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Comparative anti-hyperglycemic effects of the aqueous extracts of *Combretum molle* twigs in rats

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ABSTRACT

Aim: To evaluate the antidiabetic properties of the aqueous extracts of *Combretum molle* twigs in rats.

Methods: For the anti-hyperglycemic tests, the extracts at doses of 125, 250, and 500 mg/kg were administered orally to the normal rats and their glycemia was evaluated every 30 minutes during 4 hours. Type 1 diabetes was induced by the intra-peritoneal injection of alloxane (150 mg/kg) in rats. Type 2 diabetes was induced by the sub-cutaneous injection of the dexamethasone (1 mg/kg). Afterwards, animals were treated at doses 250 and 500 mg/kg of the decoction for 14 days (type 1 diabetes) and 8 days (type 2 diabetes). Body weight, glycemia, lipid parameters, and atherogenic index were evaluated.

Results: The decoction (250 mg/kg) produced a significant ($p < 0.05$) decrease in the postprandial glycemia at 90 minutes. However, at 120 minutes, a significant regulation of the blood glucose was observed at the dose of 500 mg/kg of the decoction ($p < 0.01$), maceration ($p < 0.05$), and infusion ($p < 0.05$). In addition, the doses 250 and 500 mg/kg of the decoction of *C. molle* prevented a significant reduction in body weight, hyperglycemia, and dyslipidemia, and a significant increase in atherogenic index, which were observed in the type 1 and 2 diabetic subjects.

Conclusion: The decoction was showed the greatest hypoglycemic and anti-hyperglycemic activities, thereby confirming his ethnopharmacological use of this extract in the management of diabetes mellitus.

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KEYWORDS

Combretum molle; diabetes mellitus; lipid profile; aqueous extracts; Wistar rats

Introduction

Diabetes mellitus is a metabolic disease responsible for the major problems of public health. It is a chronic disease that occurs when blood glucose is elevated at a rate greater than or equal to 1.26 g/l. Hyperglycemia can result in either pancreatic dysfunction, unable to produce enough sugar degradation loaded insulin in the body, either by defects of cellular uptake of glucose [1]. The rate of diabetes has increased dramatically in the last 35 years worldwide. Indeed, in 1980 nearly 108 million patients were recorded [2]. This rate was 422 million in 2014, representing 8.5% of the world population and will reach more than 438 million in 2030 or 8.82% of the world's population [3]. Deaths related to diabetes were 1.5 million in 2012 and will reach 3.7 million in 2040 [4]. Uncontrolled permanent hyperglycemia leads over time to degenerative and infectious complications. Some pharmaceutical treatments also reduce the impact of the disease and its complications. The purpose of these treatments is to reduce hyperglycemia by activating the

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endogenous insulin secretion with sulphonylureas and glitinides or improving the sensitivity of target tissues to insulin with thiazolidinediones and biguanides [5]. Unfortunately some of these products are costly and have adverse side effects on the health of patients. Given these limitations, the majority of the population converges to herbal medicine [6].

In this study, our choice fell on *Combretum molle*, graceful deciduous shrub 3–13 m in height, generally widespread in tropical Africa and used by African traditional healers as an antidiabetic, anti-inflammatory, antioxidant, and antimicrobial [7,8]. Several antidiabetic studies have already been conducted on this plant [9–11]. However, no previous antidiabetic studies have been performed on the aqueous extracts of *C. molle* twigs. The objective of this study is to assess the hypoglycemic and anti-hyperglycemic properties of the aqueous extracts of *C. molle* twigs in the rat.

Materials and Methods

Ethics approval

All animal procedures were conducted with strict adherence to the NIH Guide for the care and use of Laboratory Animals (NIH Publication #85-23 Rev. 1985).

Chemicals and drugs

Alloxan and kits for biochemical dosages were purchased from Sigma-Aldrich, St. Louis, USA. D-glucose was purchased from Edu-Lab Biology Kit, Bexwell, Norfolk PE38 9GA, UK. All chemicals and drugs were obtained commercially and were of analytical grade.

Harvest and identification of plant material

The plant material consisted of *C. molle* twigs, harvested in the month of December 2012 in Moutourwa, situated at about 55 km from Maroua-Cameroon. The harvested species was authenticated at the Cameroon Herbarium of where it was registered under N° CNH 433724. Once harvested, the twigs were cut into small pieces, washed with tap water, and dried in the open air, protected from the sun and then crushed with a mill until a fine powder is obtained.

Preparation of aqueous extracts

Decoction: 200 g of *C. molle* powder was added to 500 ml of distilled water and the whole content was boiled for 15 minutes. After cooling, the mixture was filtered with Whatman No.1 filter paper. The filtrate obtained was evaporated in an oven for 72 hours at a temperature of 45°C, resulting in 19.69 g of crude extract, i.e., a yield of 9.64%.

Maceration: 200 g of *C. molle* powder was macerated in 500 ml of distilled water and left in a sealed jar for 24 hours. Subsequently, this mixture was filtered and the filtrate obtained was evaporated in an oven under the same conditions as in the preceding case, which made it possible to obtain 26 g of crude extract, i.e., a yield of 13%.

Infusion: 200 g of *C. molle* powder was added to 500 ml of distilled water previously heated to boiling for 15 minutes. The whole content was left in a sealed jar for 30 minutes and then filtered as before. The filtrate obtained was evaporated in an oven under the same conditions as in the preceding cases, resulting in 23.74 g of crude extract, i.e., a yield of 11.93%.

Qualitative phytochemical tests

The phytochemical screening was done using conventional laboratory methods described by Vijayalakshmi and Ravindhran [12]. Indeed, Dragendorff's reagent was used to alkaloids, chloroform, and ammonia to glycosides, $FeCl_3$ to tannins, plomb acetate to phenols, ammonium hydroxide to flavonoids, chloroform and concentrated sulfuric acid to terpenoids, concentrated sulfuric acid to quinones, and distilled water to saponins.

Experimental animal

Male Wistar rats aged 12 to 16 weeks and having an average weight of 250 g were used. These animals were raised in the animal house of the Department of Animal Biology of the Faculty of Science at the University of Dschang in polypropylene cages under ambient temperature, natural light conditions, and under sufficient ventilation. They received daily drinking water and standard diet *ad libitum*.

Anti-hyperglycemic activity of the extracts of C. molle in normal rats

Sixty-six rats were fasted for 16 hours and then divided into 11 groups of six rats each and treated orally as follows [13]:

- Group 1 received 10 ml/kg of distilled water;
- Group 2 received glibenclamide at the dose of 0.3 mg/kg of body weight (b.w.);
- Groups 3, 4, and 5 received the maceration at the respective doses of 125, 250, and 500 mg/kg b.w.;

- Groups 6, 7, and 8 received the infusion at the respective doses of 125, 250, and 500 mg/kg b.w.;
- Groups 9, 10, and 11 received the decoction at the respective doses of 125, 250, and 500 mg/kg b.w.

After ninety minutes, 3 g/kg of D-glucose was administered orally to animals. Blood glucose was taken from tail vein of rats and blood glucose levels were determined by a glucose meter (OneTouch UltraMini). The variation in blood glucose was evaluated at time t_0 and every 30 minutes for 2 hours.

Effects of the decoction of C. molle twigs on insulin resistance and type 1 diabetes

Induction of insulin resistance and treatment of animals

Twenty-five rats were divided into groups of five rats each and daily treated orally for 10 days [14]:

- Group 1 (normal control) received 10 ml/kg of NaCl 0.9%;
- Group 2 (diabetic control) received 10 ml/kg of NaCl 0.9%;
- Group 3 (positive control) received 40 mg/kg of metformin;
- Groups 4 and 5 received the decoction at the respective doses of 250 and 500 mg/kg.

One hour after the above pretreatment, the rats of groups 3–5 received 1 mg/kg of dexamethasone subcutaneously each, except those of groups 1 and 2 of which received 1 ml/kg of NaCl 0.9 % each by the same route.

The body weight and fasting blood glucose of rats were taken on days 0 and 10 of the experiment.

Induction of type 1 diabetes and treatment of animals

Type 1 diabetes was induced by intraperitoneal injection of alloxane solution (150 mg/kg) [15]. Seventy-two hours later, blood glucose was evaluated and rats with a higher or equal blood glucose level to 200 mg/dl were considered diabetic.

Animals were randomly divided into five groups (five rats/group) and orally treated for 14 days as follows:

- Group 1 (normal control) received 10 ml/kg of NaCl 0.9%;
- Group 2 (diabetic control) received 10 ml/kg of NaCl 0.9%;
- Group 3 (positive control) received 2.5 mg/kg of glibenclamide;
- Groups 4 and 5 received the decoction at doses of 250 and 500 mg/kg.

The blood glucose and body weight of the animals were measured on days 1, 7, and 14 of the experiment.

Blood sampling

At the end of the treatment period, animals were fasted overnight, anesthetized with ketamine (10 mg/ml)/diazepan (5 mg/ml) and then dissected. The blood was collected by catheterization of the abdominal artery and placed in tubes without anticoagulant and then left for 1 hour at rest and centrifuged at 3,000 rpm for 15 minutes. The supernatant was used for the determination of the lipid parameters.

Determination of lipid parameters

The cholesterol assay was performed following a colorimetric enzymatic method described by Trinder using the Dialab kit [16]. The high-density lipoprotein cholesterol (HDL-C) assay was analysed by the method described by Weibe and Warnick [17] with Inmesco kit. The following triglyceride level was determined by enzymatic colorimetric method described by Cole et al. [18] with the Dialab kit. The low-density lipoprotein cholesterol (LDL-C) was deduced from the other lipids previously obtained [19].

Statistical analysis

All results were expressed as mean ± standard error of mean. The data were analyzed using Graph Pad Prism Version 5.01. The two-way analysis of variance followed by the Bonferroni *post hoc* test were used for the treatment of double-variable tests and the one-way analysis of variance followed by the Turkey's *post hoc* test were used to analyze the single-variable test data. Differences were considered as significant at the p values of 0.05.

Results

Results in Table 1 show that the classes of chemical compounds such as tannins, phenols, flavonoids, saponins, terpenoids, and glycosides were present in decoction, maceration, and infusion. The alkaloids are absent in the three extracts while the quinones are present in the decoction but absent in maceration and infusion.

The anti-hyperglycemic activity of aqueous extracts of *C. molle* on the variation in postprandial glycemia is shown in Table 2. Compared to normal control group, glibenclamide has caused a significant decrease of blood glucose at the 60th, 90th,

and 120th minute post gavage ($p < 0.01$). Similarly, the doses of 250 and 500 mg/kg of the decoction significantly decreased the glycemia at 90 and 120 minutes, respectively ($p < 0.05$ and $p < 0.01$). The dose 500 mg/kg of infusion produced a significant decrease of blood glucose at the 120th minute ($p < 0.05$). The decoction at the doses of 250 and 500 mg/kg showed a higher anti-hyperglycaemic activity in normal rats. Therefore, decoction would be the most active aqueous extracts and will be used in antidiabetic tests.

Table 1. Phytochemical screening of aqueous extracts twigs of *C. molle*.

Chemical compounds	Decoction	Maceration	Infusion
Tannins	+	+	+
Phenols	+	+	+
Flavonoïds	+	+	+
Saponins	+	+	+
Quinones	+	–	–
Terpenoides	+	+	+
Alkaloids	–	–	–
Glycosides	+	+	+

+: présence, –: absence.

The results presented in Table 3 show the evolution of the relative body weight in insulin resistance rats. Indeed, the body weight of the animals having received the different treatments remained similar during the 10 days of the experiment. However, only the diabetic control group showed a significant decrease in body weight on 9th ($p < 0.05$) and 10th day ($p < 0.01$) of treatment.

Figure 1 shows the variation of glycemia in insulin resistance animals. A significant increase of the blood glucose was recorded on day 10 in the diabetic group, compared to the normal control group ($p < 0.001$). However, metformin and decoction at doses of 250 and 500 mg/kg resulted in a significant decrease of the glucose level to the 10th day of treatment, compared to the diabetic group ($p < 0.001$).

Table 4 shows the effects of the decoction of *C. molle* on the lipid profile in rats. Dexamethasone animals showed a significant increase in total cholesterol ($p < 0.01$), triglycerides ($p < 0.001$) and LDL-C ($p < 0.001$), and a significant ($p < 0.001$) decrease on the HDL-C level, compared to the normal control group. Compared to the diabetic group, metformin induced a significant ($p < 0.001$) increase in HDL-C

Table 2. Anti-hyperglycemic effect of aqueous extracts twigs of *C. molle* in normal rats.

Groups	Dose (mg/kg)	Glucose level (mg/dl)				
		0 minute	30 minutes	60 mintues	90 minutes	120 minutes
Control	–	87.50 ± 1.95	138.33 ± 3.57	143.00 ± 1.63	130.00 ± 2.21	113.67 ± 3.07
Gliben	0.3	81.83 ± 1.14	118.67 ± 4.11	114.67 ± 2.01**	101.50 ± 4.48**	85.17 ± 3.18**
Decoction	125	80.83 ± 2.36	130.33 ± 2.93	126.17 ± 2.80	113.00 ± 2.02	103.83 ± 1.78
	250	79.17 ± 2.09	129.33 ± 2.75	128.50 ± 2.59	105.50 ± 2.70*	86.83 ± 2.80*
	500	77.67 ± 2.60	119.50 ± 3.38	118.50 ± 1.60	103.50 ± 3.03*	81.83 ± 2.54**
Infusion	125	80.50 ± 2.63	126.33 ± 1.94	131.33 ± 2.86	116.67 ± 4.90	99.83 ± 2.71
	250	82.50 ± 2.23	125.66 ± 2.23	136.00 ± 0.82	116.50 ± 1.54	97.67 ± 2.33
	500	82.16 ± 1.11	126.83 ± 2.69	128.50 ± 3.22	121.00 ± 2.21	92.17 ± 2.10*
Maceration	125	82.00 ± 2.22	136.00 ± 2.94	127.33 ± 2.99	125.17 ± 3.74	95.83 ± 3.95
	250	83.83 ± 1.64	136.83 ± 3.46	127.00 ± 1.21	123.50 ± 2.59	103.67 ± 2.14
	500	81.67 ± 2.75	129.33 ± 2.75	130.50 ± 2.49	124.66 ± 3.40	98.83 ± 1.74

Each value is expressed as mean ± S.E.M. ($n = 6$). Data analysis was performed by two-way ANOVA followed by Bonferroni's *post-hoc* test. *$p < 0.05$; **$p < 0.01$ significantly different when compared to the normal control group. Gliben: glibenclamide.

Table 3. Effect of the decoction of *C. molle* twigs on the relative body weight in type 1 diabetes and insulin resistance rats.

Groups	Body weight (g)				
	Insulin resistance rats		Type 1 diabetes rats		
	Day 0	Day 10	Day 0	Day 7	Day 14
Normal control	227.20 ± 11.53	259.20 ± 12.61	192.00 ± 9.06	199.79 ± 9.40	209.32 ± 9.40
Diabetic control	221.80 ± 12.16	219.20 ± 13.07**	232.00 ± 9.32	237.03 ± 9.24	243.89 ± 9.24**
Positive control	226.00 ± 7.46	248.20 ± 7.73	226.60 ± 9.17	234.49 ± 8.04	243.94 ± 8.60
Decoction 250 mg/kg	248.00 ± 3.39	266.60 ± 2.54	184.75 ± 14.31	192.36 ± 13.44	198.54 ± 14.97
Decoction 500 mg/kg	249.00 ± 3.13	275.00 ± 3.33	192.36 ± 13.44	249.00 ± 3.13	265.00 ± 3.63

Each value is expressed as mean ± S.E.M. ($n = 5$). Data analysis was performed by two-way ANOVA followed by Bonferroni's *post-hoc* test. **$p < 0.01$ significantly different when compared to the normal control group.

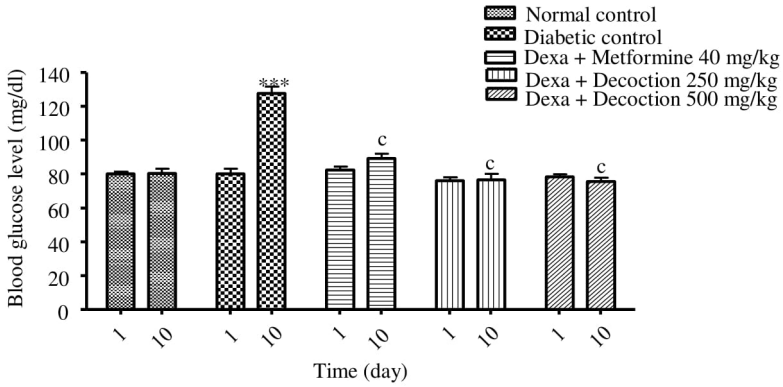

Figure 1. Effect of the decoction of *C. molle* twigs on the relative body weight in insulin resistance rats. Each value is expressed as mean ± S.E.M. (n = 5). Data analysis was performed by two-way ANOVA followed by Bonferroni's *post-hoc* test. **p < 0.01 significantly different when compared to the normal control group. Dexa: dexamethasone.

Table 4. Effect of extract on the lipid parameters in insulin resistance rats.

Groups	CT (mg/dl)	TG (mg/dl)	HDL-C(mg/dl)	LDL-C(mg/dl)
Normal control	110.95 ± 0.94	80.18 ± 2.95	57.65 ± 2.19	37.26 ± 2.05
Diabetic control	127.03 ± 1.40**	101.79 ± 4.79***	34.91 ± 3.30***	71.76 ± 3.78***
Dexa + metformine 40 mg/kg	100.95 ± 2.21^{c}	76.05 ± 1.59^{c}	53.88 ± 2.19^{c}	31.85 ± 3.22^{c}
Dexa + decoction 250 mg/kg	116.08 ± 3.53^{a}	78.48 ± 1.28^{c}	51.93 ± 1.27^{c}	48.46 ± 4.47^{c}
Dexa + decoction 500 mg/kg	99.87 ± 4.98^{b}	75.51 ± 1.62^{b}	46.48 ± 5.93^{a}	38.28 ± 3.49^{b}

Each value is expressed as mean ± S.E.M. (n = 5). Data analysis was performed by one-way ANOVA followed by Turkey's *post-hoc* test. **p < 0.01; ***p < 0.001 significantly different when compared to the normal control group. ^{a}p < 0.05; ^{b}p < 0.01; ^{c}p < 0.001 significantly different when compared to the diabetic control group. CT: total cholesterol; TG: triglycerides.

and a significant (p < 0.001) decrease in serum total cholesterol, triglycerides, and LDL-C. A decrease in total cholesterol (p < 0.05), triglycerides (p < 0.001), and LDL-C (p < 0.001) was observed in animals treated with decoction (250 mg/kg). Similarly, a significant (p < 0.001) decrease in the lipid parameters was noted at 500 mg/kg. However, there was a significant increase in HDL-C at 250 (p < 0.001) and 500 mg/kg (p < 0.05).

At the first week of treatment, relative body weight of all type 1 diabetic animals remained similar (Table 3). At the second week, a decrease in body weight was observed in all treated groups as compared to the diabetic group. Indeed, in the diabetic control group, there was a significant decrease in body weight compared to the normal control group (p < 0.01). However, the relative body weight of the animals receiving glibenclamide and different doses of the extract remained superior to those of the diabetic group.

Compared to the normal control group, there was a significant increase (p < 0.001) in blood glucose throughout the treatment period in all groups of treated animals (Fig. 2). Compared to the negative control group, at the 2nd week, there was a significant (p < 0.001) decrease in blood glucose in subjects treated with glibenclamide and varoius doses of the extract.

Table 5 shows the effects of the decoction of *C. molle* on lipid parameters. In fact, the diabetic control group rats showed a significant (p < 0.001) increase in total cholesterol, triglycerides, and LDL-C, and a significant (p < 0.001) decrease in HDL-C compared to normal control batch. Similarly, the decoction (250 and 500 mg/kg) resulted in a significant increase in total cholesterol (p < 0.01; p < 0.05) and triglycerides (p < 0.01; p < 0.01), respectively. Compared to the diabetic group, the glibenclamide resulted in a significant (p < 0.001) decrease in total cholesterol, triglycerides, and LDL-C, and a significant (p < 0.01) increase in HDL-C. Similarly, the decoction resulted in a significant decrease in serum total cholesterol (p < 0.01; p < 0.001), triglycerides (p < 0.05; p < 0.01), and LDL-C (p < 0.001; p < 0.001), and a significant (p < 0.01; p < 0.001) increase in HDL-C at the respective doses of 250 and 500 mg/kg.

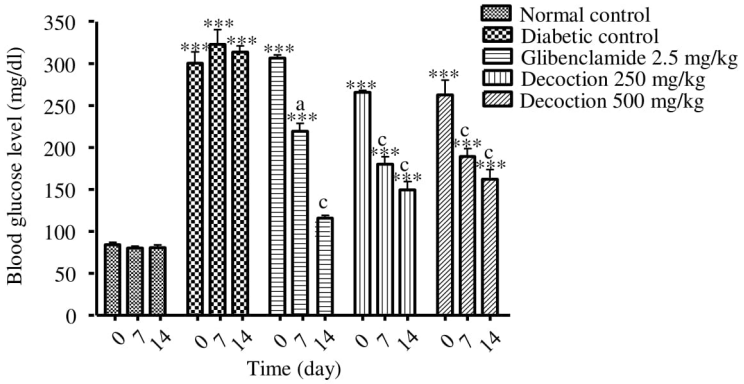

Figure 2. Effect of the decoction of *C. molle* twigs on blood glucose level in insulin resistance rats. Each value is expressed as mean ± S.E.M. (n = 5). Data analysis was performed by two-way ANOVA followed by Bonferroni's *post-hoc* test. $^{**}p < 0.01$ significantly different when compared to the normal control group. $^{c}p < 0.001$ significantly different when compared to the diabetic control group. Dexa: dexamethasone.

Table 5. Effect of extract on the lipid parameters in type 1 diabetic rats.

Groups	CT (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
Normal control	100.67 ± 1.62	83.98 ± 2.72	48.12 ± 4.75	35.76 ± 3.43
Diabetic control	129.56 ± 2.25***	119.67 ± 1.18***	35.89 ± 1.87***	76.73 ± 2.36***
Glibenclamide 40 mg/kg	108.19 ± 1.01^{c}	91.62 ± 1.31^{c}	49.21 ± 1.92^{b}	40.64 ± 0.77^{c}
Decoction 250 mg/kg	116.12 ± 2.15*^{b}	106.28 ± 3.07**^{a}	48.21 ± 3.81^{b}	46.66 ± 6.30^{c}
Decoction 500 mg/kg	111.88 ± 2.73*^{c}	103.67 ± 2.44**^{b}	51.32 ± 1.35^{c}	39.82 ± 4.00^{c}

Each value is expressed as mean ± S.E.M. (n = 5). Data analysis was performed by one-way ANOVA followed by Turkey's post-hoc test. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$ significantly different when compared to the normal control group. $^{a}p < 0.05$; $^{b}p < 0.01$; $^{c}p < 0.001$ significantly different when compared to the diabetic control group. CT: total cholesterol; TG: triglycerides.

Discussion

Phytochemical evaluation of aqueous extracts of *C. molle* twigs showed the presence of some antidiabetic compounds such as saponins, phenols, tannins, glycosides, flavonoids, and terpenoids.

Results from preliminary glucose tolerance test showed that only the decoction at dose(s) of 250 and/or 500 mg/kg resulted in a marked decrease in postprandial glucose compared to infusion and maceration. This leads us to assert that decoction is the most effective aqueous extract. In addition, doses 250 and 500 mg/kg are the most effective doses of this extract. These results corroborate those of Mahgoup et al. [20] which showed that the administration of the methanol extract of leaves of *Anogeissus leiocarpus* (Combretaceae) led to a significant drop in postprandial glucose in normal rats. The decrease in the glycemia observed is due to the presence in the extracts the compounds such as phenols, terpenoids, and flavonoids, which possess the remarkable anti-hyperglycemic properties [21,22].

The relative body weight of animals receiving dexamethasone decreased significantly from day 10 of treatment. These results support many studies that have reported that dexamethasone was able to lose weight [23]. Dexamethasone has lipolytic and proteolytic properties. Indeed, dexamethasone reduces the uptake of amino acids and protein synthesis in muscles and increase lipolysis in fat cells [24]. It is also a secretagogue of leptin, a hormone secreted by adipose tissue and involved in decreasing appetite [25]. However, metformin and the different doses of the decoction prevented this decrease by adversaries mechanisms to those of dexamethasone.

Compared to control diabetic group, the decoction and glibenclamide resulted in an increase in body weight of type 1 diabetic animals. The weight gain observed in subjects receiving substances with antidiabetic activity may be either due to insulin activity or due to insulin secretagogues activity [26]. Therefore, the extract would cause weight gain in diabetic rats by similar mechanisms.

Blood glucose level in rats treated with dexamethasone alone were found to be higher than in the normal control group. However, metformin and decoction resulted in decreased blood glucose level by counteracting the hyperglycaemic effects of dexamethasone. Indeed, the extract could act by reversing the translocation of glucose transporters

in the cell membrane to intracellular compartment, which increases the insulin sensitivity of peripheral tissues [27]. The extract could also inhibit gluconeogenesis and/or glycogenolysis of the liver, and lipolysis of dexamethasone-induced adipose tissue. Blood glucose lowering activity of the extract is due to the combined effects of bioactive present in the twigs of *C. molle*. This corrobotes the works of some researchers which have demonstrated that isolated glycosides of *C. molle* leaves possessed antidiabetic properties in rodents [9] and phenolic constituents, especially flavonoids, widely present in plants of *Combretum* genus are probably responsible for their antidiabetic activity [28].

The administration of the decoction for 14 days resulted in a significant and dose-dependent decrease in blood glucose as well as the glibenclamide. These results corroborate those obtained by Chika and Bello [29] which showed that the aqueous extract of *Combretum micranthum* leaves reduces blood glucose in type 1 diabetes rats. The recorded hypoglycemia could be explained by the presence in the extract of chemical compounds such as flavonoids, saponins, and trapeenoids which have the capacity to mimic the action of insulin or to stimulate its secretion by the pancreas β cells [30].

In this work, dyslipidemia was observed in diabetic control group. These results agree with those obtained by Jamkhande et al. [23] who observed an increased concentration in serum lipids in diabetic subjects. Moreover, Betterridge et al. [31] reported that insulin deficiency or insulin resistance may be responsible for hyperlipidemia. However, the extract improved the lipid profile by reducing the levels of total cholesterol, triglycerides, LDL-C, and increasing the HDL-C in animals. Since in adipose tissues, insulin has antilipolytic action by inhibiting hormone-sensitive lipase, the extract could either mimic the action of insulin or stimulate insulin synthesis. The extract probably acts by decreasing cholesterol biosynthesis specifically by decreasing the activity of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase and by increasing the activity of the Lecithin-Cholesterol Acyl Transferase [32]. The decoction reduced the triglyceride level either by decreasing fatty acid synthesis or by inhibiting the production of triglycerides precursors such as acetyl CoA and glycerol phosphate [32]. In addition, several authors have reported that the secondary metabolites such as saponins, flavonoids, phenolic compounds, and triterpenoids have a hypolipidemic activity [33]. The lipid-lowering properties observed might be due to the different types of active secondary metabolites present in the extract of *C. molle*.

Conclusion

The decoction is the aqueous extract which has remarkable antihyperglycemic and hypolipidemic activities, confirming his ethnopharmacological use in the management of diabetes mellitus.

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