



## RESEARCH ARTICLE

## EFFECT OF THE AQUEOUS EXTRACT OF *CLERODENDRUM THOMSONIAE* LINN (*VERBENACEAE*) LEAVES ON TYPE 2 DIABETIC WISTAR RATS INDUCED BY THE MACAPOS1 TYPE DIET AND DEXAMETHASONE

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## Abstract

**Aim and objective:** *Clerodendrum thomsoniae* leaves are used in Cameroon to manage diabetes and its related disorders. The study aimed at investigating the antidiabetic effect of the aqueous extract on diet and dexamethasone induced diabetic rats.

**Methods:** Young mature leaves of *C. thomsoniae* were dried, finely powdered and submitted to aqueous extraction. The dehydrated extract was tested in rats at 3 doses 312.5, 625 and 1250 mg/kg based on the local use of the plant. The effect of the extract on the fasting blood glucose in normoglycemic rats and MACAPOS 1 type diet induced diabetic rats, using respectively glibenclamide and metformin as positive control groups, were investigated.

**Results:** AECT significantly reduced blood glucose levels in normoglycemic rats ( $p < 0.05$ ) two hours after administration, from  $83 \pm 2$  mg/dL to  $57.39 \pm 1.7$  mg/dL with the dose of 1250 mg/kg given the highest reduction rate of 30.86%. In normoglycemic rats 30 minutes after oral glucose overload, the maximum reduction rate was observed with glibenclamide 5 mg / kg and calculated at 49.90% followed by 36.39%, for the extract at 1250 mg/kg. After 30 days of repeated oral administration, AECT produced a reduction on blood glucose levels ( $p < 0.05$ ) in type 2 diabetic rats. This reduction in blood sugar was much more expressed with the dose of 1250mg/kg ( $73.52 \pm 0.71$  mg/dL) followed by metformin 38 mg/kg ( $70.21 \pm 0.89$  mg/dL) as the normal control with no significant difference ( $p < 0.05$ ).

**Conclusion:** These results show that the antidiabetic activity of AECT can be explained by insulin stimulating effect, also give support to the traditional use of this plant.

**Keywords:** Antidiabetic, aqueous extract, *Clerodendrum thomsoniae* leaves, Dexamethasone, hypoglycemic, MACAPOS 1 diet.

## INTRODUCTION

African populations use many plants to treat diabetes type 2 and related disorders, thanks to their diversified flora. Diabetes mellitus (DM) is a metabolic disorder due to insufficiency or improper use of insulin characterized by fasting blood sugar above  $1.26 \text{gL}^{-1}$  checked twice<sup>1</sup>. While the incidence of the disease is still on progress, with an estimated increase to 72% by year 2025 and an affected population of 472.6 million

by 2045, DM is more and more a global public health problem<sup>2</sup>. According to reported data, DM is mostly frequent in rural area and type 2 accounted for about 80% of all forms of DM in both sexes<sup>3,4</sup>. Type 2 DM is a chronic and progressive syndrome characterized by metabolic abnormalities such as insulin resistance and decreased pancreatic b-cell function that modifies fuel-sensing processes in the body<sup>5</sup>. DM is primarily treated with insulin and oral antidiabetic drugs such as biguanides, alpha glucosidase inhibitors, sulphonyl-

ureas and glinides<sup>6</sup>. These drugs do not only have negative side effects, but also are expensive, in particular for individuals in developing countries given their low purchasing power. In this respect the traditional pharmacopoeia offers a solution.

Since ancient times, more than 80% of the world population used plant extracts or any other form to treat many diseases including DM<sup>7,8</sup>. At least 12 000 plants in the world are used for medicinal purposes, but less than 10% of them are investigated from pharmacological point of view<sup>9</sup>. Many antidiabetic wild plant species have been investigated for their hypoglycemic activity<sup>10</sup> and actually recommended for therapeutic treatment of DM<sup>11</sup>. The anti-diabetic effects of plants have been attributed to their contents which include carotenoids, flavonoids, terpenoids, alkaloids, glycosides<sup>12</sup>. Amongst plants studied for their antidiabetic activities we may cite *Anacardium occidentale*<sup>13</sup>, *Allium sativum*<sup>14</sup>, *Allium cepa*<sup>15</sup>. Thought *Clerodendrum* sp. are granted strong therapeutic potentials<sup>16</sup>, *Clerodendrum thomsoniae* an ornamental plant<sup>16</sup> widely used by traditional healers in Ngaoundere-Cameroon to treat diabetes, has not yet been investigated. According to the literature, the plant leaves are traditionally used in the treatment of intestinal worms and other illnesses. In addition, the hypolipidemic, the antioxidant activity<sup>17</sup> and the toxicity<sup>18</sup> of the aqueous extract of the leaves were studied. The plant activity of the plant was attributed to its high flavonoid and tannin contents<sup>17</sup>.

The general objective of this work was to evaluate the hypoglycemic and antidiabetic activities of aqueous extracts of *C. thomsoniae* on type 2 diabetic rats induced by MACAPOS 1 type diet and dexamethasone.

## MATERIALS AND METHODS

### Sampling and production of *C. thomsoniae* extract

The plant material (leaves) was collected at Mbideng, a neighborhood of Ngaoundéré, in Adamawa region of Cameroon. The plant was identified at the national herbarium (N<sup>o</sup> Letouzey 11090 from the herbarium collection NO 28476/SRF/Yaoundé, Cameroon). Young mature leaves of the plant were carefully cleaned, sorted, graded according to size and dried in a ventilated electric turning dryer (brand Riviera & Bar) at 40±2°C for 48 h. After drying, the leaves were ground to make a fine powder using an electric grinder (Culatti, Polymix, France) equipped with a sieve of diameter 500 µm mesh.

### Preparation of *C. thomsoniae* aqueous extract

The obtained powder (2.5 g) was blended with 40 mL distilled water. The different mixtures were placed in a water bath at 70±2 °C and extracted for 30 min under stirring. The mixture was then cooled for 30 min and centrifuged at 1500 g for 15 min at 20°C using refrigerated centrifuge. The supernatant was collected and the residue was solubilized in 40 mL and re-extracted as mentioned above. The supernatants were combined and concentrated under vacuum in a rotary evaporator and dried in a desiccator at 40°C. The crude extract was weighed and used to prepare 31.25, 62.5

and 125 mg/mL aqueous extract of *C. thomsoniae* (AECT) corresponding to the 3 tested doses (312.5, 625 and 1250 mg/kg).

### Animal experiments

To conduct this experiment, healthy Wistar rats all male aged between 6 -8 weeks old and weighing about 150-200 g were raised in the animal house of the Faculty of Science of the University of Ngaoundéré (Cameroon) at an ambient temperature of 22±3°C and relative humidity of 54±2% under a 12 h/12 h light/dark cycle. The animals were acclimatized to laboratory condition for four days before the experiment starts and were fed with a standard diet made of casein as a protein source and tap water *ad libitum*. The experiment was carried out as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and ethically approved by the Institutional Committee of the Ministry of Scientific Research and Innovation of Cameroon (Phone: 00(237)699870979

### Effect of single oral administration of AECT in normal healthy rats

This study was done as reported by Kouambou *et al.*,<sup>19</sup> with some modifications. Twenty rats were divided into four experimental groups with five animals in each group: normal control (NC) rats that received only distilled water 10 mL/kg; 3 test groups as used by traditional practitioners (AECT312.5 mg/kg; AECT625 mg/kg; and AECT1250 mg/kg). For this study, administration of the aqueous extract was done by gavage using a 2.5 mL gavage probe. Blood samples were collected from the tail vein periodically at t=0, 60, 90 and 120 min after the administration of extract and the glucose content determined using glucose oxidase method.

### Oral Glucose Tolerance Test (OGTT) in normal Rats

The anti-hyperglycemic effect of the AECT at doses of 312.5, 625 and 1250 mg/kg was studied as described by Nkono *et al.*,<sup>20</sup> with some modifications. In this respect, 25 rats were fasted for 16 h and treated with the AECT (test groups), glibenclamide 5mg/kg (positive control group) and water (Normal control group, NC). At time 0 min, the animals were administered orally 10 mL of the extract, glibenclamide or water. After 30 min of the treatment, all groups received glucose (2.5 g/kg b.m) orally and the blood glucose concentrations were determined from the tip of a tail at time 0, 60, 90 and 150 min..

### Induction and Treatment of Hyperglycemia

#### Diabetes induction

Diabetes was induced in Rats using the MACAPOS 1 diet and dexamethasone according to Kamgang *et al.*,<sup>21</sup> with some modifications. In the procedure, healthy rats were divided in two groups. One group (normal control) was submitted to standard diet, another group was submitted per os to Sweetened high-calorie diet (SHCD) made of dextrose 0.8 g/kg (Gwardan Laviretteet Cie, Glucose pure Anhydre) and sucrose 4 g/kg (SOSUCAM, Bandjock-Cameroon) every two days. One month after the beginning of SHCD, the animals received the dexamethasone (25 µg/kg b.m i.m.) once every 2 days during 3 weeks. During the

induction period, fasting glycemia was estimated at the beginning and at the end to confirm the onset of diabetes. In this respect the oral glucose tolerance test (OGTT) was carried out by administration of 4g/kg b.m. of D-glucose in rats of different groups. Blood sugar was monitored for 120 min. The animals with fasting total blood glycemia  $\geq 126$  mg/dL were considered as diabetic and were selected for the next stage of experiment.

#### Evaluation of antidiabetic activity of AECT

The rats were organized into 6 groups of 5 animals each: normal control, negative control group made of diabetic rats receiving water, positive control group made of diabetic rats treated with Metformin (38 mg/kg b.m: Met38), test groups composed of diabetic rats treated with aqueous extract of *C. thomsoniae* doses 312.5, 625 and 1250 mg/kg b.m (AECT312.5, AECT625, AECT1250). The animals were treated once daily by intra-gastric gavages for 30 consecutive days. During the treatment, fasting glycemia was estimated at the beginning and every fifteen days. Other parameters such as food intake, water intake and change in body mass were also measured. At the end of treatment, OGTT and organ to body mass were

evaluated as previously described. In addition, animals were sacrificed and dissected and the visceral adipose, hepatic, cardiac and testicular tissues were removed, and weighed.

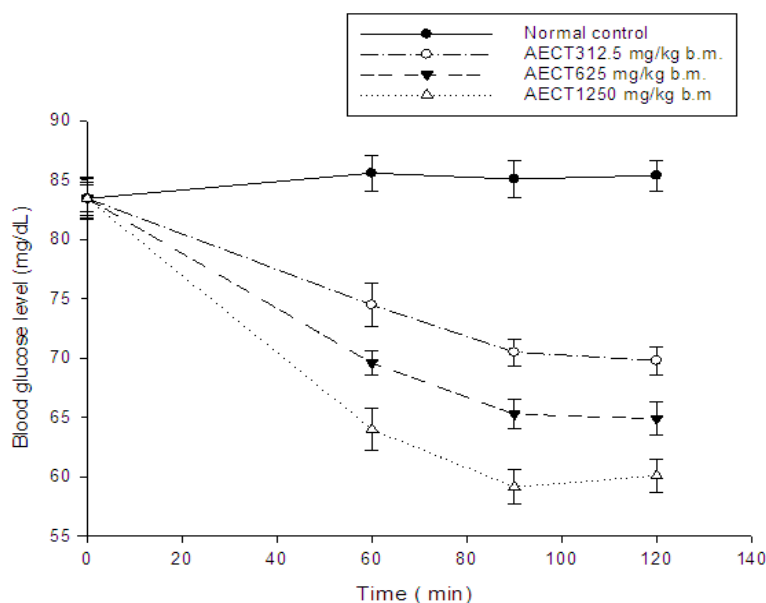
#### Statistical analysis

All data were expressed as mean  $\pm$  standard deviation and were statistically analyzed using one-way analysis of variance (ANOVA). When statistical differences were found, the Duncan's Multiple Range Test was applied in order to classify samples at the significance level of 5%. The Statgraphics Program (Statistically Graphics Educational, version 6.0, 1992, Manugistics, Inc. and Statistical Graphics Corp., USA) was used for the statistical analysis.

## RESULTS

### Hypoglycemic effect of aqueous extract of *C. thomsoniae* on normoglycaemic rats

The effect of AECT on blood glucose levels in fasting normal rats is presented in Figure 1. A single administration of AECT at all the doses exhibited a significant hypoglycemic effect after 2 hours ( $p < 0.05$ ).



**Figure 1: Effect of the aqueous extract of *C. thomsoniae* on blood glucose of normoglycemic rats.**

Value are means  $\pm$ SD (n=5) significantly different ( $p < 0.05$ ) as determined by Duncan's multiple range test. Normal: group of normal rats received distilled water; AECT312.5: group of rats receiving *C. thomsoniae* extract at dose of 312.5 mg/kg; AECT625: group of rats receiving *C. thomsoniae* extract at dose of 625 mg/kg; AECT1250: group of rats receiving *C. thomsoniae* extract at dose of 1250 mg/kg. b.m=body mass.

The extract at 1250 mg/kg produced the most significant reduction (29.1 %) ( $p < 0.05$ ) comparatively to the effect of the two others doses (15.5 %, 21.8 % respectively) 90 min after administration.

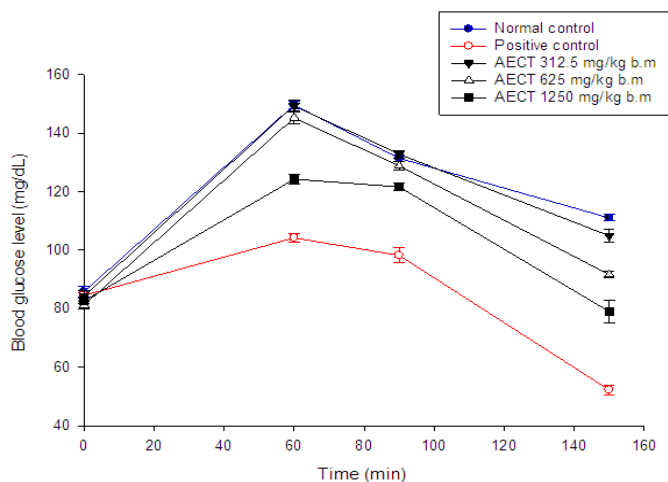
Consequently, blood sugar tended to stabilize until the 120<sup>th</sup> minute when there has been no significant change compared to the 90<sup>th</sup> minute regardless.

#### Effects of AECT on Glucose-Induced Hyperglycemia in normal rats

Blood glucose levels returned to baseline or even lower 2 hours after glucose administration in all animals. Animals treated with glibenclamide and AECT showed

decreases in blood glucose level 2 hours after glucose administration as shown in Figure 2. In particular, the rats receiving glibenclamide and AECT at 1250 mg/kg dose showed significant reductions in blood glucose level 30 min after glucose administration compared with the normal control rats.

In the acute test, the glucose load increased blood sugar in the normal control group. The basal glucose in rats in this group increased from  $85.8 \pm 2$  to  $149.6 \pm 1.43$  mg/dL at 30 min after glucose administration and returned to  $111.0 \pm 1.1$  mg/dL after 150 min.



**Figure 2: Effect of the aqueous extract of *C. thomsoniae* on oral glucose overload.**

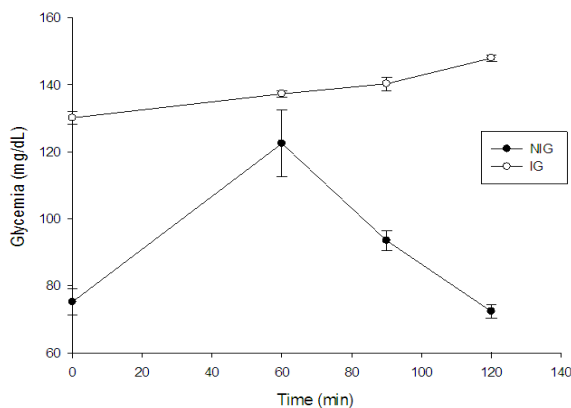
Value are means  $\pm$ SD (n=5) significantly different ( $p < 0.05$ ) as determined by Duncan’s multiple range test. Normal control: group of normal rats received distilled water; AECT312.5: group of rats received *C. thomsoniae* extract at dose of 312.5 mg/kg; AECT625: group of rats received *C. thomsoniae* extract at dose of 625 mg/kg; AECT1250: group of rats received *C. thomsoniae* extract at dose of 1250 mg/kg. Positive control: Group of rats received glibenclamide. AECT=Aqueous extract of *Clerodendrum thomsoniae*. b.m = body mass

Glibenclamide significantly prevented the rise in blood glucose throughout the experiment followed by AECT at dose of 1250 mg/kg.

**Oral glucose tolerance test at the end of induction of type 2 diabetes**

Figure 3 shows the glycemic response of rats submitted to sweetened high-calorie and dexamethasone regime

and compared to normal rats. OGTT in normal rats resulted in an increase in blood sugar at 60 min (122.50 mg/dL), then a decrease within 120 min to an identical value (72.33 $\pm$ 2.80 md/dL) at baseline blood sugar. In diabetic rats, the glycemia significantly linearly increased ( $p < 0.05$ ) from 130 $\pm$ 2 to 148 $\pm$ 2 mg/dL, passing by a value of 137.33 mg/dL at 60 min.



**Figure 3: Change in blood sugar after an oral overload of a glucose solution at the end of induction period (4g/kg b.m).**

NIG: Non-Induced Group; IG: Induced Group; min: minute; The means are significantly different ( $P < 0.05$ ); Values were expressed as mean $\pm$ standard deviation; n = 5.

**Diabetes treatment**

**Effect of *C. thomsoniae* extract on fasting glucose in type 2 diabetic rats**

Table 1 presents the effect of AECT on blood glucose level during each period of 15 days on normal and type 2 induced diabetic rats for 30 days experimental period. Administration of Sweetened high-calorie diet (MACAPOS 1) led to an increase in the blood glucose levels in induced rats compared to those of normal control. However, 30 days treatment with AECT at the three doses resulted to a marked decrease in blood glucose. For diabetics’ rats receiving placebo, glycemia remained very high compared to the normal control (128 $\pm$ 2,6 vs 74.2 $\pm$ 1.92 mg/dL). The glycemia of test groups treated AECT decreased whatever the dose (- 22.14 $\pm$ 1.67 %; - 24.73 $\pm$ 1.1 %; -43.90 $\pm$ 1.73 % and -

44.9 $\pm$ 1.35 %) respectively for AECT312.5, AECT625, AECT1250) and metformin. The reductions were significant ( $p < 0.05$ ) compared to the negative control. The observed decrease was more pronounced with the treatment AECT at dose 1250 mg/kg, leading to a glycemia comparable to that of normal control group the 30<sup>th</sup> day (73.5 $\pm$ 0.7 and 74.2 $\pm$ 1.9 mg/dL respectively). No significant ( $p < 0.05$ ) difference was observed between normal control, positive control and test group AECT dose 1250 mg/kg at the end of treatment.

**The Effects of aqueous extract of *C. thomsoniae* on gain in body mass, water intake, food intake and glycemia parameters in induced type 2 diabetic rats**

The Effects of aqueous extract of *C. thomsoniae* on change in body mass, water intake, food intake



parameters on induced type 2 diabetic rats are summarized in Table 1. During 30 days of the treatment of diabetic rats, the body mass of rats in positive control group (PC) and test groups irrespective of the dose gradually decreased at the end of the treatment, these groups also showed significant reductions ( $p < 0.05$ ). The drop in body mass was higher with the extract at the dose 1250 mg/kg and metformin (respectively  $-16.07 \pm 10.00$  g and  $-18.39 \pm 4.74$  g). It has also been observed a significant reduction in food intake and water intake in groups administered AECT as compared to the diabetic group (NC) ( $p < 0.05$ ).

#### Assessment of abdominal fat at the end of treatment

The effects of AECT administration on the abdominal fat of diabetic rats are presented in Figure 4. It appears from this figure that the relative mass of abdominal fat decreased during treatment. Administration of AECT reduced abdominal fat with the magnitude increasing with the dose with 1250 mg/kg inducing reduction 64.52% while reduction in Metformin group was 59%.

## DISCUSSION

Plants have always been the major source of drugs, thanks to their content in secondary metabolites<sup>22,23</sup>. In this vein, thousands of plants are traditionally used for the treatment of diabetes mellitus and its complications, however to the best of the knowledge, no study has been conducted on the hypoglycemic and antidiabetic properties of AECT *in vivo*. The effect of the AECT on normoglycemic animals suggested that the leaves of *C. thomsoniae* has a mild lowering effect on normal glucose levels. This effect was comparable to that of glibenclamide, an insulin secretagogue, which also lowers blood glucose in normal animals. Provided the  $\beta$ -cells are fully functional, sulphonylureas, such as glibenclamide, can cause hypoglycemia since insulin release is initiated even when glucose concentrations are below the normal threshold for glucose stimulated insulin release (approximately 5 mmol/L or 90 mg/dl)<sup>24</sup>. The results of this study showed a dose-dependent hypoglycemic activity of the aqueous extract of *C. thomsoniae* in normoglycemic rats. These results also suggested that the hypoglycemic effect may be due to water-soluble compounds. It has been established by many studies that the genus *Clerodendrum* is rich in total phenolic compounds, flavonoids, terpenoids, alkaloids, tannins, saponosides and anthraquinones<sup>25,26</sup>. Our previous studies also revealed that AECT contains these secondary metabolites<sup>17</sup>. As reported by Mamadou<sup>27</sup>, the lowering blood glucose property of *Clerodendrum capitatum* is dose dependent and based to its level in secondary metabolites. OGTT measures the ability of the body to stabilize the blood glucose to its normal level. The glycemic status of rats was shown to improve as the AECT dose increased in a dose-dependent manner. OGTT study revealed diabetic rats treated AECT and glibenclamide exhibited significant ( $p < 0.05$ ) improvements in their blood glucose levels, with the effect being more effective as the dose of AECT increased. The antihyperglycemic activity of the

aqueous extract suggested that *C. thomsoniae* extract contains compounds with a mechanism of action that may be similar to that of glibenclamide. Therefore, AECT may be considered insulin-secreting agent which stimulates the beta cells of the Langerhan islets of the pancreas for insulin production. According to Arumugam *et al.*,<sup>28</sup>, plants may act as antihyperglycemic agent through two mechanisms: increasing insulin secretions or reducing intestinal absorption of glucose. These activities may be associated to their content in some bioactive components revealed earlier in the plant extract<sup>17</sup>. The role of polyphenols in the complexation, and therefore inhibition of  $\alpha$ -glucosidase and  $\alpha$ -amylase has been pointed as a mechanism involved in hypoglycemic effect of some plants<sup>29</sup>.

In the current work, a relative stability was found in blood glucose in the diabetic control group which may be due to the insulin resistance very often encountered in obese or type 2 diabetes<sup>30</sup>. However, oral administration of AECT exhibited significant increase in blood glucose levels. Current results indicated that AECT dose 1250 mg/kg significantly ( $p < 0.05$ ) reduced the level of blood glucose within the third and fourth week of the experimental period. This result strongly supports the antidiabetic property of AECT. However, increasing insulin secretion and maintaining its level within the normal physiological range are very important for antidiabetic therapy. In this experiment, hyperglycemia induced in 10 weeks by the combined effect of MACAPOS 1 type diet and dexamethasone was associated with increase food intake and water intake body mass. Current results are in accordance with many other<sup>31</sup>. Glucocorticoids are known to have particularly significant metabolic side effects on carbohydrate metabolism<sup>32</sup>.

Dexamethasone (exogenous glucocorticoid) provokes the insulin resistance thereby induces chronic hyperglycemia and other metabolic disorders such as increase neo-glucogenesis from amino acid and glycerol in the liver, and lipolysis in adipocytes<sup>33</sup>. Dexamethasone also acts by inhibiting the gene expression of adiponectin, a hormone produced by adipocytes which promotes insulin resistance through dysfunction of hormone receptor in the liver, muscle and adipose tissue<sup>34,35</sup>. Fortunately, AECT significantly ( $p < 0.05$ ) decreased blood sugar levels of diabetic rats to normal value with a maximum decrease observed with the highest dose of AECT 1250 mg/kg dose. This result suggested that AECT may act among others like metformin, by decreasing hepatic glucose production and ameliorating the peripheral insulin sensitivity<sup>36</sup>.

This further indicates the role phytochemicals present in AECT which need investigations in order to identify the molecules responsible for the activity observed. In anticipation, flavonoids have been shown to improve the sensitivity to insulin and thereby reduced the incidence of type 2 diabetes<sup>37,38</sup>. Concerning abdominal fat, AECT reduce the quantity in a dose-dependent manner with the highest reduction observed at 1250 mg/kg of AECT compared to the group of rats treated with metformin.

Table 1: Parameters measured during treatment.

Parameters	Water intake			Food intake			Changes in body mass			Glycemia		
	D0	D15	D30	D0	D15	D30	D0	D15	D30	D0	D15	D30
Normal	136±0.71 <sup>a</sup>	129.28±0.84 <sup>b</sup>	129.71±1.92 <sup>b</sup>	91.74±0.71 <sup>a</sup>	78.51±0.84 <sup>b</sup>	77.93±1.92 <sup>b</sup>	212.2±10.9 <sup>a</sup>	222.5±8.8 <sup>e</sup>	226.6±1.4 <sup>ac</sup>	75.00±0.71 <sup>a</sup>	74.8±0.84 <sup>a</sup>	74.2±1.92 <sup>a</sup>
NC	264±1.22 <sup>a</sup>	255.8±3.97 <sup>b</sup>	255±2.61 <sup>b</sup>	135.96±1.22 <sup>a</sup>	124±3.97 <sup>b</sup>	123.00±2.61 <sup>b</sup>	261.8±11.1 <sup>ab</sup>	255.9±4.4 <sup>d</sup>	249.3±3.6 <sup>b</sup>	131±1.22 <sup>b</sup>	131.00±3.97 <sup>b</sup>	128±2.61 <sup>b</sup>
PC	262±1.67 <sup>a</sup>	136.28±1.14 <sup>ab</sup>	131.85±0.89 <sup>ac</sup>	135.88±1.67 <sup>a</sup>	76.93±1.14 <sup>b</sup>	75.32±0.89 <sup>b</sup>	257.2±15.1 <sup>ab</sup>	233.7±8.3 <sup>b</sup>	219.3±6.7 <sup>a</sup>	131±1.67 <sup>b</sup>	121.00±1.14 <sup>ab</sup>	70.2±0.89 <sup>a</sup>
AECT312.5	269±1.14 <sup>a</sup>	135.71±0.84 <sup>b</sup>	130.57±0.55 <sup>c</sup>	136.87±1.14 <sup>a</sup>	73.36±0.84 <sup>b</sup>	74.29±0.55 <sup>b</sup>	262.9±10.4 <sup>ab</sup>	240.1±5.8 <sup>ac</sup>	236.4±3.9 <sup>bc</sup>	131.00±1.14 <sup>b</sup>	126.4±0.84 <sup>c</sup>	102.4±0.55 <sup>bc</sup>
AECT625	260±1.30 <sup>a</sup>	137.57±1.00 <sup>b</sup>	132.28±1.14 <sup>c</sup>	135.83±1.30 <sup>a</sup>	74.85±1.00 <sup>b</sup>	75.26±1.14 <sup>b</sup>	260.1±13.6 <sup>ab</sup>	244.8±7.5 <sup>bc</sup>	231.7±2.4 <sup>c</sup>	131.00±1.3 <sup>b</sup>	125.4±1 <sup>ab</sup>	98.6±1.11 <sup>d</sup>
AECT1250	260±1.14 <sup>a</sup>	135.71±0.84 <sup>ab</sup>	130.85±0.71 <sup>b</sup>	135.9±1.14 <sup>a</sup>	76.09±0.84 <sup>b</sup>	74.59±0.71 <sup>c</sup>	260.2±12.8 <sup>ab</sup>	239.9±8.6 <sup>ac</sup>	221.8±5.1 <sup>ac</sup>	131.00±1.14 <sup>b</sup>	123.8±0.84 <sup>ab</sup>	73.5±0.71 <sup>a</sup>

The values entered in the table are means±standard deviation, with a sample number of "n = 5. The means with different letters are significantly different (P <0.05). AECT: aqueous extract of *Clerodendrum thomsoniae* (1250mg/kg m.c; 625mg/kg m.c; 312mg/kg b.m) N.C: Negative Control (subjected to a Normal Diet + Distilled Water during treatment); P.C: Positive control subjected to a Normal Diet + metformin.

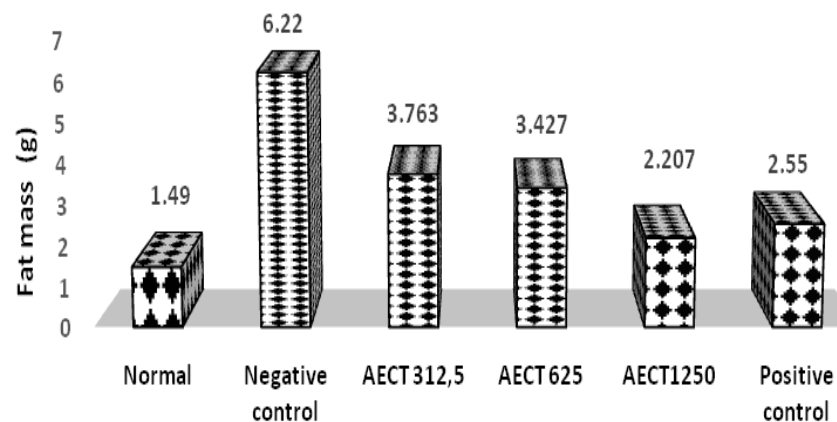


Figure 4: Evolution of abdominal fat mass during treatment.

AECT312.5: group of rats received *C. thomsoniae* extract at dose of 312.5 mg/kg; AECT625: group of rats received *C. thomsoniae* extract at dose of 625 mg/kg; AECT1250: group of rats received *C. thomsoniae* extract at dose of 1250 mg/kg. PC=Positive control: Group of rats received metformin. AECT=Aqueous extract of *Clerodendrum thomsoniae* N.C: Negative control

In normal physiological state, insulin activates the lipolytic actions of the hormones on the deposit peripheral fat, hydrolyzing triglycerides and preventing storage of free fatty acids<sup>39,40</sup>. In this experimental study, type 2 diabetic rats- showed significantly elevated quantity of abdominal fat. As expected, treatment with AECT significantly decreased the quantity of fat in the diabetic rats. Sharma *et al.*,<sup>29</sup> observed a similar hypolipidemic potential of *Garcinia pedunculata* extract polyphenols in fatty diet rats. Moreover, our previous studies<sup>17</sup> established the lipid-lowering nature of AECT in dyslipidemic rats, thanks to their content in bioactive compounds. In summary, the aqueous extract of *C. thomsoniae* appears to have insulin-stimulating property, which could be useful in the reduction of fat-related problems. According to Cryer<sup>41</sup> the decrease in fluid intake observed in rats treated with the extract and those with metformin could be linked to the restoration of blood glucose homeostasis. Indeed, the reduction-in blood glucose probably resulted from a decrease in blood osmolarity which is accompanied by a reduction in need for water and consequently, a decrease in fluid intake.

## CONCLUSIONS

On the basis of the current investigation, it could be concluded that aqueous extract of the leaves of *C. thomsoniae* possess hypoglycaemic and antidiabetic properties, in both normal and diabetic rats. The increase in activity is dose-dependent up to a maximum dose of 1250 mg/kg. To establish the antidiabetic principle(s) however, the putative compound(s) have to be isolated and evaluated. It is therefore, suggested that further purification steps would be necessary to isolate and further evaluate the antidiabetic principles of the plant on animal models.

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## AUTHORS'S CONTRIBUTION

**Ngounou EMD:** writing-review, editing, lab work. **Mang YD:** lab work, data interpretation. **Dongmo F:** lab work, formal analysis. **Malla OWI:** lab work. **Dongmo SS:** visualization, editing. **Yanou NN:** supervision. All authors revised the article and approved the final version.

## DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## CONFLICT OF INTEREST

None to declare.

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