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Effects of *Dracaena arborea* (Dracaenaceae) on sexual dysfunction in 4 weeks hyperglycemic male rats

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ABSTRACT

Objective: To investigate the effects of *Dracaena arborea* (*D. arborea*) on the sexual behavior parameters in experienced type-1 diabetic rats. **Methods:** Aqueous and ethanol (100 and 500 mg/kg respectively) extracts of dried root barks of *D. arborea*, sildenafil citrate (1.44 mg/kg), trimethylamine-N-oxide (TMAO, 20 mg/kg) and distilled water (10 mL/kg) were orally administered to 4 weeks streptozotocin-induced diabetic rats. Mount latency and frequency (ML, MF), intromission latency and frequency (IL, IF) and post-ejaculatory interval (PEI) were measured by ejaculatory series during 90 min once a week for 4 weeks. Glycemia was determined at the beginning and at the end of the treatment. **Results:** *D. arborea* did not show any major antihyperglycemic effects. Compared to the control group, a significant (P<0.05-0.001) increase in MF and IF was noticed in rats treated with sildenafil citrate (89.71% and 90.07% respectively), aqueous (500 mg/kg, 88.08% and 88.74% respectively) and ethanol (100 mg/kg; 89.53% and 89.17 respectively) extracts of *D. arborea* after two weeks (series 1) of treatment. ML, IL and PEI were significantly (P<0.05-0.001) decreased after 4 weeks of daily treatment [sildenafil citrate (96.31, 96.31% and 34.98%), and *D. arborea* aqueous 500 mg/kg (94.33, 94.33% and 66.60%) and ethanol extracts 100 mg/kg (96.98, 97.08% and 64.26%)]. **Conclusions:** These aphrodisiac potentials of *D. arborea* in experienced diabetic rats could be due to the antioxidant and androgenic properties of phenols, flavonoids, saponins and sterols revealed in the plant extracts.

1. Introduction

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both; also, hyperglycemia is still considered as the principal cause of diabetic complications[1,2]. Sustained higher levels of blood glucose cause damage to nerves and blood vessels, leading to complications such as erectile dysfunction[3-5]. Erectile dysfunction (ED) is defined as the inability of the male to attain and maintain erection of penis sufficient to permit satisfactory sexual intercourse[6]. DM is one of the predominant risk factors of ED and also one of the most difficult to treat[7]. Diabetes mellitus may cause erectile dysfunction through a number of pathophysiologic changes, including neuropathy, endothelial dysfunction, cavernosal smooth muscle structural/functional changes, hormonal changes[8,9]. Although pathophysiologic changes may be more pronounced in type 1 diabetes than in type 2, they are mainly due to oxidative stress, through the formation of oxygen free radicals and advanced glycation end-products (AGEs)[10]. Oxygen free radicals and AGEs have been shown to contribute to the neurodegeneration, reduction of endothelium-dependent vasorelaxation by

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altering the endothelial nitric oxide synthase synthesis and have been associated with impaired endothelium-dependent vasodilation in Type 2 diabetic patients[11-15]. In addition, endothelial dysfunction might be the link between diabetes mellitus and erectile dysfunction[16] since it takes a minimum of 4 weeks for a rat to develop erectile and nitrergic dysfunctions, whereas endothelial dysfunction can potentially develop in days as a direct consequence of hyperglycaemia[17]. Due to multiple action of streptozotocin intoxication, understanding how uncontrolled hyperglyceamia impacts the sexual function and seeking for efficient drugs able to alleviate diabetes-induced complications are yet important areas of inquiry. However, despite the increasing availability of effective conventional medical treatments for erectile dysfunction in diabetic patients, plant-derived and herbal remedies continue to provide a popular alternative for diabetic men seeking to improve their sexual life[18-20]. Cameroonian traditional medicine indicates that the mixture of the roots of *Dracaena arborea* (*D. arborea*)(Wild) Link (Dracaenaceae), a tall tree native to West Africa, with palm wine possess aphrodisiac potentials. Also, in a pilot study, we demonstrated that *D. arborea* extracts and especially its ethanolic extract (100 mg/kg) stimulate the copulatory activity of normal and androgen-deprived (castrated) rats through dopaminergic and/or cholinergic pathways[21]. The aim of the present study was to evaluate the aphrodisiac effects of the aqueous and ethanol extracts of *D. arborea* in streptozotocin-induced type 1 diabetic rats. Streptozotocin-induced type 1 diabetes in rats provides a relevant model to study the reproductive dysfunction under diabetic conditions, as they exhibit a number of reproductive deficits that resemble those seen in human diabetics[22].

2. Materials and methods

2.1. Chemicals

Streptozotocin, trimethylamine-N-oxide (TMAO), estradiol benzoate and progesterone were purchased from Sigma (USA), sildenafil citrate (Kamagra®) from Ajanta Pharma Limited (India), diazepam from Renaudin (France), ketamine from Rotex Medica (Germany) and penicillin G from Clarion Medicals (Nigeria).

2.2. Plant material collection and preparation of extracts

The plant material was harvested in Bagnoun, West Region of Cameroon and authenticated at the Cameroon National Herbarium (CNH) under the voucher number 25361/SFR/Cam. The harvested fresh root barks were cut into small pieces, dried at room temperature and ground into a fine powder. For the aqueous extraction, eight hundred grams (800 g) of the powdered roots were dissolved in 5 L of distilled water and kept for 72 h at 25 ℃, and occasionally stirred. After filtration, the filtrate was concentrated in an oven (40 ℃) to give 39.68 g of brownish residue corresponding to an extraction yield of 4.96%. In order to obtain the ethanolic extract, ground root bark (1 kg) of *D. arborea* was macerated with ethanol (95%) (5 L, 2×) for 72 h to yield, after solvent evaporation under reduced pressure, 30 g of a brownish extract corresponding to an extraction yield of 3%. The working extracts were prepared at a final concentration of 100 mg/mL in distilled water. The doses used in the study were 100 and 500 mg/kg.

2.3. Phytochemical screening

Qualitative phytochemical evaluation was performed on aqueous and ethanolic extracts of *D. arborea* to determine the presence of flavonoids (test of Shinoda), sterols (Libermann Buchard test), phenols (ferric chloride test), alkaloids (Dragendorff test), or saponins (Saponification test). All these tests were performed as described by other authors[23].

2.4. Animals

A total of 176 adult healthy albino rats of Wistar strain of either sex (48 males and 128 females) were used for the present study. Rats were obtained from the animal house of the Faculty of Science, University of Dschang, Cameroon. They were maintained at room temperature with a natural light: dark cycle (12 h: 12 h) and provided with standard Laboratory rat diet and water ad libitum. The experiments were performed in accordance with the internationally accepted standard ethical guidelines for laboratory animal use and care as described in the European Community guidelines; EEC Directive 86/609/EEC, of the 24th November 1986[24].

2.4.1. Male training procedure

Male rats were trained for sexual experience prior to diabetes induction. To provide sexual experience, each male was allowed 1 h exposure to a receptive female rat (used as mating stimulator) in behavioral estrus for 5 consecutive days and only those exhibiting good copulatory behavior (active males) were selected for the study.

2.4.2. Ovariectomy

Ovariectomy was performed following the technique of

Cariton[25] with minor modifications as described by Watcho and colleagues[21].

2.4.3. Estrus induction

One month after ovariectomy, female rats were brought into estrus by sequential subcutaneous injection of 30 μg of estradiol benzoate and 600 μg of progesterone, 48 h and 6 h respectively before testing[21]. In ovariectomized rat, it was shown that estradiol benzoate induced a specific urge to seek contact with a sexual active male[26]. They were further screened with non-experimental vigorous males and only those exhibiting good sexual receptivity and no rejection behaviour were employed in the tests.

2.4.4. Diabetes induction

Diabetes was induced in 16 h fasted adult male rats by a single intraperitoneal injection of a buffered solution (0.1 M citrate, pH 4.5) of streptozotocin at the dose 50 mg/kg. To prevent hypoglycemia, animals were given a 10% glucose solution for the next 48 h. Blood glucose level was measured 7 d after diabetes induction using reagent strips (Accu-Chek®, Roche,). Blood was collected from tail vein and rats with blood glucose values more than 200 mg/dL were considered diabetics. Forty two rats were made diabetic in this way and kept for four weeks before starting the experiment. Initial and final fasting blood glucose levels were recorded in this study.

2.5. Experimental design

A total of 48 rats (42 diabetics and 6 non diabetic rats) were randomly divided into 8 groups of 6 animals each and treated as follows: Group 1, normal rats receiving the vehicle (10 mL/kg of distilled water). Group 2, diabetic rats receiving 10 mL/kg of distilled water. Group 3, diabetic rats receiving 1.44 mg/kg of sildenafil citrate. Group 4, diabetic rats receiving 20 mg/kg of trimethylamine-N-oxide (TMAO). Groups 5 and 6, diabetic rats receiving 100 mg/kg and 500 mg/kg of the aqueous extract of *D. arborea*. Groups 7 and 8, diabetic rats receiving 100 mg/kg and 500 mg/kg of the ethanol extract of *D. arborea*. The vehicle (distilled water) as well as the reference drugs (Sildenafil citrate and TMAO) and plant extracts were orally administered once a day for four weeks.

2.6. Sexual behavior testing procedure

The sexual behavior of each rat was monitored for 4 consecutive weeks in a dark and quiet room for 1 h and 30 min duration. After 30 min of acclimatization in the copulation cage (rectangular glass cage), a stimulus-receptive female was presented to each male by dropping it gently into the cage. The following parameters were recorded by ejaculatory series according to standard methods[21,27]: mount (ML) and intromission latency (IL), the time elapsed from the introduction of a female into a cage until the first mount and intromission respectively; mount (MF) and intromission frequency (IF), the number of mounts and intromissions preceding ejaculation respectively in one series; post-ejaculatory interval (PEI), the elapsed time between an ejaculation and the first intromission of the next ejaculatory series. Further, the test was force-ended when ML equaled 20 min.

2.7. Statistical analysis

Data are expressed in mean±SEM. Data from blood glucose levels were analysed using Two ways ANOVA followed by

Table 1

Effects of *D. arborea*, sildenafil citrate and TMAO on fasting blood glucose level.

Groups	Initial blood glucose level (mg/dL)	Final blood glucose level (mg/dL)
Control	52.38±5.76^{a}	57.38±3.29^{a}
STZ	283.67±10.57^{a***}	399.17±44.03^{b***}
STZ+Sildenafil	318.00±28.62^{a***}	220.17±39.38^{bC**}
STZ+TMAO	344.83±30.01^{a***}	289.17±57.63^{a***}
STZ+AQ100	416.17±44.38^{a***}	428.83±39.20^{a***}
STZ+AQ500	275.00±17.01^{a***}	270.50±15.82^{aA***}
STZ+ETH100	280.29±22.87^{a***}	243.71±36.15^{aB***}
STZ+ETH500	326.17±28.47^{a***}	272.67±87.38^{aA***}

Values of blood glucose level are means±SEM, n = 6. Control = normal rats receiving distilled water (10 mL/kg). STZ = diabetic rats receiving distilled water (10 mL/kg). STZ+Sildenafil = diabetic rats treated with sildenafil citrate (1.44 mg/kg). STZ+TMAO = diabetic rats treated with trimethylamine-N-oxide (20 mg/kg). STZ+AQ100 or AQ500 = diabetic rats treated with aqueous extract of *D. arborea* (100 or 500mg/kg). STZ+ETH100 or ETH500 = diabetic rats treated with ethanol extract of *D. arborea* (100 or 500 mg/kg). On the same line, the values of blood glucose level assigned by the same lowercase letter are not significantly different. In the same column, **P<0.01, *** P<0.001 significantly different compared to the corresponding normal control. Always in the same column, ^{A}P<0.05; ^{B}P<0.01, ^{C}P<0.001 significantly different compared to the corresponding STZ control.

Bonferroni all pair comparism test. The effect of the duration of the treatment on each copulatory parameter was analyzed using two ways ANOVA repeated measures followed by Bonferroni all pair comparism test when necessary. Within the same week of treatment, two ways ANOVA followed by Bonferroni all pair comparism test was used to compare the treated groups to normal and diabetic control animals respectively. *P* values of 0.05 or less were taken to imply statistical significance between the means. All these analysis were performed using Graphpad Prism version 5.1.

3. Results

3.1. Phytochemical analysis

Qualitative phytochemical screening of both aqueous and ethanol extracts of *D. arborea* dried roots showed the presence of saponins, phenols, flavonoids and sterols whereas alkaloids were absent in the two extracts.

3.2. Fasting blood glucose level

Table 1 shows that after four weeks of treatment, apart

Table 2

Effects of *D. arborea*, sildenafil citrate and TMAO on mount frequency.

Ejaculatory series	Groups	Treatment period			
		Week 0	Week 1	Week 2	Week 4
Series 1	Control	17.60±1.88^{a}	9.40±1.29^{a}	16.00±2.52^{a}	47.20±9.17^{b}
	STZ	13.00±6.00^{a}	3.60±3.60^{ab}	3.60±3.60^{ab}	0^{b***}
	STZ+ Sildenafil	20.00±1.25^{a}	42.00±18.15^{abC**}	35.00±7.07^{aB}	66.00±8.53^{bC}
	STZ+TMAO	16.75±6.16^{a}	30.75±3.73^{acA}	28.50±5.25^{acA}	45.25±8.36^{cC}
	STZ+AQ100	21.80±6.30^{a}	21.60±8.05^{a}	27.40±9.01^{a}	11.60±3.59^{a**}
	STZ+AQ500	15.83±5.70^{a}	30.40±8.70^{aA}	30.20±8.39^{aB}	29.80±9.18^{aB}
	STZ+ETH100	18.20±2.97^{a}	22.80±5.65^{a}	34.40±5.88^{aB}	23.60±3.91^{a***}
	STZ+ETH500	13.40±5.51^{a}	7.40±5.11^{a}	11.40±4.73^{a}	9.60±4.30^{a}
Series 2	Control	14.00±2.28^{a}	7.60±0.59^{a}	13.60±2.56^{a}	19.80±2.91^{a}
	STZ	0^{a}	2.60±2.60^{a}	2.00±2.00a	0^{a**}
	STZ+ Sildenafil	13.75±8.05^{a}	19.75±5.96^{aB}	23.25±2.17^{aC}	29.75±2.69^{aC}
	STZ+TMAO	7.75±5.20^{a}	20.25±5.17^{aB}	14.25±4.80^{a}	15.50±7.66^{aA}
	STZ+AQ100	7.20±1.98^{a}	12.60±4.15^{a}	12.80±2.71^{a}	8.60±2.73^{a}
	STZ+AQ500	6.00±2.60^{a}	19.80±5.27^{abB}	28.40±9.19^{bC*}	15.80±3.99^{abA}
	STZ+ETH100	5.80±1.21^{a}	11.00±0.71^{a}	19.40±4.10^{aB}	13.40±2.28^{a}
	STZ+ETH500	3.80±2.33^{a}	4.40±2.69^{a}	5.00±3.26^{a}	3.40±2.14^{a*}
Series 3	Control	15.00±5.05^{a}	8.40±1.21^{a}	13.00±2.59^{a}	30.00±8.26^{a}
	STZ	0^{a}	0^{a}	2.20±2.20^{a}	0^{a***}
	STZ+ Sildenafil	7.50±4.41^{a}	17.25±6.42^{abA}	23.75±3.59^{abB}	26.75±4.33^{bC}
	STZ+TMAO	2.72±2.75^{ab}	9.25±3.50^{ab}	23.50±12.90^{aB}	0
	STZ+AQ100	9.80±3.15^{a}	10.80±5.36^{a}	11.80±4.16^{a}	3.00±2.00^{a***}
	STZ+AQ500	4.00±1.50^{a}	14.80±2.74^{a}	24.40±18.09^{aB}	26.60±12.11^{aC}
	STZ+ETH100	2.40±1.90^{a}	15.00±2.66^{b}	16.80±3.21^{b}	6.40±1.36^{ab**}
	STZ+ETH500	6.00±2.51^{a}	5.20±3.20^{a}	0	2.20±2.20^{a***}
Series 4	Control	10.20±2.9^{a}	14.40±1.93^{a}	9.40±2.80^{a}	6.00±4.74^{a}
	STZ	0^{a*}	0^{a***}	0^{a*}	0^{a}
	STZ+ Sildenafil	0^{a*}	8.25±4.77^{a}	4.25±4.25^{a}	0^{a}
	STZ+TMAO	0^{a*}	11.25±4.33^{bdA}	15.25±5.56^{cd}	0^{a}
	STZ+AQ100	1.60±1.60^{a}	1.40±1.40^{a**}	1.20±1.20^{a}	4.60±2.80^{a}
	STZ+AQ500	0^{a*}	3.40±1.95^{a*}	1.20±1.10^{a}	2.00±1.83^{a}
	STZ+ETH100	0^{a*}	4.80±2.76^{a*}	12.40±3.64^{a}	3.80±2.16^{a}
	STZ+ETH500	2.20±2.20^{a}	3.00±3.00^{a**}	0^{a*}	0^{a}
Series 5	Control	2.00±1.58^{a}	4.20±2.04^{a}	0^{a}	0^{a}
	STZ	0^{a}	0^{a}	0^{a}	0^{a}
	STZ+ Sildenafil	0^{a}	0^{a}	0^{a}	0^{a}
	STZ+TMAO	0^{a}	10.75±6.92^{aC**}	3.00±3.00^{a}	0^{a}
	STZ+AQ100	0^{a}	0^{a}	0^{a}	0^{a}
	STZ+AQ500	0^{a}	0	0^{a}	0^{a}
	STZ+ETH100	0^{a}	3.40±1.69^{a}	0^{a}	0^{a}
	STZ+ETH500	0^{a}	0^{a}	0^{a}	0^{a}

Values of mount frequency are means±SEM (*n*=6).

from the untreated diabetic rats where the blood glucose continued to increase significantly ($P<0.05$), those of all other groups remained statistically unchanged ($P>0.05$) compared to their respective baseline values (initial blood glucose level) but remained high compared to normal control rats.

3.3. Sexual behavior test

3.3.1. Effects on mount and intromission frequencies

Tables 2 and 3 clearly indicate the tendency to decrease in the mount frequency (MF) and intromission frequency (IF) as the ejaculatory series evolved. It can also be observed that compared to the baseline value (week 0) and to the normal control group, the untreated diabetic rats showed a significant ($P<0.05-0.001$) decrease in these two sexual parameters particularly in the ejaculatory series 1 to 3 after four weeks.

Sildenafil citrate, TMAO, aqueous (500 mg/kg) and ethanol (100 mg/kg) extracts of *D. arborea* produced a significant increase ($P<0.05-0.001$) in the mount and intromission frequencies especially at the first ejaculatory series, on weeks 1, 2 and 4 of treatment when compared to the untreated diabetics and week 0. The ejaculatory series 1, 2 and 3 were the most important in these recordings; with

Table 3

Effects of *D. arborea*, sildenafil citrate and TMAO on intromission frequency.

Ejaculatory series	Groups	Treatment period			
		Week 0	Week 1	Week 2	Week 4
Series 1	Control	16.80 ± 1.83^{a}	9.40 ± 1.29^{a}	16.80 ± 1.40^{a}	46.20 ± 9.06^{b}
	STZ	12.00 ± 5.00^{a}	3.40 ± 3.40^{a}	3.40 ± 3.40^{a}	0^{b***}
	STZ+ Sildenafil	18.00 ± 1.68^{a}	$40.25\pm17.24^{abC**}$	34.25 ± 6.73^{aC}	66.00 ± 8.53^{bC}
	STZ+TMAO	15.75 ± 5.68^{a}	30.25 ± 3.71^{aB}	26.75 ± 3.45^{aB}	44.25 ± 8.25^{bC}
	STZ+AQ100	17.80 ± 6.15^{a}	18.20 ± 6.42^{a}	22.20 ± 5.94^{aA}	$11.60\pm3.59^{a***}$
	STZ+AQ500	15.60 ± 5.70^{a}	30.40 ± 8.70^{aA}	30.20 ± 8.39^{aB}	29.80 ± 9.18^{aC}
	STZ+ETH100	15.80 ± 1.97^{a}	21.20 ± 5.46^{a}	31.40 ± 5.57^{aB}	$18.00\pm2.17^{a**}$
	STZ+ETH500	13.20 ± 5.43^{a}	9.40 ± 5.78^{a}	10.80 ± 4.49^{a}	$9.20\pm4.09^{a***}$
Series 2	Control	13.80 ± 2.34^{a}	7.60 ± 0.59^{a}	13.20 ± 2.42^{a}	19.80 ± 2.91^{a}
	STZ	0^{a*}	2.60 ± 2.60^{a}	2.00 ± 2.00^{a}	0^{a***}
	STZ+ Sildenafil	13.75 ± 8.05^{aA}	19.75 ± 5.96^{aB}	23.25 ± 2.17^{aC}	29.75 ± 2.69^{aC}
	STZ+TMAO	7.75 ± 5.20^{a}	20.25 ± 5.17^{aB}	14.25 ± 4.80^{a}	15.50 ± 7.66^{aB}
	STZ+AQ100	7.20 ± 1.98^{a}	12.60 ± 4.15^{a}	12.80 ± 2.71^{a}	8.60 ± 2.73^{a}
	STZ+AQ500	6.00 ± 2.60^{a}	19.80 ± 5.27^{abA}	28.40 ± 9.19^{bC}	15.80 ± 3.99^{abA}
	STZ+ETH100	5.40 ± 1.19^{a}	10.60 ± 0.73^{ab}	18.40 ± 3.86^{bB}	11.60 ± 1.16^{ab}
	STZ+ETH500	3.80 ± 2.33^{a}	4.40 ± 2.69^{a}	5.00 ± 3.26^{a}	$3.40\pm2.14^{a**}$
Series 3	Control	13.80 ± 1.53^{ab}	8.20 ± 1.31^{a}	13.00 ± 2.59^{ab}	29.80 ± 8.24^{b}
	STZ	0^{a}	0a	2.00 ± 2.00^{a}	0^{a***}
	STZ+ Sildenafil	7.25 ± 4.31^{a}	16.25 ± 6.03^{abA}	23.50 ± 3.43^{abB}	26.75 ± 4.33^{bC}
	STZ+TMAO	2.50 ± 2.50^{ab}	9.00 ± 3.49^{ab}	23.25 ± 12.67^{aB}	0^{a***}
	STZ+AQ100	8.40 ± 3.08^{a}	9.80 ± 4.96^{a}	10.00 ± 3.58^{a}	2.80 ± 1.96^{a}
	STZ+AQ500	4.00 ± 1.50^{a}	14.80 ± 2.74^{a}	24.40 ± 8.09^{aB}	26.60 ± 12.11^{aC}
	STZ+ETH100	2.20 ± 1.74^{a}	14.60 ± 2.48^{b}	16.00 ± 3.18^{b}	$6.20\pm1.48^{ab***}$
	STZ+ETH500	3.40 ± 2.23^{a}	5.20 ± 3.20^{a}	0^{a}	$2.20\pm2.20^{a***}$
Series 4	Control	10.00 ± 2.92^{a}	13.80 ± 1.84^{a}	9.40 ± 2.80^{a}	5.80 ± 4.59^{a}
	STZ	0^{a*}	0^{a***}	0^{a*}	0^{a}
	STZ+ Sildenafil	0^{a*}	7.75 ± 4.52^{a}	4.00 ± 4.00^{a}	0^{a}
	STZ+TMAO	0^{a*}	11.25 ± 4.33^{abB}	15.25 ± 5.56^{bC}	0^{a}
	STZ+AQ100	0^{a*}	$1.20\pm1.20^{a**}$	1.00 ± 1.00^{a}	4.40 ± 2.71^{a}
	STZ+AQ500	0^{a*}	$3.40\pm1.95^{a**}$	1.20 ± 1.10^{a}	2.00 ± 1.83^{a}
	STZ+ETH100	0^{a*}	$4.20\pm2.45^{a*}$	11.80 ± 3.48^{aB}	3.80 ± 2.16^{a}
	STZ+ETH500	2.20 ± 2.20^{a}	$3.00\pm3.00^{a*}$	0^{a*}	0^{a}
Series 5	Control	2.00 ± 1.58^{a}	3.60 ± 1.76^{a}	0^{a}	0^{a}
	STZ	0^{a}	0^{a}	0^{a}	0^{a}
	STZ+ Sildenafil	0^{a}	0^{a}	0a	0^{a}
	STZ+TMAO	0^{a}	$10.75\pm6.92^{aC***}$	3.00 ± 3.00^{a}	0^{a}
	STZ+AQ100	0^{a}	0^{a}	0a	0^{a}
	STZ+AQ500	0^{a}	0^{a}	0^{a}	0^{a}
	STZ+ETH100	0^{a}	3.40 ± 1.69^{a}	1.00 ± 0.79^{a}	0^{a}
	STZ+ETH500	0^{a}	0^{a}	0^{a}	0^{a}

Values of intromission frequency are means±SEM ($n=6$).

regard to the ejaculatory series 4 and 5, only TMAO-treated rats showed similar effects on week 1 compared to week 0 ($P<0.05$) and to the untreated diabetic group ($P<0.01-0.001$) respectively.

3.3.2. Effects on mount and intromission latencies

In the first four ejaculatory series, mount and intromission latencies were significantly increased ($P<0.01-0.001$) in the untreated diabetic group. On the contrary, when compared to week 0 and to the untreated diabetic animals respectively, especially in the first ejaculatory series of week 4, mount latency (ML) and intromission latency (IL) significantly decreased ($P<0.05-0.001$) after treatments with sildenafil citrate (75.52% and 96.31% of decrease for ML; 65.63% and 96.31% of decrease for IL), TMAO (46.92% and 77.89% for ML; 48.11% and 76.77% of decrease for IL), aqueous 500 mg/kg (88.95% and 94.33% of decrease for ML; 89.02% and 94.33% of decrease for IL) and ethanol 100 mg/kg (86.41% and 96.98% of decrease for ML; 89.08% and 97.08% of decrease for IL) extracts of *D. arborea* (Tables 4 and 5).

3.3.3. Effects on post-ejaculatory interval

As observed in Table 6, the post-ejaculatory interval (PEI) was significantly increased ($P<0.05-0.001$) in diabetic rats

Table 4

Effects of *D. arborea*, sildenafil citrate and TMAO on mount latency.

Ejaculatory series	Groups	Treatment period			
		Week0	Week1	Week2	Week4
Series 1	Control	67.40±35.83^{a}	22.60±13.95^{a}	7.40±1.26^{a}	17.00±8.20^{a}
	STZ	1 148.80±51.20^{a***}	1 200.00±0.00^{a***}	1 008.00±192.00^{a***}	1 200.00±0.00^{a***}
	STZ+ Sildenafil	180.75±64.00^{aC}	52.75±16.50^{bC}	30.75±9.22^{bC}	44.25±30.61^{bC}
	STZ+TMAO	499.75±238.71^{aB}	16.50±8.10^{bC}	160.00±8.71^{bC}	265.25±194.78^{abC}
	STZ+AQ100	177.40±21.50^{aC}	394.20±224.15^{aC}	6.00±1.95^{bC}	253.60±236.61^{aC}
	STZ+AQ500	615.60±258.38^{aA}	117.00±57.92^{aC}	241.40±59.24^{aC}	68.00±8.02^{aC}
	STZ+ETH100	266.40±59.85^{aC}	70.60±16.07^{abC}	158.40±74.59^{abC}	36.20±5.78^{bC}
	STZ+ETH500	565.60±260.49^{aA*}	736.20±284.20^{a**}	612.20±255.03^{a**}	520.60±278.00^{aB*}
Series 2	Control	405.60±34.61^{a}	359.60±16.55^{a}	424.40±21.11^{a}	632.40±33.32^{b}
	STZ	1 148.80±51.20^{a***}	1 200.00±0.00^{a***}	1 008.00±192.00^{a**}	1 200.00±0.00^{a**}
	STZ+ Sildenafil	670.25±181.75^{aA}	495.00±55.17^{aC}	607.50±179.93^{a}	780.25±267.32^{a}
	STZ+TMAO	878.50±186.41^{a*}	874.75±383.20^{aB*}	667.50±186.49^{a}	736.50±166.52^{aA}
	STZ+AQ100	711.40±150.47^{a}	787.20±177.46^{aB}	483.80±27.84^{aA}	741.80±143.23^{aA}
	STZ+AQ500	819.20±163.50^{a}	428.20±15.95^{bC}	475.80±54.85^{abA}	400.80±28.25^{bC}
	STZ+ETH100	915.60±95.65^{a*}	559.40±82.20^{abC}	473.00±57.42^{bA}	436.80±45.03^{bC}
	STZ+ETH500	937.20±161.45^{a*}	915.00±177.93^{aA**}	966.80±167.70^{a*}	982.20±136.75^{a}
Series 3	Control	436.60±23.78^{a}	466.00±22.74^{a}	551.00±37.84^{a}	912.2 0±240.0^{2b}
	STZ	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}
	STZ+ Sildenafil	944.00±149.20^{a**}	861.25±116.14^{a*}	823.75±151.92^{aA}	925.00±173.11^{a}
	STZ+TMAO	1 104.75±95.25^{ab***}	856.75±172.87^{ab*}	678.75±178.59^{aB}	1 200.00±0.00^{b}
	STZ+AQ100	890.80±102.46^{a**}	856.00±143.50^{a*}	762.60±118.81^{aC}	957.40±150.27^{a}
	STZ+AQ500	951.40±116.72^{a**}	735.8 0±67.19^{aB}	765.00±111.75^{aA}	681.40±75.53^{aB**}
	STZ+ETH100	1 154.00±36.35^{a***}	715.60±98.19^{bB}	687.20±106.92^{bB}	373.20±79.46^{bC**}
	STZ+ETH500	937.60±161.56^{a**}	1 014.20±123.09^{a***}	1 200.00±0.00^{a***}	1 138.00±62.00^{a}
Series 4	Control	793.60±95.95^{a}	568.60±70.49^{a}	948.60±96.95^{a}	1122.00±61.66^{a}
	STZ	1200.00±0.00^{a**}	1200.00±0.00^{a***}	1200.00±0.00^{a***}	1200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a**}	1 045.25±106.17^{a**}	1 151.00±49.00^{a**}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a**}	754.00±162.51^{bB}	880.75±133.93^{ab}	1 200.00±0.00^{ab}
	STZ+AQ100	1 087.60±112.40^{a}	1 073.60±126.40^{a***}	1 089.60±110.40^{a*}	1 119.80±151.88^{a}
	STZ+AQ500	1 200.00±0.00^{a**}	1 030.20±95.19^{a**}	1 072.20±116.64^{a*}	109.80±82.32^{a}
	STZ+ETH100	1 200.00±0.00^{a**}	949.00±123.58^{a*}	736.00±98.91^{aB}	1 028.60±94.76^{a}
	STZ+ETH500	1 154.60±45.40^{a*}	1 161.40±38.60^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}
Series 5	Control	793.60±95.95^{a}	568.60±70.49^{a}	948.6 0±96.95^{a}	1 122.00±61.66^{a}
	STZ	1 200.00±0.00^{a**}	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a**}	1 045.25±106.17^{a**}	1 151.00±49.00^{a**}	200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a**}	754.00±162.51^{bB}	880.75±133.93^{ab}	1 200.00±0.00^{ab}
	STZ+AQ100	1 087.60±112.40^{a}	1 073.60±126.40^{a***}	1 089.6 0±110.40^{a*}	1 119.80±151.88^{a}
	STZ+AQ500	1 200.00±0.00^{a**}	1 030.20±95.19^{a**}	1 072.20±116.64^{a*}	1 109.80±82.32^{a}
	STZ+ETH100	1 200.00±0.00^{a**}	949.00±123.58^{a*}	736.00±98.91^{aB}	1 028.60±94.76^{a}
	STZ+ETH500	1 154.60±45.40^{a*}	1 161.40±38.60^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}

Values of mount frequency are means±SEM (n=6).

treated with distilled water during the first three ejaculatory series compared to normal rats. However, this parameter was significantly lowered (P<0.05-0.001) mostly in the first ejaculatory series of 4 weeks-treated diabetic rats with aqueous 500 mg/kg (66.60% of decrease) and ethanol 100 mg/kg (64.26% of decrease) extracts of *D. arborea*. A lack of ejaculatory activity was noticed in the series 4 and 5.

4. Discussion

Streptozotocin has long been used as a tool for creating experimental diabetes in animal. An advantage of the streptozotocin-model is that it closely mimics type 1 diabetes in humans rather than type 2[2,28]. Sustained hyperglycemia is one of the main causes of sexual dysfunction[29]. Hypogonadism, neuropathy, arterial insufficiency, progressive loss of both endothelium and smooth muscle tissue, and impaired regulation of smooth muscle tone are the most common predictors of erectile dysfunction in patients or animals with diabetes[9,30]. In our previous article, we have shown through electron micrograph examinations that, streptozotocin-induced diabetes in rats caused testicular dysfunction, leading to the dramatic

Table 5

Effects of *D. arborea*, sildenafil citrate and TMAO on intromission latency.

Ejaculatory series	Groups	Treatment period			
		Week0	Week1	Week2	Week4
Series 1	Control	67.80±36.14^{a}	22.60±13.95^{a}	7.40±1.26^{a}	17.00±8.20^{a}
	STZ	1 159.40±40.60^{a***}	1200.00±0.00^{a***}	1008.00±192.00^{a***}	1200.00±0.00^{a***}
	STZ+ Sildenafil	128.75±44.58^{aC}	52.75±16.50^{bC}	30.75±9.22^{bC}	44.25±30.61^{bC}
	STZ+TMAO	537.25±221.64^{aB}	16.50±8.10^{bC}	16.00±8.71^{bC}	278.75±208.01^{abC}
	STZ+AQ100	199.80±23.29^{aC}	429.00±220.11^{aC}	6.00±1.95^{bC}	253.60±236.61^{aC}
	STZ+AQ500	619.40±256.80^{aA*}	133.00±53.11^{aC}	244.80±59.16^{aC}	68.00±8.02^{aC}
	STZ+ETH100	320.60±50.91^{a}	97.80±9.72^{abC}	158.40±74.59^{abC}	35.00±7.31^{bC}
	STZ+ETH500	606.80±242.36^{aA*}	736.20±284.02^{a**}	690.80±261.12^{a**}	520.60±278.00^{aB*}
Series 2	Control	405.60±34.61^{a}	359.60±163.55^{a}	424.60±20.96^{a}	632.40±33.32^{b}
	STZ	1 200.00±0.00^{a***}	1056.80±143.20^{a***}	1030.40±169.60^{a**}	1200.00±0.00^{a**}
	STZ+ Sildenafil	846.75±196.33^{a*}	495.00±55.17^{aB}	582.50±154.95^{aA}	780.25±267.32^{a}
	STZ+TMAO	878.50±186.41^{a*}	874.75±383.20^{a*}	667.50±186.49^{a}	736.50±166.52^{aA}
	STZ+AQ100	732.80±143.46^{aA}	796.20±173.91^{a}	505.20±36.09^{aA}	774.40±136.73^{a}
	STZ+AQ500	819.20±163.50^{a}	437.60±16.24^{bB}	475.80±54.85^{abB}	400.80±28.25^{bC}
	STZ+ETH100	847.00±90.21^{a*}	559.40±82.20^{abA}	473.60±57.21^{bB}	452.20±42.73^{bC}
	STZ+ETH500	947.40±156.11^{a**}	915.00±177.93^{a**}	968.40±167.03^{a**}	982.20±136.75^{a}
Series 3	Control	476.60±24.91^{a}	466.00±22.74^{a}	551.00±37.84^{a}	1 152.20±158.73^{b}
	STZ	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}
	STZ+ Sildenafil	945.500±148.52^{a*}	811.25±140.34^{a}	823.75±151.92^{aC}	925.00±173.11^{a}
	STZ+TMAO	1 104.75±95.25^{ab***}	857.25±172.95^{a}	678.75±178.59^{aC}	1 200.00±0.00^{b}
	STZ+AQ100	920.2±101.56^{a*}	857.20±142.9^{ab}	764.60±118.23^{aC}	959.00±149.12^{a}
	STZ+AQ500	972.20±119.95^{a**}	738.40±66.56^{aA}	756.80±115.93^{aC}	681.40±75.53^{aB}
	STZ+ETH100	1 154.00±36.35^{a***}	715.60±98.19^{bA}	668.40±106.66^{bC}	767.20±142.53^{bA}
	STZ+ETH500	938.00±161.35^{a*}	1 014.20±123.09^{a**}	1 200.00±0.00^{a***}	1 138.00±62.00^{a}
Series 4	Control	793.60±95.95^{a}	568.60±70.49^{a}	948.60±96.95^{a}	1 122.00±61.66^{a}
	STZ	1 200.00±0.00^{a**}	1 200.00±0.00^{a***}	1 200 .00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a**}	1 045.25±106.17^{a***}	1 151.00±49.00^{a}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a**}	754.00±162.51^{bB}	880.75±133.93^{abA}	1 200.00±0.00^{ab}
	STZ+AQ100	1 099.60±100.40^{a}	1 073.60±126.40^{a***}	1 090.40±109.60^{a}	1 119.80±151.88^{a}
	STZ+AQ500	1 200.00±0.00^{a**}	1 031.40±94.59^{a**}	1 072.20±116.64^{a}	1 109.80±82.32^{a}
	STZ+ETH100	1 200.00±0.00^{a**}	951.80±122.49^{a*}	740.20±98.86^{aB}	1 028.60±94.76^{a}
	STZ+ETH500	1 154.60±45.40^{a*}	1 161.40±38.60^{a***}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
Series 5	Control	1 138.00±49.02^{a}	1 050.40±76.22^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ	1 200.00±0.00^{a}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a}	1 200.00±0.00^{a*}	1 200.00±0.0 0^{a}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a}	970.00±138.11^{aC}	1 075.75±124.25^{a}	1 200.00±0.00^{a}
	STZ+AQ100	1 200.00±0.00^{a}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+AQ500	1 200.00±0.00^{a}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ETH100	1 200.00±0.00^{a}	1 079.00±58.94^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ETH500	1 200.00±0.00^{a}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}

Values of intromission frequency are means±SEM (n=6).

Table 6

Effects of *D. arborea*, sildenafil citrate and TMAO on post-ejaculatory interval.

Ejaculatory series	Groups	Treatment period			
		Week0	Week1	Week2	Week4
Series 1	Control	405.60±34.61^{a}	=359.60±16.55^{a}	424.60±20.96^{a}	632.40±33.32^{b}
	STZ	1 066.00±134.00^{a**}	1 056.80±143.20^{a**}	1 030.40±169.60^{a**}	1 200.00±0.00^{a*}
	STZ+ Sildenafil	858.75±364.11^{a}	495.00±55.17$^{a\alpha}$	607.50±179.93^{a}	780.25±267.32^{a}
	STZ+TMAO	878.50±186.41^{a}	874.75±383.20^{a*}	667.50±186.49^{a}	787.25±214.44^{a}
	STZ+AQ100	710.00±125.60^{a}	796.20±173.91^{a}	505.20±36.09^{aA}	774.40±136.73^{a}
	STZ+AQ500	710.20±139.07^{a}	437.60±16.24^{aB}	475.80±54.85^{aA}	400.80±28.25^{aC}
	STZ+ETH100	779.60±92.86^{a}	559.40±82.19^{aA}	473.00±57.41^{aA}	428.80±48.06^{aC}
	STZ+ETH500	869.80±143.49^{a}	915.00±177.93^{a}	968.40±167.03^{a}	982.20±136.75^{a}
Series 2	Control	476.60±24.91^{a}	466.00±22.74^{a}	551.00±37.83^{a}	912.20±240.02^{a}
	STZ	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a***}	1 200.00±0.00^{a}
	STZ+ Sildenafil	945.50±148.52^{a*}	811.25±140.34^{a}	823.75±151.92^{a}	925.00±173.10^{a}
	STZ+TMAO	1 104.75±95.25^{ad***}	857.25±172.95^{a}	678.75±178.59^{bB}	1 200.00±0.00^{cd}
	STZ+AQ100	920.20±101.56^{a}	758.00±115.14^{aA}	764.60±118.23^{aA}	959.00±149.12^{a}
	STZ+AQ500	972.20±119.95^{a**}	738.4 0±66.56^{aA}	766.80±11.69^{aA}	681.40±75.53^{aB}
	STZ+ETH100	1 121.80±38.81^{a***}	675.60±102.04^{bcB}	740.20±98.86^{cA}	647.20±114.42^{bcB}
	STZ+ETH500	938.00±161.35^{a*}	1 014.20±123.34^{a**}	1 099.00±101.00^{a}	1 138.00±61.99^{a}
Series 3	Control	793.60±59.95^{ab}	568.60±70.49^{b}	843.80±89.61^{ab}	1 122.00±61.66^{ac}
	STZ	1 200.00±0.00^{a**}	1 200.00±0.00^{a***}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a**}	1 045.25±106.17^{a**}	1 151.00±49.00^{a}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a**}	754.00±162.51^{bB}	880.75±133.93^{b}	1 200.00±0.00^{ac}
	STZ+AQ100	1 099.60±100.40^{a}	1 073.60±126.40^{a***}	1 013.60±117.50^{a}	1 069.00±131.00^{a}
	STZ+AQ500	1 102.60±88.89^{a}	1 110.00±82.14^{a***}	1 072.20±116.64^{a}	1 109.80±82.33^{a}
	STZ+ETH100	1 154.00±36.34a**	715.60±98.19^{a*}	668.40±106.66^{aB}	767.20±142.53^{a}
	STZ+ETH500	1 049.40±103.63^{a}	1 161.40±38.60^{a***}	1 200.00±0.00^{a*}	1 200.00±0.00^{a}
Series 4	Control	1 025.80±89.98^{a}	1 066.80±82.12^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a*}	970.00±138.11$^{a\beta}$	1 075.75±124.25^{a}	1 200.00±0.00^{a}
	STZ+AQ100	1 157.80±42.20^{a}	1 131.40±68.60^{a}	1 108.40±91.60^{a}	1 134.80±65.20^{a}
	STZ+AQ500	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ETH100	1 200.00±0.00^{a*}	951.80±122.49^{a}	740.20±98.86^{a}	1 028.60±947.60
	STZ+ETH500	1 200.00±0.00^{a*}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
Series 5	Control	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ Sildenafil	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+TMAO	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+AQ100	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+AQ500	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ETH100	1 200.00±0.00^{a}	1 079.00±58.94^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}
	STZ+ETH500	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}	1 200.00±0.00^{a}

Values of post-ejaculatory interval are means±SEM (n=6).

changes in the testicular morphology and the alteration of spermatogenic process which were corrected by *D. arborea* treatment[31]. The main objective of this work was to evaluate the effect of *D. arborea* on the sexual behavior of 4 weeks hyperglycemic rats. In the present work, we show that an intraperitoneal injection of streptozotocin to rats always brought out severe hyperglycemia. However, the minor drop of glycemia observed 4 weeks after various treatments is of less importance since all recorded glycemic values were within the range of the pre-defined glycemic status (>200 mg/dL).

As expected, an impairment of the sexual function of the untreated diabetic rats was noticed under diabetic condition; this sexual dysfunction was indicated by a significant decrease in the sexual performance/vigor parameters (frequency of mounts and intromission) whereas an increase in the sexual motivation parameters (latency of mount and intromission, post-ejaculatory interval) was observed. It is known that diabetes has the potential to impact all components of the erectile response in patients and in the streptozotocin-induced diabetic rat model. These deleterious effects of diabetes in the copulatory activity of rats could be due to the impairment in smooth muscle relaxation leading to the decrease of the arterial inflow in

the penile circulation and corpora cavernosa, resulting to the down-regulation of the neuronal and endothelial isoforms of nitric-oxide synthase[12,32,33].

Treatment of diabetic rats with sildenafil citrate, TMAO, aqueous (500 mg/kg) and ethanol (100 mg/kg) extracts of *D. arborea* enhanced the behavioural parameters impaired under diabetic condition. Sildenafil citrate, a standard drug against erectile dysfunction (ED), was the most active in this study. This beneficial effect of Sidenafil citrate on rat copulatory activity may firstly be attributed to its steroidogenic activity since it was demonstrated that, inhibition of phosphodiesterase activity during prolonged sildenafil treatment increased serum testosterone level and Leydig cells' steroidogenic capacity by coordinated stimulatory action on cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) signaling pathways[34]. Moreover, sildenafil citrate for erectile dysfunction is effective through an increased percentage of successful attempts at intercourse and well tolerated among men with type 1 diabetes[35]. Also, it is reported that acute and chronic administrations of sildenafil may improve endothelium-dependent cavernosal relaxations and erectile functions when altered by various pathophysiological mechanisms such as diabetes and, the antioxidant properties of this drug may be responsible for these effects[36-41].

Several findings have shown that oxidative stress has a relevant role in the pathophysiology of diabetic erectile dysfunction and provides a rationale for the use of antioxidant therapy in the treatment of erectile dysfunction in diabetes[42]. Many chemicals molecules are known to possess antioxidant potentials responsible for the regulation of the endothelium dysfunction induced by oxidative stress through the regeneration of antioxidant enzymes[43,44]. Trimethylamine N-oxide (TMAO), a chemical chaperone used in this work could also enhanced the sexual behavior of diabetic rats through its antioxidant properties since Lupachyk and collaborators demonstrated that TMAO attenuated endoplasmic reticulum stress, peripheral nerve dysfunction, intraepidermal nerve fiber loss, and sciatic nerve and spinal cord oxidative-nitrative stress in streptozotocin diabetic rats[45].

The enhancement of the sexual behavior observed in diabetic rats after *D. arborea* application (increase in sexual performance associated to a decrease of the motivation parameters) is indicative of the aphrodisiac potential of this plant[46,47]. Phenols, flavonoids, saponins and phytosterols revealed in these extracts, could be responsible of this sexual improvement. Many studies have shown that flavonoids and phenols are capable of relaxing the corpus cavernosum of both normal and diabetic rats[48-51]. Another possibility is that flavonoids may increase the level of testosterone, the main hormone that controls sexual behaviour[52,53]. As previously proposed in our earlier studies, sterols could again improve the sexual ability of the streptozotocin-diabetic rats through an androgenic pathway[54]. Similarly, saponin revealed in the plant extracts, which may belong to the steroidal family[55], could possess an androgen increasing property[20,27,56]. Many other plants or plant components are known to improve and protect erectile tissues from the oxidative stress-induced degeneration via an antioxidant mechanism[57,58]. Results obtained in this work are similar to those obtained by other authors[59,60].

With regard to the ejaculatory series, it appeared that the proposed treatments were more efficient during the first three ejaculatory series for both the frequency and latency of mounts and intromissions; this view could be pharmacologically explained by the exposure-response relationship during which a decrease in the response (effect) is recorded as the time is increased.

Our results confirmed that *D. arborea* extracts possess aphrodisiac property capable of alleviating erectile dysfunction caused by streptozotocin-induced diabetes in rats without having major anti-hyperglycemic effects. Bioactive components such as phenols, saponins, flavonoids and sterols present in this plant could be useful molecules for the treatment of erectile dysfunction in severe diabetic patients; however, further investigations using long-term diabetic rats need to be conducted in order to better appreciate the efficiency of this plant.

Conflict of interest statement

We declare that we have no conflict of interest

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