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Antidiabetic and antidiarrhoeal potentials of ethanolic extracts of aerial parts of *Cynodon dactylon* Pers.

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ABSTRACT

Objective: To explore the antidiabetic and the antidiarrhoeal effects of ethanolic extracts of *Cynodon dactylon* Pers. aerial parts (EECA) in Wistar rats.
Methods: To assess the antidiabetic activity of EECA, oral glucose tolerance test (OGTT) model and alloxan induced diabetic test (AIDT) model were performed. The EECA was used at the doses of 2 g/kg, 1 g/kg and 500 mg/kg body weight in OGTT model and 1.5 g/kg was used for AIDT model. Castor oil-induced diarrhoeal model and gastrointestinal motility test with barium sulphate milk model were performed for evaluating the antidiarrhoeal effects at doses of 1 g/kg, 750 mg/kg respectively.
Results: The dose 2 g/kg in OGTT and 1.5 g/kg in AIDT model blood glucose levels decreased significantly ($P < 0.01$) in Wistar rats that showed antidiabetic effect of EECA. After administration of EECA at the dose of 1 g/kg, the extract showed significant ($P < 0.05$) antidiarrhoeal activity in castor oil-induced diarrhoeal model. The results were also significant ($P < 0.05$) in barium sulphate milk model for the same dose by using above mentioned animals.
Conclusions: It is concluded that EECA contains both antidiabetic and the antidiarrhoeal properties.

1. Introduction

Diabetes mellitus is a continual metabolic disorder which leads to the deficiency in the production of insulin by the pancreas and has resulted significant morbidity and mortality because of microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular complications (heart attack, stroke and peripheral vascular disease) of patients [1]. Now it is expected that all over the world at least 171 million people have diabetes, and this number is probable to more than double by 2030. In addition, per year nearly 3.2 million deaths are attributable to complications of diabetes; six deaths every minute [2]. On the other hand diarrhoeal diseases are one of the major causes of morbidity and mortality in developing countries and each year 1.5 million children who are under five years old are died because of the disease [3]. Now existing available drugs for the treatment of diabetes and diarrhoea are not free from side effects. So, it is very important to identify and assess usually available natural drugs as alternatives to currently used antidiabetic and antidiarrhoeal drugs. In this view, plants are cheaper and much effective, and are completely free from adverse effects. Traditionally a number of medicinal plants are used as antidiabetic and antidiarrhoeal agent, and some of them have shown their efficacy through pharmacological evaluation. In addition, depending on traditional medical practices, the World Health Organization encouraged to study for the treatment and prevention of diabetes and diarrhoeal diseases [3,4].

Cynodon dactylon Pers. (*C. dactylon*) (Bengali name “dubla”, “durbaghas”, English name bermuda grass) belonging to the family Poaceae is a slender, perennial creeping grass forming matted tufts with slender erect flowering branches. The plant is vulnerary, expectorant and styptic. It is a very common plant in Bangladesh and contains various medicinal properties [5]. This plant has been used as anti-inflammatory, anticystitis, antihypertensive [6]. The juice of the plant is astringent and frequently used

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to fresh cuts and wounds. It is also functional in the action of catarrhal ophthalmia, dropsy, insanity, hysteria, epilepsy, chronic diarrhoea, and dysentery. The rhizome of the plants is used as an anti-inflammatory, antiemetic, purifying agent, diuretic and also in the treatment of dysentery. The plant, *C. dactylon* is a folk medicine for anasarca, calculus, carbuncles, cancer, cough, hypertension, snakebites, gout, fever, stones, skin diseases, and rheumatic infections [7]. The present study aims to explore the antidiabetic and antidiarrhoeal activity of ethanolic extract of aerial parts of *C. dactylon* in normal Wistar rat, which is first report from Bangladesh.

2. Materials and methods

2.1. Plant materials and extraction

The aerial parts of *C. dactylon* were collected from Bangladesh Council of Scientific and Industrial Research (BCSIR) laboratories, Chittagong, Bangladesh campus in September 2013. The voucher specimen (S-0026/2013) of this plant was deposited at the Herbarium, Industrial Botany Research Division, BCSIR Laboratories, Chittagong, Bangladesh. The collected plants were washed, chopped, dried, powdered, extracted with 98.00% ethanol and concentrated with the help of rotary vacuum evaporator. In terms of dried starting material the yield of the extract was 0.99% (w/w) that was preserved in refrigerator at 4 °C for using the experiment purposes.

2.2. Experimental animals

To evaluate the antidiabetic and the antidiarrhoeal activity of ethanolic extracts of *C. dactylon* aerial parts (EECA), male Wistar rats weighting between (180 ± 10) g were brought from animal house of BCSIR Laboratories, Chittagong. Standard laboratory conditions were maintained for the experiments. Drinking water *ad libitum* and standard diet were supplied for the animals. The ethical guidelines of Pharmacological Research Division, BCSIR Laboratories, Chittagong, Bangladesh were followed in all aspect of animal care.

2.3. Chemicals

Commercially available analytical grade chemicals and drugs like alloxan tetrahydrate (Merck, India), barium sulfate (Merck, India Ltd.), castor oil (Shengyang Kaiyingsheng Chemical Co. Ltd., China), diethyl ether (Sigma–Aldrich, India), glibenclamide [Marion Roussel Ltd., (Aventis, Bangladesh)], glucose powder (Dextrose monohydrase, GlaxoSmithKline, Chittagong, Bangladesh Ltd.), Loperamide (Opsonin, Bangladesh) and Tween 80 [Polyoxyethylene (20), Loba Chemie Pvt. Ltd., India] were used for this experiment.

2.4. Experiments

2.4.1. Oral glucose tolerance test (OGTT) model

Overnight fasted normal albino Wistar rats were used for the OGTT as per maintained the reported method [8]. The rats were randomly divided into five groups marked as Group I to V. Each group contains five rats. Group I and Group II assigned as control and positive control group respectively. Groups III to V recognized as treated group for EECA treatment. Blood was collected from the tip of tail and blood glucose level (BGL) was measured of all groups of rats with the help of a blood glucose meter (Accu-chek active, Roche Diagnostics, Germany). After then only 2 mL/rat distilled water was supplied for control group and reference antidiabetic drug glibenclamide was given orally at a dose of 4.15 mg/kg body weight for positive control group. Groups III, IV and V of rats were treated orally with EECA at the doses of 2 g/kg, 1 g/kg and 500 mg/kg body weight respectively. After 30 min of water, drug and extract administration BGL was measured. Then 10 g/kg (body weight) glucose solution was provided orally for all these animals and BGL was observed of all rats after 30, 60, and 120 min of glucose administration.

2.4.2. Alloxan induced diabetic test (AIDT) model

With the help of intraperitoneal injection, alloxan tetrahydrate (100 mg/kg *i.p.*) was provided in overnight fasted male Wistar rats for inducing diabetes. After 24 h BGL was measured and separated them who were contained BGL more than 15 mmol/L and assigned as diabetic rats. These rats were used for the experiment. Diabetic induced rats were randomly divided into three experimental groups and each with five rats, marked as Group II to IV. Group II indicated as diabetic control supplied only distilled water. Reference antidiabetic drug glibenclamide (4.15 mg/kg) was provided for Group III marked as positive control. Group IV was treated with EECA at the dose of 1.5 g/kg. Previously selected Group I marked as control which had no diabetes. At first, BGL of all groups of rats was measured before administration of water, extract and drug which indicated the time 0 h, after then water, drug and extract were provided according to mentioned group and BGL were determined after 3, 6 and 9 h respectively by following above mentioned system. During blood collection from experimented rats, diethyl ether was used for anaesthesia. Favourable humidity and room temperature were maintained for increasing the survival capacity of experimental rats.

2.4.3. Castor oil-induced diarrhoea (COID) model

Antidiarrhoeal activity of EECA was estimated with COID model as per reported method [9]. Wistar rats were divided into four groups by random selection and each group contained five rats. Group I assigned as control. Group II marked as positive control and the rest of Groups III and IV recognized as treated groups. At first, extract and drugs were provided orally and after 1 h castor oil (2 mL/rat) was supplied for inducing diarrhoea. Only distilled water (2 mL/rat) was supplied for the control group and standard drug loperamide (2 mg/kg) was provided for the positive control group. Treated Groups III and IV received EECA at the dose of 1 g/kg and 750 mg/kg respectively. Separate cages were used for each rat and sheets of paper were placed below the cage for collection of fecal matters. The presence of stool with fluid material that stained the paper was placed beneath the cages indicated diarrhoea. At every hour the numbers of both hard and soft pellets were counted up to 6 h period for each rat and finally moisture content of all faeces was measured.

2.4.4. Gastrointestinal motility test with barium sulfate milk (BSM) model for diarrhoea

BSM model was done as per published method [10]. By random selection Wistar rats (over night fasted) were divided into four groups each with five rats. Only distilled water of 2 mL/rat was supplied orally for Group I recognized as control group. Commercially available reference antidiarrhoeal drug loperamide at the dose of 2 mg/kg was provided orally for Group II marked as positive control group. EECA orally treated at dose of 1 g/kg and 750 mg/kg for Groups III and IV respectively assigned as treated groups. After 30 min, 2 mL of 10% barium sulfate solution was administered in all groups of rats. Rats were sacrificed after 30 min of extract and drug administration. Finally, the distance travelled by BSM was measured and showed as a percentage of the total length of small intestine (from pylorus to the ileo-cecal junction).

2.5. Statistical analysis

The values of antidiarrhoeal and antidiabetic tests were expressed as mean ± SEM. Student's *t*-test was used to analyse statistical differences between the mean of the various groups. Microsoft Excel 2007 was used for statistical calculations. Mean values were considered significantly different if $P < 0.05$, $P < 0.01$ and $P < 0.001$.

3. Results

3.1. Effect of EECA on OGTT model

In the present study, the results of OGTT of EECA on Wistar rats are documented in the Table 1. In the positive control group BGL were 4.54, 3.60, 8.66, 6.42 and 2.88 mmol/L whereas the group received EECA at the dose of 2 g/kg, BGL were 4.98, 4.64, 12.02, 9.00 and 7.36 mmol/L at different times mentioned in Table 1. It was observed that glibenclamide at dose of 4.15 g/kg were effective to the decreased BGL in all interval with the increasing exposure time. On the other hand among three treated groups (Groups III, IV and V), Group III showed significant ($P < 0.05$ and $P < 0.01$) result to decrease the BGL at the dose of 2 g/kg.

Table 2
Effect of EECA on alloxan induced model.

Groups	0 h	3 h	6 h	9 h
Group I (control)	6.78 ± 0.29	6.54 ± 0.51	6.70 ± 0.38	6.14 ± 0.22
Group II (diabetic control)	19.46 ± 0.59$^{###}$	22.72 ± 0.99$^{###}$	24.90 ± 1.06$^{###}$	29.03 ± 1.81$^{###}$
Group III (positive control)	21.44 ± 1.52	16.14 ± 1.74	9.30 ± 1.81**	5.36 ± 0.59***
Group IV (EECA 1.5 g/kg)	22.64 ± 0.63	19.74 ± 0.82	15.80 ± 0.45**	14.84 ± 0.53**

Values are expressed mean ± SEM; $^{###}$: $P < 0.001$ means significant difference compared diabetic control with control; **: $P < 0.01$; ***: $P < 0.001$ refers to positive control and extract compared with diabetic control.

3.2. Effect of EECA on AIDT model

The effects of EECA on AIDT model of treated rats are shown in Table 2. It was observed that the BGL increased after administration of alloxan in diabetic control group in all counted intervals at 3, 6 and 9 h respectively. The BGL of the positive control group were 21.44, 16.14, 9.30 and 5.36 mmol/L at different times mentioned in Table 2. Whereas the values (BGL) for the plant extract at the dose of 1.5 g/kg were 22.64, 19.74, 15.80 and 14.84 mmol/L. Compared to control EECA showed effective result in reduction of BGL in the alloxane induced diabetic rats ($P < 0.01$).

3.3. Effect of EECA on COID model

Table 3 enumerated the results of antidiarrhoeal effect of loperamide and EECA in on Wistar albino rats. Compared to the control group the results shown that EECA at the dose of 1 g/kg was effective to inhibit the frequency of wetting faeces ($P < 0.01$ and $P < 0.05$) and defecation as well as inhibit the moisture content of total faeces.

Table 1
Effect of ethanol extract of *C. dactylon* aerial parts on OGTT.

Test samples groups		Dose	Mean blood glucose concentration (mmol/L)				
			Fasting BGL (pretreatment)	BGL after 30 min extract administration	BGL after glucose administration		
					30 min	60 min	120 min
Control (Group I)		2 mL/rat	4.18 ± 0.34	4.56 ± 0.16	12.70 ± 1.21	12.08 ± 1.13	10.10 ± 0.58
Positive control (Group II)		4.15 mg/kg	4.54 ± 0.45	3.60 ± 0.34*	8.66 ± 0.58**	6.42 ± 0.58**	2.88 ± 0.34***
EECA treated	Group III	2 g/kg	4.98 ± 0.34	4.64 ± 0.21	12.02 ± 1.59	9.00 ± 1.33*	7.36 ± 0.74**
	Group IV	1 g/kg	4.36 ± 0.24	4.78 ± 0.18	15.70 ± 1.40	13.52 ± 0.91	9.04 ± 0.86
	Group V	500 mg/kg	4.86 ± 0.34	4.76 ± 0.19	15.10 ± 0.95	14.70 ± 1.42	10.50 ± 0.73

Values are expressed mean ± SEM; *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$ mean significant difference compared positive control and extract with control.

Table 3
Effect of EECA on COID model.

Groups	Dose	Total faeces in 6 h	% Inhibition of defecation	No. of wet faeces in 6 h	% Inhibition of defecation	Water content of total faeces (g)	Inhibition (%) of water content	Moisture content of total faeces (%)
Control (water)	2 mL/rat	21.60 ± 2.07		18.60 ± 4.09		5.71		20.34
Positive control (loperamide)	2 mg/kg	8.40 ± 0.14***	61	4.20 ± 0.83**	78	2.90	49.21	10.75
EECA	1 g/kg	15.40 ± 1.14**	29	13.60 ± 1.14*	27	3.72	34.85	13.71
	750 mg/kg	21.20 ± 1.92	2	16.00 ± 1.58	14	4.92	13.83	18.13

Values are expressed mean ± SEM; *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$ mean significant difference compared positive control and extract with control.

Table 4
Effect of EECA on gastrointestinal motility with BSM on Wistar rat.

Group	Dose	Length of GIT (cm)	Distance passed by $BaSO_4$ cm	$BaSO_4$ transverse (%)	Inhibition (%)
Control (distilled water)	2 mL	117.80 ± 6.80	69.00 ± 5.00	58.57	
Positive control (loperamide)	2 mg/kg	113.70 ± 4.50	40.20 ± 12.10	35.38**	39.60
EECA	1 g/kg	106.60 ± 6.17	50.25 ± 8.22	47.12*	19.55
	750 mg/kg	103.60 ± 2.38	49.85 ± 9.70	48.12	17.84

Values are expressed mean ± SEM. *: $P < 0.05$; **: $P < 0.01$ mean significant difference compared positive control and extract with control. GIT: Gastro intestinal tract (from pylorus to the ileo-cecal junction).

3.4. Effect of EECA on BSM model

The gastrointestinal motility test with BSM of EECA and loperamide results on Wistar rats are illustrated in Table 4. At 30 min study, the highest reduction of gastrointestinal motility (from 58.57% to 35.38%) was for loperamide at dose of 2 mg/kg and inhibition of the distance travelled by $BaSO_4$ milk was 39.6%. It was observed that the plant extracts decreased the distance of gastrointestinal motility of rats that was moderately significant ($P < 0.05$), from 58.57% (control group) to 47.12% as well as the inhibition of distance travelled by $BaSO_4$ milk was 19.55% at the dose of 1 g/kg compared to control.

4. Discussion

The aqueous extract of *C. dactylon* (whole plant) lowers BGL around 31% after 4 h of administration in normal rats and the dose 500 mg/kg was evaluated as the most effective dose [11]. At the dose of 500 mg/kg after 7 days, the ethanolic extract of *C. dactylon* root stalks showed a good antidiabetic activity against the treated model [12]. The aqueous crude extract of *C. dactylon* (whole plant) at the dose of 400 mg/kg showed significant activity to decrease the BGL after 2 h of administration [13]. The present study, the ethanolic extracts of the aerial parts of *C. dactylon* at the dose of 2 g/kg after 120 min the extract showed a significant result ($P < 0.01$ and $P < 0.05$) to reduce the BGL with OGTT model as well as with AIDT model at the dose of 1.5 g/kg after 6 h of administration.

Methanolic extract of *C. dactylon* (whole plants) exhibited considerable reduction in inhibition of castor oil induced diarrhoea at the dose of 200 mg/kg and 300 mg/kg [14]. The present work with castor oil induced diarrhoea model, the ethanolic extract of *C. dactylon* (aerial parts) significantly ($P < 0.05$) reduced the number of wet faeces and inhibited the total moisture of total faeces at the dose of 1 g/kg. The plant extract also decreased the number of stools between 1st and 6th h significantly ($P < 0.01$) at the dose of 1 g/kg compare to control. In gastrointestinal motility with charcoal meal test, methanolic extract of *C. dactylon* (whole plant) also expressed significant result against dysentery [14]. The present result with BSM model, at the dose of 1 g/kg of *C. dactylon* ethanolic extract (aerial parts) significantly decreased ($P < 0.05$) in intestinal transmit and inhibited by 19.55% compared to control.

Alloxan as well as over loaded glucose damage the beta cells of pancreas and create diabetes due to selectively inhibiting glucose-induced insulin secretion and hampering the activity of the beta cell glucose sensor glucokinase [15].

Castor oil reduces normal fluid absorption due to inhabiting the N^+ K^+ APTase activity of intestinal tract and inhibiting the mucosal cAMP-mediated active secretion. However, Castor oil contains active component ricinoleic acid which is mostly responsible for inducing diarrhoea through a hypersecretory response [16].

Phytochemical observations of *C. dactylon* show the presences of flavonoids, alkaloids, aminoacids, triterpenoids, phenolics, coumarins, iridoids, polysaccharides, glycopeptides and guanidines and sterols [7,12,17,18]. These chemicals are known to be bioactive for the management of diabetes [19] and diarrhoea [14]. It is well established that certain flavonoids shows hypoglycemic activity [20] and are also recognized for their capability of beta cell regeneration of pancreas [21] and have the ability to inhibit intestinal motility and hydroelectrolytic secretions [22]. Sterols also have ability to reduce blood sugar in experimental animal models [23]. Saponins, tannins, flavonoids, alkaloids and terpenes are shown as antidiarrhoeal agents [24,25]. So, the significant antidiabetic and antidiarrhoeal effects of ethanolic extract of aerial parts of *C. dactylon* may be due to the presence of more than one antihyperglycemic and antidiarrhoeal principle, and their synergistic properties.

By this study we can finally affirm that ethanolic extract of aerial parts of *C. dactylon* has shown significant effects to reduce the BGL and increase fluid accumulation of intestinal tract, and act as antidiabetic and antidiarrhoeal agents. There was no acute toxic effect at high dose level (4 g/kg body weight) of plant extract that observed for 24 h and next 10 days investigation, and there was no delayed toxic effects. Food consumption and growth rate of experimented rats were also examined once daily

up to 10 days, and finally there was no abnormality. In addition, pharmacological and biochemical investigations are ongoing to explicate the mechanism of the antidiabetic and antidiarrhoeal effects in *C. dactylon*.

Conflict of interest statement

We declare that we have no conflict of interest.

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