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

Konkon NG, Mohamadou LD, Kpan WB, Orsot BB, Ouattara D, Nguessan KE and Kouakou TH

Abstract

*Aloe buettneri* was evaluated to confirm its hypoglycemic activity. The presence of quinone which seem to leave the hypoglycemic activity. Lyophilisate of *A. buettneri* 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 soar 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 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; Kooit 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 believed 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 ethnomedical plants 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 decocate was frozen and then lyophilized. The lyophilisate of A. buettneri (Lₐₐ) 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].

2.5. Experimental conditions

Glibenclamide (1 mg/mL) was dissolved in saline in an amount of 10 mg (2 tablets) to 10 mL of saline serum (SS). 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) [18]. 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 mice 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 (L₄ treatment) receives the DMTL₄ 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 (L₃). 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-diabetes 
- After single administration

It is performed under the same conditions as the single dose test in normoglycemic mice (three lots of five mice). The 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 mice

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 (L₄) 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

<table>
<thead>
<tr>
<th>N° of mice</th>
<th>Blood glucose (mg/dL)</th>
<th>Normal value of fasting blood glucose level (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>128</td>
<td>129.4</td>
</tr>
<tr>
<td>2</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>153</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Fasting blood glucose (mg/dL)</th>
<th>Time (h)</th>
<th>Administered solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1/2</td>
</tr>
<tr>
<td>Serum saline (10 g/kg/vo)</td>
<td>129.8 ± 11.1a</td>
<td>129.4 ± 12.8a</td>
</tr>
<tr>
<td>Glibenclamide (10 g/kg/vo)</td>
<td>129 ± 14.7a</td>
<td>128.8 ± 16.3a</td>
</tr>
<tr>
<td>L_A (12.5 g/kg/vo)</td>
<td>126.8 ± 19.5a</td>
<td>117.2 ± 9.4b</td>
</tr>
</tbody>
</table>

(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

<table>
<thead>
<tr>
<th>Fasting blood glucose (mg/dL)</th>
<th>Time (days)</th>
<th>Administered solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1/2</td>
</tr>
<tr>
<td>Serum saline (10 g/kg/vo)</td>
<td>127.8 ± 7.4a</td>
<td>128.3 ± 9.1a</td>
</tr>
<tr>
<td>Glibenclamide (10 g/kg/vo)</td>
<td>128.1 ± 8.5a</td>
<td>128.5 ± 7.9a</td>
</tr>
<tr>
<td>L_A (12.5 g/kg/vo)</td>
<td>129.3 ± 10.1a</td>
<td>127.9 ± 9.8a</td>
</tr>
</tbody>
</table>

(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.
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 red

cusset to a value of 348.2 mg/dL to D5 mg/dL in D2 to D4 i.e. (23.4 to 27.4% reduction). Then rises that was originally 431 mg/dL decreases 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 Lₐ 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 Lₐ affects glucose level in the mice by starting the decrease at D2 and become more important with time. However, Lₐ has a greater hypoglycemic potential than Glibenclamide.

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

<table>
<thead>
<tr>
<th>Administered solutions</th>
<th>Fasting blood glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Serum saline (10 g/kg/vo)</td>
<td>428.2 ± 52.8 *</td>
</tr>
<tr>
<td>Glibenclamide (10 g/kg/vo)</td>
<td>429.2 ± 48.9 *</td>
</tr>
<tr>
<td>Lₐ (12.5 g/kg/vo)</td>
<td>428 ± 44.8 *</td>
</tr>
</tbody>
</table>

(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 Lₐ significantly reduced glucose levels in mice at D2 post-administration. Lₐ causes a more glucose level 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 Lₐ 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 Lₐ affects glucose level in the mice by starting the decrease at D2 and become more important with time. However, Lₐ has a greater hypoglycemic potential than Glibenclamide.

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

<table>
<thead>
<tr>
<th>Administered solutions</th>
<th>Fasting blood glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time (days)</td>
</tr>
<tr>
<td></td>
<td>D0</td>
</tr>
<tr>
<td>Serum saline (10 g/kg/vo)</td>
<td>430.2 ± 64.8 *</td>
</tr>
<tr>
<td>Glibenclamide (10 g/kg/vo)</td>
<td>431 ± 55.4 *</td>
</tr>
<tr>
<td>Lₐ (12.5 g/kg/vo)</td>
<td>430.6 ± 57 *</td>
</tr>
</tbody>
</table>

**Discussion**

Phytochemistry and blood glucose levels were performed on Aloe buettneri leaf extracts (Lₐ) 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 hypomyocemia induced by gibenclamide have been proposed. Subsequently, the screening of the hypoglycemic activity of Lₐ 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 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) [21]. 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 free 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-CRÉDO (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 Tourn (1991) [30] and then Guillausseau (1994) [31] show that diagnosis of diabetes is made when the laboratory assays provide 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 L₄, 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 antihyperglycemic 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) [25]. 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]. L₄ has potential antidiabetic activity. L₄ also has a hypoglycemic activity both in normoglycemics 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. L₄ 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, Ghanam 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 L₄ 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 decoct obtained from the leaves of Aloe buettneri. Ghanam 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 normoglycemics 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 normoglycemics 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 Gibenclamide 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 fraxa of the Leguminous family (Awah, 2006; El-Abbar and Schaal, 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 charantia (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 normoglycemics mice where glibenclamide should be active beyond 24 h and D2 (chronic essay) because of the cumulative effect. It is the same for the L₄ 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 normoglycemics 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.

References
32. WHO. Model List of Essential Medicine, 18th Ed. http://apps.who.int/iris/bitstream/10665/93142/1/EML_1