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The effect of *Maerua pseudopetalosa* ethanolic extract on glucose tolerance and glucose uptake in rat hemidiaphragm

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Abstract
Maerua pseudopetalosa (Gilg and Bened.) De Wolf (Family: Capparaceae) is a medicinal plant of great repute in South Central Sudan. The roots are used for cough and for treatment of tumors. The roots of *M. pseudopetalosa* showed activity against some bacterial strains. The present study was carried to evaluate the effect of 100, 200 and 400 mg/kg of ethanolic extract (80%) of *Maerua pseudopetalosa* roots in glucose-loaded wistar albino rats and dose of 0.1% of the extract in glucose uptake by using isolated rats hemidiaphgrams. The effect of the three doses 100, 200 and 400mg/kg was studied 1, 2 and 4 hours after loading the fasting rats with glucose. Their effects were compared to control rats administered with the vehicle and to a standard group administered with the standard drug glibenclamide 10mg/kg. The dose 100 mg/kg of the extract was found to be the most effective dose in models of experiments while the dose of 0.1% of aqueous extract showed significant effect on the glucose reuptake by the hemidiaphragm when administered together with insulin than the effect attained by either insulin or extract alone. The study concluded that *M. pseudopetalosa* ethanolic extract was found to have antihyperglycemic effect *in vivo* when evaluated in wistar albino rats and enhanced re-uptake of glucose when used together with insulin in isolated rat hemidiaphragm.

Keywords: *Maerua pseudopetalosa,* ethanolic extract, hypoglycemic, rats, hemidiaphragm.

1. Introduction

Diabetes mellitus (DM), a state of chronic hyperglycemia, is a common disease affecting over 124 million individuals worldwide (Laakso, 2001) [9]. DM is associated with high risk of atherosclerosis, renal, nervous system and ocular damage (Habif *et al.,* 1997) [5]. Uncontrolled hyperglycemia appears to be the principal biochemical abnormality that underlies the increased oxidative load in DM. Increased oxidative stress may contribute to the pathogenesis of the diabetic complication. In addition, increased oxidative injury has been implicated in the premature age related changes in DM (Hasanian, 2002) [6]. Multiple studies (Laight *et al*., 2000) [11] have shown that type 2 diabetes is accompanied by increased oxidative damage to all bio-molecules, especially lipids. Results of studies in animal models and in humans have demonstrated that diabetes is associated with oxidative stress, which is exhibited by elevated blood levels of lipid per-oxidation products (markers of oxidative stress), especially associated with poor blood glucose control (Garg *et al*., 1996) [3]. Prevalence of diabetes in adults (20-79 years) in Sudan is 16.2%, Cost per person with diabetes180.9 USD according to IDF (2014) [8]. While worldwide prevalence of diabetes for all age-groups was estimated to be 2.8% in 2000 and 4.4% in 2030 (Sara Wild *et al*., 2004) [15]. Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature mentioned the use of plants in treatment of various human ailments. India has about 45000 plant species and among them, several thousands have been claimed to possess medicinal properties. Indian plants which are most effective and the most commonly studied in relation to diabetes and their complications are: *Allium cepa, Allium sativum, Aloe vera, Cajanus cajan, Coccinia indica, Caesalpinia bonducella, Ficus bengalenesis, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpus marsupium, Swertia chirayita, Syzigium cumini, Tinospora cordifolia* and *Trigonella foenum graecum*. *Maerua pseudopetalosa* (Gilg and Bened.) De Wolf (Family: Capparaceae) is a medicinal plant of great repute in South Central Sudan. It is commonly known locally as "Kordale". The roots are used for cough and for treatment of tumors. The roots of *M. pseudopetalosa* showed activity against some bacterial strains (Henry, 1948) [7]. The present study is conducted to validate the anti-diabetic potential of M. *pseudopetalosa*, family Capparaceae as its use in Sudanese folkloric medicine. In Sudan, its vernacular name is kordallah. The foliage of this plant provides much-relished browsing for goats in Somalia. In parts of southern Sudan it is eaten but only as a famine-food after careful preparation to remove the toxic principle. Tetramethylammonium iodide, known as tetramine for short, is reported to be present in the tuberous root, shoot and leaf. This substance has proved fatal to humans within a

quarter hour. Di-, tri- and tetra-methylamine hydroxide have also been found. Fruits are eaten in Sudan 'to make one strong'. Roots when chewed are at first bitter, then sweetness follows, and the Sudanese use roots to make sweet drinks. Fruits and roots are used in topical application to the chest for treatment of coughs in Nigeria. The bark is used by Masai medicine men, and the plant's toxic properties appear to be well known in E Africa. The seed-husk and seed-kernel are also oil-bearing. The root is said to be an efficient precipitant of suspensions in water and is used in Sudan in water purification and storage in rural areas. The roots are chopped up and thrown into the water. This plant carries heavy charge of ions (Grover *et al*., 2002) [4]. The present study was carried to evaluate the effect of 100, 200 and 400 mg/kg of ethanolic extract of *M. pseudopetalosa* (roots) in glucose-loaded wistar albino rats and dose of 0.1% of the extract in glucose uptake by using isolated rats hemidiaphgrams.

2. Materials and Methods

Plant materials

The root of *M. pseudopetalosa* were collected from Blue Nile state (Damazin) between July 2014 and February 2015. The plant was identified and authenticated by the taxonomists Mr.: Yahiya Suleiman (Medicinal and Aromatic Plants and Traditional Medicine Research Institute, Khartoum, Sudan). The specimen was deposited in the Herbarium of the Institute.

Preparation of extract

Preparation of crude extracts

Extraction was carried out for the root of *M. pseudopetalosa* by using overnight maceration techniques according to the method described by Harbone (1984). About 50 g were macerated in 250 ml of ethanol for 3 h at room temperature with occasional shaking for 24 h at room temperature, the supernatant was decanted and clarity field by filtration through a filter paper, after filtration, the solvent was then removed under reduced pressure by rotary evaporator at 55 °C. Each residue was weighed and the yield percentage was calculated then stored at 4 °C in tightly sealed glass vial ready for use. The remaining extracts which is not soluble by successively extracted by Ethanol using the previous technique. Extracts kept in deep freezer for 48 h, then induced in freeze dryer (Virtis, USA) until completely dried. The residue was weighed and the yield percentage was calculated. The extracts were kept in 4°C until the time of their use. The yield percentages were calculated as follow:

Weight of extract / weight of sample

Table 1: Preliminary quantitative data on yield percentage (%) of *M. pseudopetalosa* (root).

Scientific name of plant	Family name	Part used	Weight of sample	Weight of extract (g)	Yield (%)
M. pseudopetalosa	Capparaceae	Root	450 g	135.95	30.211

Effect of *M. pseudopetalosa* ethanolic extract on glucose-loaded rats

Healthy male Wistar albino rats (180- 240g) were housed under standard environmental conditions at temperature (25 ± 2º C) and light and dark (12/12 h). Rats were fed with standard pellet diet. Rats were fasted for 18 hours and divided into five groups each of six rats. All rats received glucose at a dose of 2g/kg body weight intraperitoneally. Control group was administered with distilled water orally at a dose of 10ml/kg body weight.

The standard group has received glibenclamide orally at a dose of 10mg/kg body weight (Ladrière *et al*., 1997) [10] the third group received orally *M. pseudopetalosa* ethanolic extract at a dose of 100mg/kg, the fourth group received orally 200mg/kg body weight of the plant extract and the fifth group received a dose of 400mg/kg body weight of the plant extract.

Plasma glucose level was monitored at 0 hour, 1st hour, 2nd hour and 4th hour after treatment for the five groups under study (Abdolreza *et al*., 2012) [1].

Effect of *M. pseudopetalosa* ethanolic extract on glucose reuptake by using isolated rats hemi-diaphragm tissues

Eight albino rats were fasted overnight and killed by decapitation. The diaphragms were dissected out quickly with minimal trauma and divided into two halves. Two diaphragms from the same animal were not used for the same set of experiment. Four numbers of diaphragms were used for each group. The hemi-diaphragms were placed in test tubes and incubated for 30 min at 37 ºC in an atmosphere of 95% oxygen-5% CO_2 with shaking at 140 cycles/min. Glucose uptake per gram of tissue was calculated as the difference between the initial and final glucose content in the incubated medium.

Glucose uptake by rat hemi-diaphragm was estimated by the methods described by (Walaas, 1952; Chattopadhyay, 1992) [2, 17]. with some modification. Four sets containing four numbers of graduated test tubes (n=4) each, were taken as follows:

Group 1: 2 ml of Tyrode solution with 2% glucose. Group 2: 2 ml of Tyrode solution with 2% glucose and regular insulin (Nova Nordisk) 0.62 ml of 0.4 units per ml solution.

Group 3: 2 ml of Tyrode solution and 2% glucose and 1.38 ml of plant extract (0.1%).

Group 4: 2 ml of Tyrode solution with 2% glucose and regular insulin 0.62 ml of 0.4 units per ml solution and 1.38 ml of plant extract (0.1%).

The volumes of all the test tubes were made up to 4 ml with distilled water to match the volume of the test tubes of Group 4. The hemi diaphragms were taken out and weighed. Glucose uptake was calculated as the difference between the initial and final concentration of the glucose in the incubation medium.

Statistical analysis

All data were presented as means ± S.D. Statistical analysis for all the assays results were done using one-way ANOVA followed by Dennett's test. The level of significance was set at $P \leq 0.05$.

3. Results

The roots of *M. pseudopetalosa* (family: Bombacaceae) was carried to evaluate the effect of 100, 200 and 400 mg/kg of ethanolic extract (80%) of *M. pseudopetalosa* roots in glucose-loaded wistar albino rats and dose of 0.1% of the extract in glucose uptake by using isolated rats hemidiaphgrams, after the evaluation of the yield percentage of the plant which was found to be 30.211%. Table (1, 2 & 3).

Table 2: Effect of *M. pseudopetalosa* roots of ethanolic extract on glucose loaded rats

Groups	0 hour	1 hour	2 hour	4 hour
	µ±S.E.M	**µ±S.E.M**	**µ±S.E.M**	**µ±S.E.M**
Control group	67.6±1.89	107.40±2.62	98.20±8.11	87.60±8.370
glibenclamide 10 mg /kg	84.8±4.21	130.60±3.11	107.60±7.42	83.400±5.77
100 mg/kg	108.4±15.263	119.20±18.260	114.40±9.174	103.20±9.330
200 mg/kg	107.20±11.271	146.40±13.600`	144.00±8.854	139.20±8.523
400 mg/kg	97.60±8.790	121.60±18.683	122.00±15.700	98.40±14.400

Key: S.E.M= standard error of mean. **µ**= mean of values in each group.

Table 3: Effect of *M. pseudopetalosa* roots of ethanolic extract on glucose uptake by isolated rat diaphragm

Incubation medium	Glucose uptake (mg/g/30 min)
Tyrode solution with glucose (2g%)	34
Tyrode solution with 2% glucose and regular insulin 0.4unit/ml	45
Tyrode solution and 2% glucose and plant extract (100 mg/ml)	22
Tyrode solution with 2% glucose and regular insulin 0.4 units/ml and plant extract (100 mg/ml).	62

4. Discussion

In this study the effect of three different doses of *M. pseudopetalosa* (roots) of ethanolic extract was evaluated for blood glucose lowering activity. Dose of 100 mg/kg of the ethanolic extract showed the highest hypoglycemic effect in induced hyperglycemia in rats even at four hours after the glucose load compared to glibenclamide.

After oral administration of *M. pseudopetalosa* extract at a dose of 100 mg/kg the increase of blood sugar in the overnight fasted rats' blood at the end of the first hour was the least beyond the three doses (9.96%). This increase was found to be statistically significant when compared to the increase of blood glucose in the control group (58.88%) at the first hour ($p = 0.003$). Doses 200 mg/kg and 400 mg/kg the increase in blood glucose was (36.57% and 24.59%) which was also significant when compared to the increase (9.96%) caused by dose of 100 mg/kg. In the fourth hour, 100 mg/kg, 400 mg/kg and of the extract caused the glucose level to return to approximately the normal level at the zero hour before loading the rats with the glucose almost in the same level with glibenclamide. The effect of dose of 200 mg/kg did not return the glucose to the zero level could be explained by the presence of high levels of sugars and carbohydrates in the extract (Nicolas Cyrille Ayessou *et al*., 2011) [13]. which did not apply for dose 400 mg/kg, as could be expected. This could be explained by the increase in toxic compounds like tetraethyl ammonium chloride with the increment in the dose to 400 mg/kg, causing rat exhaustion and pathogenic hypoglycemia (Mariano Licciandi *et al*., 2006) [12]. Glucose uptake by rat hemi diaphragm cells when using the extract alone was found to be weak in comparison when using insulin alone while using the extract together with insulin caused a remarkable increase in the glucose uptake. This could be explained by the fact that the extract worked synergistically with insulin by increasing its receptors sensitivity and therefore could be a good candidate drug in treating diabetes type two. Work on this plant was comparable to work done on *Olea europaea* by Omer Musa *et al*., (2015) [14].

5. Conclusion

The study concluded that the ethanolic extract of *M. psedopetalosa* has anti-hyperglycemic effect in vivo and enhanced glucose re-uptake *in vitro* when used together with insulin which could imply its synergism with insulin. The extract could therefore be a potential source for anti-diabetic drug.

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7. References

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