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Phytochemical and evaluation of hypoglycemic effect of leaves extract of *Aloe buettneri* A. Berger (liliaceae) in normal and alloxan-induced diabetic mice

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Abstract
Aloe buettneri was evaluated to confirm its hypoglycemic activity. The presence of quinone which seem to leave the hypoglycemic activity. Lyophilisate of *A. buettn*eri leaf (LA) causes hypoglycemia only 2 h after its administration and is linked to the presence of quinone. Glycemia reduction with LA was significantly higher than that of Glibenclamide, the control. Glibenclamide and LA negatively affects blood glucose in the mice by decreasing it continuously over time. However, LA exhibited significant hypoglycemic activity in normal and alloxan-induced diabetic mice. LA has a greater hypoglycemic potential than Glibenclamide, a pharmaceutical drug used in the treatment of diabetes. *A. buettneri* is then a potential good hypoglycemic drug because it may provide clues for the development of new and better oral drugs for treatment of diabetes mellitus in the context of improved traditional medicines.

Keywords: *Aloe buettneri*; Alloxan; Diabetes mellitus; Leaf; Hypoglycemic activity.

1. Introduction
Diabetes mellitus is a chronic disease caused by deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves (Kitabchi *et al*., 2009; Mamun-or-Rashid *et al*., 2014) [1, 2]. Diabetes mellitus has now become an epidemic with a worldwide incidence of 5% in the general population. More than 100 million of the world's population has already reached the diabetic mark and the number of people suffering from is expected to soared up to 366 million (Hussain and Marouf, 2013)[3]. Lack of physical activity, obesity, stress and diet are currently the main phenomena involved in high prevalence of this metabolic (Konkon *et al*., 2008) [4]. Currently, there are no known effective therapies (Verrotti *et al*., 2012) [5], although in conventional therapy type I diabetes is treated with exogenous insulin and type 2 with of oral hypoglycemic agents (Pepato *et al*., 2005) [6]. Management focuses on keeping blood sugar levels as close to normal, without causing low blood sugar levels. However, there is a growing demand for patients to use natural products with antidiabetic activity using traditional pharmacopoeia plants (Eddouks *et al*., 2002; Lans, 2006; Kooti *et al*., 2016)[7-9].
The herbal remedies are essential health care throughout the world. One of the largest scientific and medical concerns is finding new ways to fight against diseases such as cancer or diabetes. The number of deaths attributed to diabetes was previously estimated at just over 800 000 a year, but we have long known that this figure has been widely underestimated. In reality, it is more likely that it is around 4 million deaths per year, or 9 % of total mortality (Oga *et al*., 2006; Sy and Cissé, 2007) [10, 11]. The search for a therapy that can help to overcome definitively diabetes remains currently a major concern of modern medicine. Facing with the expansion of this disease whose support is high, the World Health Organization (WHO), in its resolution AFR/RC50/R3 of 31 August 2000, encouraged African countries including Côte d'Ivoire to develop strategies on traditional medicine to undertake research on medicinal plants and promote their optimal uses in health care delivery systems. So, create awareness and adopt plans on how to reduce risk of diabetes mellitus prevalence were necessary. There are several means of managing and treating diabetes, however, researchers reveal that natural remedies are more viable unlike the synthetic drugs and oral medications that may pose undesirable side effects to the body.
In Africa, the traditional medicine accounts for over 85% of health coverage of the population. The lack of modern medicine treatments, the high cost of modern medicine treatments and socio-cultural habits of the population explain the use of traditional practices based on

medicinal plants (Sanogo, 2006) [12]. In Côte d'Ivoire a large part of the population still rely on the medicinal plants to treat a diverse variety of pathologies such as diabetes mellitus. The efficient traditional use of the plants in diabetes treatment has been little proven so far. Moreover, a considerable number of ethnobotanical studies state that the plant extracts were also found active against diabetes by traditional practitioners (Konkon *et al.*, 2017) [13]. Knowing the effectiveness of plant extract in diabetes mellitus treatment would be a useful technique in the development of new drugs. Indeed, a crude extract of plant may prove better therapeutically than the modern medications, less toxic and inexpensive.

The present studies was designed to evaluate and prove the effectiveness i.e. the hypoglycemic activity of *Aloe buettneri* extract used in Ivorian pharmacopoeia to treat diabetes mellitus.

2. Materials and Methods

2.1. Plant material

The leaves of *Aloe buettneri* are made powder. It is an herbaceous plant with non-fibrous succulent leaves in rosette, 40 cm long and 15 cm wide, spurred margin; the leaf bases form a bulb in the ground around a bulbous rhizome unbranched. This species grows in the area humid of the savannas.

2.2. Experimental animals

The animals used in this study were the male Swiss albino mice (7-8 weeks old), weighing between 20-25 g were obtained from Pasteur Institute of Côte d'Ivoire. These mice were housed in cages in the animal house of the Biosciences Training and Research Unit, at room temperature. They had free access to food (pellets from Ivograin, Côte d'Ivoire) and water. All the experimental procedures were approved by the Ethical Committee of Health Sciences, Félix Houphouët Boigny University of Abidjan. These guidelines were in accordance with the European Council Legislation 87/607/EEC for the protection of experimental animals.

2.3. Preparation of extract

Leaves of *Aloe buettneri* are dried in the shade at room temperature for 4 weeks, then reduced to powder. Approximately 10 g of powder were placed in a container and then 100 ml of water were added and the mixture was boiled for 15 to 30 min. After filtration, the obtained decoctate was frozen and then lyophilized. The lyophilisate of *A. buettneri* (L_A) is then dissolved in saline serum (SS) at the rate of 0.04, 0.24 and 1.2 g/mL according to the method of Houghton and Raman (1998)[14].

2.4. Phytochemical screening

The presence of some phytoconstituents was highlighted by standards phytochemical methods. Phytochemical analysis of alkaloids, flavonoids, quinones, saponins, sterols, tannins and terpenes were performed according to the methods described by Senguttuvan *et al.* (2014)[15].

2.6. Determination of the maximum tolerated dose of lyophilisate *Aloe* (MTDL_A)

To carry out the study of the acute toxicity of the extracts, three solutions prepared from the crude extract of the leaves of *A. buettneri* (L_A) were performed. Thus, the concentrations of 0.048, 0.24, 1.2, 1.25, 1.5, 1.8 and 2 g/mL of L_A were obtained. After the mice were subjected to a 12 h fast, the solutions were administered by gavage, using an intubation cannula with a slightly curved tip. Gavage was done with a volume of 0.2 mL per 20 g of body weight. The dose of extract to be administered is then expressed in milligrams per kilogram of body weight and orally (mg/kg/vo). Then lots of 10 fasted mice were made. Each lot corresponds to a concentration of extract. A control mice watered with distilled water was made. After administration of the extract, at different concentrations The dead animals were counted in each batch for 48 h. This acute toxicity experiment was conducted to determine the maximum tolerated dose (MTD) that represents the maximum dose that does not kill any animals when the extract is administered (Frank *et al*., 2012) [16].

2.5. Experimental conditions

Glibenclamide (1 mg/mL) was dissolved in saline in an amount of 10 mg (2 tablets) to 10 mL of saline serum (S.S.). It was used was used as the reference standard and the negative control lot animals received only vehicle. The solutions were administered orally at 0.2 mL to mice having 20 g of body weight.

Alloxan-induced diabetic models were selected to confirm the utility of the active antihyperglycemic extracts in diabetic conditions. Diabetes was induced in mice by injecting a solution of 70 mg/mL alloxan monohydrate intraperitoneally in S.S. into overnight fasted mice. The mice were then kept for the next 24 h on 10% glucose solution bottles, in their cages to prevent hypoglycemia. After 48 h of the injection, fasting blood glucose level was measured (Verma *et al.*, 2010; Saha *et al*., 2012) [17, 18].Animals which did not develop more than 200 mg/dL glucose levels, were rejected (Mohammed, 1990; Konkon *et al.*, 2008) [4, 19].

2.6. Blood sampling

Blood samples were taken by puncturing the orbital sinus of the eye using microhematocrit capillary tubes (0.20 ± 0.02 mL) on fasted mice since the day before (food removed from the cages 14 h before dosages) (N'guessan, 2009; Kolawole, 2012) [20, 21].

2.7. Determination of glucose in whole blood samples

The blood sugar level was measured using A Glucometer ENCORE®. Fasting blood glucose (FPG) was determined within 1 minute of taking blood. The assay was carried out on a batch of 10 mice (Franck *et al.*, 2012) [16].. Drop of blood was deposited on the reactive surface of the strip and then it is introduced into the reading chamber of the Glucometer.

2.8. Normal value of fasting blood glucose level in mice

In this experiment, 10 fasted mice for 12 h were used. The blood was sampled and the blood glucose level was measured with a meter to find the normal value of the blood glucose level in the mice used in the experiments. The normal value of the blood glucose is obtained by calculating the average of these 10 measured values.

2.9. Evaluation of hypoglycemic activity of *Aloe buettneri* lyophilisate

2.9.1. Normoglycemics mice

- After single administration

Three lots of five fasted mice (food is removed from the cages 14 h before blood was taken, while water is allowed at will) was selected and one lot of normal non-alloxanized mices was also included in the study. Blood samples were collected to determine FPG prior to administration of different products

(FPG0). Thus, lot No. 1 (control) receives the saline serum, lot No. 2 was treated with Glibenclamide as the hypoglycemic reference (reference lot) and lot No. 3 (L_A treatment) receives the $DMTL_A$ from Aloe lyophilisate. Then, the FPGs are assayed for 30 min after administration (FPG at + 1/2 h); 2 h after administration (FPG at + 2 h); 4 h after administration (FPG at + 4 h); 6 h after administration (FPG at + 6 h); 8 h after administration (FPG at + 8 h); 24 h after administration (FPG at + 24 h).

- After repetitive administrations (during five days)

Three lots of five fasted mice were also used. The control (lot No. 1) receives the saline serum (SS) the reference lot No. 2 receives Glibenclamide and the lot No. 3 receives the Aloe lyophilisate of Aloe (L_A). These products were administered daily at the same dose and by the same route as for single administration and for five days. Then blood glucose is determined before administration (FPG0); two days after administration (FPG2); three days after administration (FPG3); four days after administration (FPG4); five days after administration (FPG5).

2.9.2. Mice alloxan-diabetics

- After single administration

It is performed under the same conditions as the single dose test in normoglycemic mice (three lots of five mice). The control lot (Lot No. 1) receives the S.S., the reference lot (lot No. 2) receives the Glibenclamide and lot No. 3 receives the L_A. FPGs were assayed (before administration) at + 1/2h, +2 h; +4 h, +6 h; +8 h; +24 h after administration.

- After repetitive administrations (during five days)

It was carried out under the same conditions as the chronic test in normoglycemic mice (three lots of five mice). The different products were administered to each lot of mice at the same daily dose and by the same route of administration, during five days. The FPGs were dosed at two days (D2), three days (D3) and four days (D4) after administration.

2.10. Statistical analysis

The values are expressed as mean ± standard error of mean (SD). The results were analyzed for statistical significance using one-way analysis of variance (ANOVA) followed by Newman-Keuls's test; $P<0.05$ was considered significant.

3. Results

3.1. Phytochemical screening

The phytochemicals present of leaves extracts are given in table 1. Results shown that leaves of *Aloe buettneri* are rich in quinone substances. By cons, alkaloids, flavonoids, saponins, sterols, terpenes and tannins are absent**.**

Table 1: Phytochemical constituents of leaves extract of *Aloe buettneri*

	Constituents					
	Alkaloids	**Flavonoids**	**Quinones**	**Saponins**	**Sterols and terpenes**	**Tannins**
L_A	-	-	++++	-	-	-

(L_A) lyophilisate of *Aloe buettneri* leaf extract; (+) presence; (-) absence

3.2. Maximum tolerated dose of lyophilisate *Aloe* ($MTDL_A$

A few moments after gavage of the extract of the leaves of Aloe at doses ranging from 0.048 to 2 g/mL L_A, ie 0.48 to 2 mg/kg/vo, changes in the general appearance of the mice were not observed during these two days of observation. With L_A concentrations of 0.48 to 1.25 g/mL no mortality was observed. The concentrations of 1.5, 1.8 and 2 g/mL caused 1, 2 and 3 mice deaths, respectively. Maximum tolerated dose of lyophilisate *Aloe* ($MTDL_A$) was 1.25 g/ mL i.e 12.5 g/kg/vo (Table 2).

Table 2: Mortality of mice after gavage by different concentrations of L_A

Lots	Concentrations of L_A (g/mL)	Equivalent doses (g/kg)	Number of deaths
1	0	0	0
2	0.048	0.48	0
3	0.24	2.4	0
4	1.2	12	0
5	1.25	12.5	0
6	1.5	15	1
7	1.8	18	2
8	2.0	20	3

(L_A) lyophilisate of *Aloe buettneri* leaf extract

3.3. Normal value of fasting blood glucose level in mice

Fasting, as the name implies, means refraining from eating liquids other than water pendant eight hours. It is used as a diabetes test. After fasting, a carbohydrate metabolism test is performed to measure blood glucose levels. Thus, Table 3 shows the blood glucose values obtained in each mouse as well as the normal level of glycemia in mice which is the mean value. The blood glucose values obtained are very variable from one mouse to another and oscillate between 115 and 153 mg/dL. However, the average blood glucose level which represents the normal blood glucose level in our experimental mice is 129.4 mg/dL.

3.4. Normoglycemic mices

3.4.1. After single administration

The results reported in Table 4 show that saline (SS) serum does not significantly affect blood glucose levels in mice after single administration of the solutions although a decrease is observed between the 6th to the 8th hour. But it returns to normality at 24 h. However, Glibenclamide causes a significant decrease in blood glucose 4 h after its administration to mice. This with a rate of 65.5 mg/dL to 8h. After this time, the blood sugar level returns to normal as in the control mice. With lyophilisate of *Aloe buettneri* leaf extract

(L_A) level, significant decrease in blood glucose was observed from 2 h after gavage to 98.2 mg/dL to reach its lowest level at 8h to 74.8 mg/dL. Beyond this time, the blood glucose level rises to reach 101.6 mg/dL at 24 h but it remains significantly low by comparison with the controls.

Table 3: Blood glucose level in mice

N° of mices	Blood glucose (mg/dL)	Normal value of fasting blood glucose level (mg/dL)
1	128	129.4
2	147	
3	130	
4	128	
5	116	
6	123	
7	115	
8	153	
9	132	
10	122	

The normal blood glucose value was obtained by calculating the average of the ten values only 2 h after its administration and thus seems to persist with the Glibenclamide.

Table 4: Fasting blood glucose level obtained after single administration of the solutions with normoglycemic mice

	Fasting blood glucose (mg/dL)						
	Time (h)						
Administered solutions	0	1/2	2	4	6	8	24
Serum saline (10 g/kg/vo)	129.8 ± 11.1[a]	129.4 ± 12.8[a]	127.8 ± 13.3[a]	122.0 ± 10.5[a]	110.4 ± 16.1[b]	102.8 ± 13.3[b]	127.4 ± 17.6[a]
Glibenclamide (10 g/kg/vo)	129 ± 14.7[a]	128.8 ± 16.3[a]	115.2 ± 10.1[b]	87.5 ± 8.2[c]	85.3 ± 12.3[c]	65.5 ± 14.6[d]	134.3 ± 16.3[a]
L_A(12.5 g/kg/vo)	126.8 ± 19.5[a]	117.2 ± 9.4[b]	98.2 ± 13.3[c]	87.2 ± 8.5[c]	80.4 ± 9.6[c]	74.8 ± 8.8[d]	101.6 ± 12.3[b]

(L_A) lyophilisate of *Aloe buettneri* leaf extract; Data are expressed as mean of three replicates; ±SD: standard deviation; on a line and in a column, means followed by a different letter are significantly different according to Duncan's multiple range test at 5 % (Test of Newman-Keuls).

3.4.2. After repetitive administrations

With regard to the repetitive administration of the solutions, the results reveal in Table 6 that the saline serum (SS) has no effect on the blood glucose of the mice. Glibenclamide caused a drop in blood glucose content from day 3 to 88.1 mg/dL (a decrease of 31.8% from day 0) to the lowest value (69.4 mg/dL) at D5, with 46.41% of a rate decrease. The effect of L_A follows the same evolution as that of Glibenclamide. However, the decrease in blood glucose was less pronounced at D3 (96.9 mg/dL, with 24.8% reduction) and D5 (88.4 mg/dL, 31.7% reduction). Thus, the effect of Glibenclamide and L_A affects blood glucose in the mice by starting the decrease at D3 and become more important with time.

Table 5: Fasting blood glucose level obtained after repetitive administration of the solutions with normoglycemic mice

	Fasting blood glucose (mg/dL)				
	Time (days)				
Administered solutions	D0	D2	D3	D4	D5
Serum saline (10 g/kg/vo)	127.8 ± 7.4[a]	128.3 ± 9.1[a]	128.9 ± 10.3[a]	129.0 ± 11.2[a]	129.4 ± 16.1[a]
Glibenclamide (10 g/kg/vo)	128.1 ± 8.5[a]	128.5 ± 7.9[a]	88.1 ± 6.5[b]	82.8 ± 8.1[b]	69.4 ± 5.3[c]
L_A (12.5 g/kg/vo)	129.3 ± 10.1[a]	127.9 ± 9.8[a]	96.9 ± 8.7[d]	90.7 ± 7.2[d]	88.4 ± 6.8[b]

(L_A) lyophilisate of *Aloe buettneri* leaf extract; Data are expressed as mean of three replicates; ±SD: standard deviation; on a line and in a column, means followed by a different letter are significantly different according to Duncan's multiple range test at 5 % (Test of Newman-Keuls).

3.5. Alloxan-diabetics mice

3.5.1. After single administration

The results reported in Table 6 show with alloxan-diabetics mice that saline (SS) serum has no effect on blood glucose levels in mice after single administration. However, Glibenclamide and L_A significantly reduced blood glucose levels in mice at 4 h and 2h post-dosing, respectively and up to 24 h. L_A causes a greater reduction compared to Glibenclamide. But at 24 hours after administration, both substances produce a statistically identical blood glucose level. Between 4-8h after administration, L_A (309.2 mg/dL) has a greater hypoglycemic effect than Glibenclamide (304 mg/dL). The Glibenclamide and L_A reach their maximum activity after administration 8 h and remain active 24 h after their administration. Furthermore, the rate of glycemia reduction reached between 6-8 h after administration, 30.3-32.6% for Glibenclamide and 48-53.1% for L_A.

Table 6: Fasting blood glucose level obtained after single administration of the solutions with alloxan-diabetics mice

	Fasting blood glucose (mg/dL)						
	Time (h)						
Administered solutions	0	1/2	2	4	6	8	24
Serum saline (10 g/kg/vo)	428.2 ± 52.8[a]	426 ± 51.1[a]	428 ± 55.8[a]	426.2 ± 47.9[a]	426.4 ± 32.3[a]	426 ± 32.5[a]	425.8 ± 40.6[a]
Glibenclamide (10 g/kg/vo)	429.2 ± 48.9[a]	417.4 ± 53.3[a]	403.2 ± 50.3[a]	383.4 ± 35.9[b]	299.2 ±49.1[d]	289.2 ± 45[d]	304 ± 37.9[d]
L_A(12.5 g/kg/vo)	428 ± 44.8[a]	423.6 ± 47.8[a]	345.4 ± 32.7[c]	269.2 ± 39.1[e]	222.4 ± 42.8[f]	200.6 ± 39.1[f]	309.2 ± 21[d]

(L_A) lyophilisate of *Aloe buettneri* leaf extract; Data are expressed as mean of three replicates; ±SD: standard deviation; on a line and in a column, means followed by a different letter are significantly different according to Duncan's multiple range test at 5 % (Test of Newman-Keuls).

3.5.2. After repetitive administrations

The results reported in Table 7 show with alloxan-diabetics mice that saline (SS) serum has no effect on blood glucose levels in mice after repetitive administrations. Glibenclamide and L_A significantly reduced blood glucose levels in mice at D2 post-administration. L_A causes a more blood glucose reduction than Glibenclamide. With. Glibenclamide the rate that was originally 431 mg/dL decreased to 330.2 to 313 mg/dL in D2 to D4 i.e. (23.4 to 27.4% reduction). Then rises to a value of 348.2 mg/dL to D5 (19.2 % of reduction) which is always significantly lower than control. As far as L_A is concerned, its action on blood glucose is more pronounced. Indeed, from D2-D4 the blood glucose level of 339-260.2 mg/dL while initially it is 430.6 mg/dL in the control, ie 21.3 to 39.6% reduction. To D5, the blood glucose level continues to fall to 238 mg/dL i.e. 44.7% reduction rate. Glibenclamide and L_A affects blood glucose in the mice by starting the decrease at D2 and become more important with time. However, L_A has a greater hypoglycemic potential than Glibenclamide.

Table 7: Fasting blood glucose level obtained after repetitive administration of the solutions with alloxan-diabetics mice

	Fasting blood glucose (mg/dL)				
	Time (days)				
Administered solutions	D0	D2	D3	D4	D5
Serum saline (10 g/kg/vo)	430.2 ± 64.8[a]	431.2 ± 52.5[a]	431.2 ± 48.5[a]	432.4 ± 48.9[a]	432.8 ± 57.3[a]
Glibenclamide (10 g/kg/vo)	431 ± 55.4[a]	330.2 ± 37.5[b]	315.8 ± 24.5[b]	313 ± 20.9[b]	348.2 ± 34.3[b]
L_A(12.5 g/kg/vo)	430.6 ± 57[a]	339 ± 60.1[b]	334.8 ± 36.6[b]	260.2 ± 34.6[c]	238 ± 37.2[c]

(L_A) lyophilisate of *Aloe buettneri* leaf extract; Data are expressed as mean of three replicates; ±SD: standard deviation; on a line and in a column, means followed by a different letter are significantly different according to Duncan's multiple range test at 5 % (Test of Newman-Keuls).

Discussion

Phytochemistry and blood glucose levels were performed on *Aloe buettneri* leaf extracts (L_A) to confirm or validate traditional claims as a plant with hypoglycemic activity. Diabetes is a major health problem that affects major populations worldwide. Epidemiological studies and clinical trials strongly confirm that hyperglycemia is the main cause of complications. Effective glucose control is the key to preventing or reversing diabetic complications and improving the quality of life in patients with diabetes. Thus, a sustained reduction in hyperglycemia will reduce the risk of developing vascular complications (Muniappan *et al.*, 2004) [22]. Based on these observations, we selected the hyperglycemic model induced by alloxane and hypomycemia induced by gibenclamide have been proposed. Subsequently, the screening of the hypoglycemic activity of L_A was carried out. Any drug that is effective in diabetes will have the ability to control the rise in glucose level by different mechanisms, and the ability of the extracts to prevent hyperglycemia could be determined by the glucose-loaded hyperglycemic model.

The phytochemical analysis helped identify different chemical groups present in the extracts of the leaves of the *Aloe buettneri*. Quinones are highly reactive molecules with aromatic rings, with two substitutions ketone (Dongmo, 2009) [23]. The quinones are compounds which regenerate free radicals and therefore, are irreversibly complexed to the nucleophiles' amino acids of proteins. The quinones are ubiquitous and generally have antimicrobial properties. Their main targets in the microbial cell are adhesins, polypeptides, and membrane enzymes (Dongmo, 2009) [23]. The present study did not reveal the presence of alkaloids, which are toxic substances known even lower dose (Bruneton, 2000) [24]. They can have therapeutic effects known to limited uses (Djedioui, 2010) [25]. The alkaloids found in several plant families. They act directly on the nervous system "sympathetic, parasympathetic and central" with the effects on consciousness and motor skills (Chen *et al*., 2014; Lee *et al*., 2015) [26, 27]. This study has not revealed the presence of sterols and terpenes, but these molecules are a large family of natural compounds (Bruneton, 2003) [28]. The therapeutic value of many medicinal plants is their use for the extraction of active molecules, to obtain simple galenic forms. The tannins have not been revealed in this study; they are the non-nitrogenous compounds of the polyphenols groups. They act on diabetes itself at the cellular level, promoting the action of insulin and diabetes complications by their antioxidant and anti-enzymatic, neutralizing the effect of frees radicals and limits the inflammatory response in different tissues (Hertel, 2003) [29]. The normal value of blood glucose of mice is 129.4 mg/dL. This value is higher than that reported by IFFA-CREDO (Center for Research and Breeding of ocins) which is 94 mg/dL, obtained by the photometric method of laboratory to glucose oxidase, on the same type of mice. This difference is not related to the nature of the enzyme used (hexokinase for the Glucometer, glucose oxidase for the photometric method), but rather due to the fact that the methods of blood glucose by strips and Glucometer give significantly higher than the standard laboratory method. Indeed, Thivolet and Tourniaire (1991) [30] and then Guillausseau (1994) [31] show that diagnosis of diabetes is made when the laboratory assaysprovide a plasma glucose greater than 140 mg/dL whereas the blood glucose test strips gives a value greater

than 200 mg/dL.

In the hyperglycemic model, the plant tested for hypoglycemic activity showed significantly higher hypoglycemic activity than glibenclamide, an antidiabetic drug used to treat type 2 diabetes, which is part of the World Organization's list of essential drugs (WHO, 2013) [32]. An excessive amount of glucose in the blood induces insulin secretion. This secreted insulin appears to stimulate peripheral glucose consumption and control glucose production through various mechanisms, as mentioned by Andrew (2000) [33]. However, from the study (glucose control), it was clear that secreted insulin takes two to eight hours to restore the glucose level to normal. In the case of L_A, glucose levels did not exceed those in the control group, indicating the supportive action of the extract in the use of glucose. The effect of glibenclamide, the standard drug used in this study, on glucose tolerance was attributed to increased beta cell activity in the pancreas, resulting in increased secretion of insulin. Thus, the mechanism behind this antihyperglycaemic activity of plant extracts and fractions implies an insulin-like effect, probably due to peripheral glucose consumption or increased beta cell sensitivity to glucose, resulting in an increase of insulin release (Muniappan *et al*., 2004) [22]. In these contexts, a number of other plants have also been reported to have hypoglycemic effects (Leila *et al.*, 2007; Jarald *et al*., 2013) [34, 35]. L_A has potential antidiabetic activity. L_A also has a hypoglycemic activity both in normoglycaemics mice than in alloxan-diabetics mice. The amount of time is between 30 min and 2 h, while that of glibenclamide is between 4 and 6 hours after administration, with a biological action longer than 22 h and maximum activity that appears 8 h after oral administration. L_A has a certain advantage over glibenclamide. Indeed, it is much faster than glibenclamide (onset of action between 4 and 6 h after administration). It shows in alloxan-diabetics mice the superior activity to that of glibenclamide. However, duration of biological action is superimposed with the two cumulative. The action of *Aloe buettneri* resides in the nature of their chemical compositions whose quinone substances. *Aloe* lyophilisate thus has an intermediate-acting hypoglycemic agent as glibenclamide but with stronger activity. In the literature, there is no mention of *Aloe buettneri* but two related species that are *Aloe barbadensis* Miller (Liliaceae), native to the Mediterranean and the Arabian peninsula, and *Aloe arborescens* Miller (Liliaceae) of Asian origin. These two plants have given rise to satisfactory experimental diabetes in their country of origin. Indeed, Ghannam *et al*. (1986) [36] tested the solid residue, obtained by evaporating the latex flowing from *Aloe barbadensis* leaves on blood glucose alloxan-diabetics mice. It appears from this study that *Aloe barbadensis* significantly lowers blood sugar in alloxan-diabetics mice with an activity greater than that of glibenclamide. Single administration of L_A causes either weight loss, or purgation while during the chronic test, there was a slight drop weight without purging. The results are consistent with those of Mohammed (1990) [19] which reported the lack of purgative effect of the solid residue in both single that repetitive administration, with a slight drop weight only when the chronic assay. This weight fall would probably linked to prolonged fasting, imposed on mice during the chronic assay including the reduction of their daily food intake. However, Mohammed (1990) [19] highlighted a purgative effect during chronic treatment with the bitter extract of the solid residue in the alloxan-diabetics mice. This disagreement between our results and that of Mohammad could be explained by the nature of the extracts used. Indeed, we tested decocte obtained from the leaves of *Aloe buettneri*. Ghannam *et al*. (1986) [36] were used the residue obtained by evaporation of the latex of the leaves of *Aloe barbadensis* while Mohammed tested the bitter extract from the solid residue. This extract therefore contains more anthracene derivatives as the other two extracts.

The decrease in FPG in normoglycaemics and alloxan-diabetics mice confirmed that *Aloe buettneri* has antidiabetic activity and justifies their use in traditional medicine. However, these results do not explain the mechanism of their anti-diabetic activity. Some herbs with antidiabetic activity to act by increasing insulin levels circulating in normoglycaemics rats (Leila *et al.*, 2007; Hossain *et al*., 2012) [34, 37]. In addition, alloxan causes irreversible destruction of pancreatic beta cells; and it is difficult to determine the degree of destruction of these cells and their ability to release insulin in the conditions of our study (Mbagwu *et al*., 2011; Joshi *et al*., 2013) [38, 39]. Since glibenclamide is active only in case of partial destruction of beta cells by alloxan (Henquin, 2005; Natarajan *et al*., 2012; Triana *et al*., 2016) [40-42] and that *A. buettneri* has some differences in their activity compared to glibenclamide. Thus, hypotheses such as leaves of plant act as Glibenclamide and are therefore more effective in stimulating insulin secretion or that leaves have a mechanism of action different from that of Glibenclamide. Indeed, other mechanisms of action can be envisaged, namely, increasing the peripheral use of glucose as is the case with increased peripheral glucose utilization as is the case with *Prosopis fracta* of the Leguminous family (Awah, 2006; El-Abhar and Schaalan, 2014)[43,44], increased activity of liver enzymes involved in the metabolism of carbohydrates (insulin-like action) with the charantin isolated of the fruits of *Momordica charantica* (Baby and Jini, 2013)[45] and decreased intestinal absorption of carbohydrates as advanced by Boudreau and Beland (2006)[46] with *Aloe arborescens* and attributed to anthracene derivatives that stimulate intestinal peristalsis. But, this mechanism was reconsidered later by the same author, which showed that the laxative action of *Aloe* is predominant in the large intestine. As suggested by our results of further studies are desirable to identify the active ingredients and determine their mechanism of action for a more rational use of this plant, even their active constituents in antidiabetic therapy in like oral antidiabetic already available. During our study we got some conflicting results especially in normoglycaemics mice where glibenclamide should be active beyond 24 h and D2 (chronic essay) because of the cumulative effect. It is the same for the L_A that has activity 24 h after administration, whereas the same activity is not detected at D2. So we superimposed the results in the latter the results of alloxan-diabetics mice as they are evocative. These inconsistent results are not an artifact related to methodology, since this is the one that gives satisfactory results in alloxan-diabetic mice. Rather, they are inherent to the experimenter to the extent that there is no prior training and that the study was started on these normoglycaemics mice.

Conclusion

This study is a contribution to the valorisation of African pharmacopeia. It has established a draft monograph for this plant comes in, by their leaves, a traditional antidiabetic preparation. It appears that this species has a completely different chemical composition. For *Aloe buettneri* are only quinone that we have highlighted. The preliminary toxicity assay showed that the leaves of this plant were not toxic to the

conditions of this study. As for the pharmacodynamic study, it showed that *A. buettneri* has potential antidiabetic activity. After this study we suggest that further in-depth studies be undertaken to determine their mechanism of action for rational use in the anti-diabetic therapy.

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