (Roos *et al*., 1998; Liu *et al*., 2000). Glibenclamide, a sulfonylurea on the other hand, is a popular anti-diabetic drug used widely to treat Type 2 diabetes and works by inhibiting adenosine triphosphate (ATP)-sensitive potassium channels in pancreatic beta cells. This inhibition causes cell membrane depolarization and opening of voltage-dependent calcium channels, thus triggering an increase in intracellular calcium into the beta cell which stimulates insulin release. The specific mechanism in which the crude extract of *B. micrantha* leaves induced hypoglycemic effect in diabetic rats was not fully understood but it was possible that the extract mediated its action either through the prevention of STZ-induced O-GlcNAcase inhibition or indirect stimulation of insulin release or early regeneration of **β**-cells of the islets. Conventional anti-diabetic agents can affect several pathways of glucose metabolism such as insulin secretion, glucose uptake by target organs as well as nutrient absorption (Frode and Medeiros, 2008). STZ-induced **β**-cell toxicity is completely blocked by GlcNAc which also prevents STZ-induced O-GlcNAcase inhibition (Konrad *et al*., 2001). The O-linked glycosylation is reversed by OGlcNAc **β**-acetylglucosaminidase (O-GlcNAcase) (Kaneto *et al*., 2001). Other plant parts specifically evaluated with proven antidiabetic potentials were documented. The roots of *Panax ginseng* Mey (Araliaceae), bark of *Pterocarpus marsupium* (Leguminosae), tubers of *Dioscorea japonica* Thunb. (Dioscoreaceae), aerial parts of *Ephedra distachya* L. (Ephedraceae), root barks of *Morus alba* L., roots of *Oryza sativa* L. (Gramineae), bulbs of *Allium cepa* L. (Liliaceae), fruits of *Capsicum annuum* L. (Solanaceae), seeds of *Galega officinalis* L. (Leguminosae) (Ivorra *et al*., 1989) are some of the few worth mentioned.

The crude ethyl acetate extract of *B. micrantha* leaves demonstrated appreciable potency as revealed by the *in vivo* antioxidant studies (CAT, GSH and lipid peroxidation). All doses (150, 300 and 600 mg kg^{-1}) of the extract exhibited significant ($p<0.05$) potency comparable to glibenclamide in preserving endogenous serum catalase and reduced glutathione. Diabetic rats that were treated with the extract and glibenclamide had higher concentration of CAT and GSH compared to untreated ones that received distilled water alone (Table 2). GSH also functions as free radical scavenger and in the repair of radical-induced biological damage (Meister, 1984). It was remarkable that high doses (300 and 600 mg kg^{-1}) of the extract were also found to have equipotency with glibenclamide in the significant ($p<0.05$) reduction of MDA values (lipid peroxidation) compared to the control. Recent evidence indicates that some saturated and unsaturated aldehydes, including malondialdehyde (MDA), hydroxyaldehydes and other short chain carbonyl compounds contribute to peroxidative cell damage by reacting with sensitive biomolecules (Kim *et al*., 1999). Increased oxidative stress generates reactive oxygen species (ROS) which are implicated in a variety of pathologies including heart attacks, strokes, renal failure, diabetes, neurodegenerative diseases, etc. (Kalaivanam *et al*., 2006). STZ-diabetic animals exhibit most of the diabetic complications including myocardial, nervous, gastrointestinal, kidney and urinary bladder dysfunction through oxidative stress (Palsamy and Malathi, 2007).

All the test doses (150, 300 and 600 mg kg^{-1}) of the extract were significantly ($p<0.05$) potent in reducing total serum triglyceride but only the higher doses (300 and 600 mg kg^{-1}) became effective at decreasing the concentration of total serum cholesterol in the experimental animals. The high concentration of serum lipids in the diabetic untreated rats may be due to increase in the

mobilization of free fatty acids from peripheral fat depots, since insulin inhibits the hormone sensitive lipase (Jasmine and Daisy, 2007). Deficiency of insulin results in failure to activate the enzymes thereby causing hypertriglyceridemia (Mahesh and Brahatheeswaran, 2007).

Conclusively, the study has established the presence of pharmacologically active anti-diabetic, hypolipidemic and antioxidant compounds in the crude extract of *B. micrantha* leaves. The findings support the view that diverse medicaments including anti-diabetics abound in the plant kingdom and the empirical knowledge of such medicinal substances are sometimes passed on through folkloric use. The study of indigenous remedies provides chemists with the platform to use plant-derived drugs as prototypes in the development of more effective and less toxic chemotherapeutics.

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