

## ANTIDIABETIC ACTIVITY AND CHEMICAL SCREENING OF THE AQUEOUS EXTRACT OF SEEDS OF *STRYCHNOS CAMPTONEURA* GILG & BUSSE (LOGANIACEAE)

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### ABSTRACT

This contribution studies concern the antidiabetic activity and chemical screening of the aqueous extract of the seeds of *S. camptoneura*. The antidiabetic activity was evaluated respectively in normal and hyperglycemic rats by overdose of glucose 10% at 3g/kg by oral way and, in the rat made diabetic by intravenous injection of the streptozotocine 50mg/kg. The results show a significant reduction ( $p < 0.01$ ) of glycemia in the normal rats at 3<sup>rd</sup> hour (47.37% at 400 mg/kg of extract against -04.44% for distilled water). The administration of aqueous extract one hour before the overdose of glucose caused 30 mn after, a significant hyperglycemia ( $p < 0.05$ ) compared with the control group (distilled water). In diabetic rats

treated with the extract, the glycemia decreases significantly ( $p < 0.05$ ) from 2<sup>nd</sup> until the 5<sup>th</sup> hour at 54.17; 60.65 and 40.71% respectively at the doses of 200; 400 and 800 mg/kg against -0.01% for control group (distilled water). The chemical screening by tube reactions revealed the presence of alcaloids, saponosids, flavanons, sterols/triterpens and mucilages. These results can justify the use of these species in traditional medicine against diabetes.

**KEYWORDS:** *Strychnos camptoneura*, aqueous extract, antidiabetic, chemical screening.

## 1. INTRODUCTION

Diabetes is a chronic metabolic disease which results in high rate of glucose in blood. It occurs when the concentration of glucose at fast, becomes higher than 1,4g/l. This chronic hyperglycemia in the organism is caused either by a dysfunction of the pancreas, which does not produce sufficient insulin, or by a misuse of glucose in the muscular cells, or by the hereditary and environmental factors as by other pathologies (**Deteix, 2005**). The incidence of diabetes on the organism appears in the form of serious metabolic, degenerative, infectious, cardiovascular and renal complications which have a negative impact on the life of the patient and can lead to his death. According to WHO, one estimates at 135 million the number of diabetic in the world with a forecast of 300 million people likely to be reached at 2025. This prevalence is in continuous increases in the industrialized and the developing countries (**WHO, 2002**). In Africa, the epidemiologic data of the diabetes are estimated at 14 million in 2011 and in 2030 this number will reach 28 million diabetic (**Sambo, 2011**). In the Republic of Congo, according to Diabaction Association of Congo, the prevalence is estimated at 7% (**ADC, 2015**). The clinical evolution of this disease requires diabetic life treatment, followed well and a regular self-monitoring, very expensive in hospital area, calling upon the association of several therapies (**Deteix, 2005**). The prohibitory costs of the modern treatment for the populations of the poor countries, and the difficulties of access to the modern drugs lead the patients towards the traditional remedies. WHO encourages the intensification of the research of the tracks also including those which resort to the traditional treatments containing medicinal plants (**WHO, 1995**). *S. camptoneura* is abundantly used in traditional medicine in the zone of Makoua, Itoumbi, Mbomo, Kelle and Mbama (North of Brazzaville) in the treatment of paludism, ulcers, rheumatisms, diabetes, fever, microbial infections, hernia, parasitoses and sexual failures (**Morabandza et al, 2016**). If other curative effects were already checked scientifically, its antidiabetic properties were not done yet. Thus, we intend to evaluate its potential antidiabetic in order to contribute to the development of an improved traditional drug with antidiabetic potentiality.

## 2. MATERIALS AND METHODS

### 2.1. Plant collection

The seeds of *S. camptoneura* were collected at M'voula, a village of Itoumbi (Cuvette ouest in Congo) located at 765 km from Brazzaville, in June 2015. The specimen was identified in the Research Institute of Exact and Natural Sciences (I.R.E.N.S.) of Congo registered under

the N° 2271. They were previously washed, air dried during 10 days at laboratory temperature ( $25\pm 1^{\circ}\text{C}$ ).

## 2.2 Experimental Animals

To carry out this study, we used male Wistar rats, from 2 to 3 months weighing between 150 and 200g. Animal comes from the animalery of the Laboratory of Biochemistry and Pharmacology Faculty of Health Sciences at Marien Ngouabi University (Brazzaville-Congo). They had free access to water and food.

## 2.3 Preparation of aqueous extract

100 g of seeds was subjected to magnetic maceration extraction in 1000 ml of distilled water during 72 hours. The macerate was filtered three (3) times with the absorbent cotton and the filtrate concentrated at  $50^{\circ}\text{C}$  until obtaining 09.65g of dry extract; corresponding to the yield extraction of 09.65%. The concentrate tightly closed and kept to  $4^{\circ}\text{C}$  to the refrigerator for pharmacological tests.

## 2.4 Hypoglycemic test

Normal rats were divided into 4 groups of 5 rats each one and treated orally. Control group (group 1) treated with 10 ml/kg of distilled water; group 2 received glibenclamide at 5 mg/kg; groups 3 and 4 received respectively the doses of 400 and 800 mg/kg of aqueous extract of the seeds of *S. camptoneura*. A follow-up glycemic was made after administration, during 3 hours by taking the glycemia of each animal each hour.

## 2.5 Antihyperglycemic test

An overdose of glucose 10% at 3g/kg was made to cause an hyperglycemia in the normal rats after the fasting period of 16 hours. 5 groups of 5 male rats each one were made and treated orally as follows: Control group (group 1) received 10 ml/Kg of distilled water; group 2, received glibenclamide at 5 mg/kg; groups 3, 4 and 5 received respectively the doses of 200, 400 and 800 mg/kg of the aqueous extract of seeds of *S. camptoneura*.

At  $t_{-1/2\text{h}}$ , the animals received distilled water and the extracts; at  $t_0\text{h}$ , animals received the overdose of glucose after taking the glycemia; at  $t_{1/2\text{h}}$ ;  $t_1\text{h}$ ;  $t_2\text{h}$  and  $t_3\text{h}$  after overload of glucose, the rats glycemia were taken.

## 2.6 Induction of diabetes of the type II

After a 14 hour fasting, male rats received via the penis vein, a single dose of streptozotocine at 50 mg/kg proportionally with their body weight. Three days after, the rats glycemia were evaluated in order to confirm the appearance of diabetes. The rats having a glycemia after fasting higher than 1.40 g/l were considered as one diabetics of type II and were confirmed at the 5<sup>th</sup> day by the persistence of the hyperglycemia.

### 2.7 Antidiabetic activity

After a 16 hour of fasting, 5 groups of 5 diabetic rats by injection of the streptozotocine were made: group1, the rats were treated with 10 ml/kg distilled water; group 2 treated with glibenclamide at 5mg/kg; groups 3, 4, and 5 received respectively by oral way 200, 400 and 800 mg/kg aqueous extract of *S. camptoneura*. After administration of various products, a follow-up glycemie 5 hours was made by taking the glycemia of the rats after each hour.

### 2.8 Treatment of the results

The results were treated with Excel, the statistical analysis was made with the tests of opposite Student. The percentage of reduction of glycemia (P.R.G) was obtained starting from the formula:

$$PRG = \frac{\text{Glycémie 0h} - \text{Glycémie xh}}{\text{Glycémie 0h}} \times 100$$

### 2.9 Chemical screening

The various great chemical groups contained in macerated seeds of *S. camptoneura* were identified by colored reactions in tubes method (Cuilei, 1982; Sofowora, 1996).

## 3. RESULTS

### 3.1 Hypoglycemic test of aqueous extract of the seeds of *S. camptoneura*

The aqueous extract of the seeds of *S. camptoneura* at the dose of 400 mg/kg decreases the basic glycemia of the rats (table II). Indeed, the administration of the extract at 400 mg/kg involves at the 1<sup>st</sup> hour, a significant reduction ( $p < 0.05$ ) of glycemia with the P.R.G. of 13.68%, compared to the control group (distilled water). From the 2<sup>nd</sup> hour until the 3<sup>rd</sup> hour, the reduction is significant and more marked ( $p < 0.01$ ) with the percentages 27.37% and 47.37% respectively for the 2<sup>nd</sup> and 3<sup>rd</sup> hour, compared to the control group. For the one who received glibenclamid (5mg/kg), the reduction becomes significant only from the 2<sup>nd</sup> hour ( $p < 0.05$ ) and is more significantly marked ( $p < 0.01$ ) at 3<sup>rd</sup> hour with percentages of 21.70

and 41.51% respectively. However, the dose of 800 mg/kg remains ineffective until the 3<sup>rd</sup> hour (table II).

**Table II: Effect of aqueous extract of the seed of *S. camptoneura* on average glycemia of the normal rats.**

Products	Means values of glycemia (g/l) (Percentage of reduction)			
	0 h	1 h	2 h	3 h
Distilled water (10mL/kg)	0.99±0.081	1.16±0.10 (-18.88%) <sup>ns</sup>	1.09±0.09 (-11.11%) <sup>ns</sup>	1.032±0.08 (-4.44%) <sup>ns</sup>
Glibenclamid (5 mg/kg)	1.06±0.05	1.01±0.01 (04.72%) <sup>ns</sup>	0.83±0.03 (21.70%)*	0.62±0.03 (41.51%)**
Aqueous extract (400 mg/Kg)	0.95±0.01	0.82±0.03 (13.68%)*	0.69±0.05 (27.37%)**	0.50±0.07 (47.37%)**
Aqueous extract (800 mg/Kg)	1.04±0.05	1.01±0.07 (02.88%) <sup>ns</sup>	0.86±0.05 (17.31%) <sup>ns</sup>	0.80±0.07 (23.08%) <sup>ns</sup>

Significative difference by report to the control group treated with distilled water

\* $p < 0.05$ ; \*\* $p < 0.01$ ; ns: no significative; (%): percentage of reduction of glycemia

### 3.2 Effect of the aqueous extract of the seeds of *S. camptoneura* on the glycemia of the subjected rats to the hyperglycemia proof

The evolution of the average glycemia of normal rats subjected to the hyperglycemia proof shows that the administration of different doses of the aqueous extract and the glibenclamid before the overdose of glucose, induced 30 mn after, a weak decrease of the glycemia (-0.5h to 0h) compared to the starting glycemia. The administration of glucose to 10% *per os*, showed for all of the groups an increase of the average of glycemia at 0.5h later. One notes that however the peak of the average glycemia presented by the rats of control group (distilled water) is significantly higher ( $p \leq 0.05$ ) to that presented by the glibenclamide group and the one receiving the extract (200, 400 and 800 mg/kg). Three (3h) hours after the overload, the average glycemia of the rats treated with the glibenclamide and 200 and 400 mg/kg of the extract were significantly reduced ( $p \leq 0.05$ ) compared to the average glycemia of the control group (distilled water).

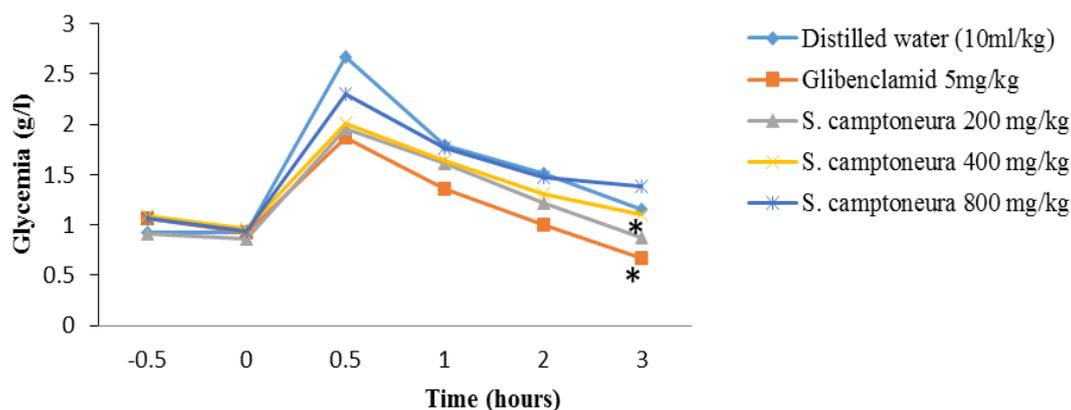


Figure 4 : Evolution of average glycemia of normal rats subjected to the hyperglycemia proof via oral way

### 3.4 Effect of the aqueous extract of the seeds of *S. camptoneura* on the glycemia of the rats made diabetic by the streptozotocine

Table III shows the effect of various doses (200, 400, and 800 mg/kg) of the extract on the glycemia of the diabetic rats of type II. One hour after the administration of the products, one observes a significant decrease ( $p < 0.05$ ) of the average of glycemia to the diabetic rats treated with 400 mg/kg of extract and the glibenclamide, compared to the rats which received only distilled water (control group). The two other doses (200 and 800 mg/kg) of extract are still ineffective. Two hours later, all the doses of the extract become effective until the 5<sup>th</sup> hour; but one notes that the dose of 400 mg/kg remains more effective than the two others (60.65% for 400 mg/kg against 54.17% and 40.77% respectively for 200 and 800 mg/kg). The glibenclamid, produced pure remains more effective ( $p < 0.01$ ) that all dose of the extract with a percentage of reduction of the glycemia of 77.40% at 5<sup>th</sup> hour.

**Table III: Effect of Aqueous extract of the seeds of *S. camptoneura* on average glycemia to diabetics rats of type II.**

Products	Means values of glycemia (g/l) (percentage of reduction of glycemia)					
	0h	1h	2h	3h	4h	5h
Distilled water (10 mL/kg)	2.02±0.09	2.12±0.02 (-04.95%) <sup>ns</sup>	2.26±0.17 (-11.88%) <sup>ns</sup>	2.29±0.28 (13.36%) <sup>ns</sup>	2.16±0.27 (-06.93%) <sup>ns</sup>	2.04±0.30 (-01.00%) <sup>ns</sup>
Glibenclamid (5 m/kg)	2.08±0.14	1.49±0.12 (28.36%) <sup>**</sup>	0.69±0.70 (66.83%) <sup>***</sup>	0.60±0.07 (71.15%) <sup>***</sup>	0.53±0.06 (74.52%) <sup>***</sup>	0.47±0.06 (77.40%) <sup>**</sup>
Aqueous extract (200 mg/kg)	2.40±0.13	1.97±0.16 (17.91%) <sup>ns</sup>	1.65±0.05 (31.25%)*	1.47±0.05 (38.75%)*	1.36±0.06 (43.33%)*	1.10±0.07 (54.17%)*
Aqueous extract (400 mg/kg)	2.77±0.26	1.86±0.24 (32.85%)*	1.81±0.23 (34.66%)*	1.45±0.14 (47.65%)*	1.33±0.07 (51.98%)*	1.09±0.06 (60.65%)*
Aqueous extract (800 mg/Kg)	2.06±0.23	1.74±0.08 (15.53%) <sup>ns</sup>	1.55±0.11 (24.75%)*	1.40±0.10 (32.04%)*	1.33±0.09 (35.43%)*	1.22±0.06 (40.77%)*

*Significative difference by report to the control group treated with distilled water:*

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ; ns: no significative; (%): percentage of reduction of glycemia.

### 3.5 Chemical profile of the aqueous extract of seeds of *S. camptoneura*

The tube reactions revealed different secondary metabolites in the aqueous extract of the seeds of *S. camptoneura*. The results in table I show that this extract contains alkaloids, saponosids, sterols and tri-terpens, mucilages and the flavanons in great quantity. One notes an absence of flavones, flavonols and flavanols, tanins, anthocyanes and reducing compounds.

**Table I: Chemical profile of aqueous extract of the seeds of *S. camptoneura*.**

Familles chimiques		Test results
Alcaloids		+
Saponosids		+
Free flavonoids	Flavons	-
	Flavanons	++
	Flavonols and flavanols	-
Tanins		-
Anthocyanes		-
Sterols/terpens		++
Mucilags		+
Reducing compounds		-

+ = presence ; ++ = abundance ; - = absence.

## 4. DISCUSSION

*S. camptoneura* is a medicinal plant of traditional Congolese pharmacopoeia widely used against several pathologies among which diabetes (Morabandza et al., 2016). The results show a reduction of the average of glycemia of the treated rats with the aqueous extract, compared to there which received distilled water (control group). This reduction is more remarkable at the dose 400 mg/kg of the extract; what lets think an hypoglycemiant effect. The analyzis of figure 4 what is, the test of hyperglycemia caused by oral way or test of tolerance to glucose, reveals an hyperglycemia in all rats, 30 mn after the glucose overdose; particularly to the rats having received distilled water. Yet to the one that received glibenclamid and the extract (200, 400 and 800 mg/kg), one observes at the same time, less low peaks of glycemia. This presupposes the plant extract as the glibenclamid would prevent the treated animals to make very high peaks of glycemia, compared to the control which received only distilled water. It would increase the tolerance of cells to glucose and protect the animals against the occurrence of a great hyperglycemia. The same results were obtained

in the rats with the extracts of *Trilepisium madagascariense* (Ampa *et al*, 2013); *Cogniauxia podolaena* (Badila, 2003) and *Ceiba pentandra* (Dzeufiet-Djomeni, 2007).

The table III shows that the administration of the extract at various doses provoke one hour later, a reduction of the average of glycemia in all the diabetic rats compared to the average starting glycemias but, this reduction is significant only for the diabetic rats having received glibenclamid and aqueous extract at 400 mg/kg ( $p < 0.05$ ), compared to the diabetic rats having received distilled water. The reduction of the average glycemia at 200 and 800 mg/kg of the aqueous extract becomes significant only 2 hours later. From the 3<sup>rd</sup> until the 5<sup>th</sup> hour, all doses of the aqueous extract (200, 400 and 800 mg/kg) become significant ( $p < 0.05$ ), compared to the control (distilled water), with variable percentages of reduction. It is noted that the dose of 400 mg/kg remains the one which has higher percentages of 47.65%; 51.98% and 60.65% respectively at 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> hour. One can thus deduce from these results that the seeds of *S. camptoneura* have an antidiabetic activity on the rats made diabetic by the streptozotocin. The dose of 400 mg/kg acts quickly and more effectively by reducing the glycemia average of diabetic rats and this activity decreases slightly with the time one confirms that the antidiabetic activity of these seeds is dependent on dose. The activity of this extract is at long duration, because above to 4 hours, the glycemia average continues to decrease. The similar results were obtained with hydroethanolic extracts of *Trilepisium madagascariense* (Ampa *et al*, 2013) and with macerated of *Zizyphus mauritania* leaves (Yassambou<sup>[26]</sup>). These results also approach with those obtained with the aqueous extract *Icacina senegalensis* leaves what the dose 400 mg/kg reduced better and significantly the glycemia average of the animals that the dose of 800 mg/kg (N'diaye *et al*, 2008).

These results suggest that the extract contains active substances which induce in the rats a very active use of glucose by peripheral muscle. The results of chemical screening showed the presence of alkaloids, saponosids, flavonoids, sterols/terpens and the mucilags; with higher concentration of free flavonoids. The absence of another substances can be explained by the weak capacity of water extraction. Thus, the reduction of glycemia can be related to the presence of the flavonoids in the aqueous extract of seeds of *S. camptoneura*. Indeed, the anti-hyperglysemic capacity of the flavonoids was announced with the aqueous extracts of the roots of *Bridelia ferruginea* (Bakoma *et al*, 2012). and also with *Citrus* what flavonoids could have hyperglysemic antiproperties while acting on the enzymatic activity intervening in the hepatic metabolism of glucose (Jung *et al*, 2004) It was also shown that flavonoids can

increase the glucotransporter activity GLUT4 of the adipocytes for the synthesis of glycogen on the level of the liver (**Jung et al, 2006**). The dose of 400 mg/kg of the extracts of the seeds of *S. camptoneura* could thus act by using these same ways. Indeed, the flavonoids equipped with antidiabetic activity were identified in the extracts from some plants (**Iwu et al, 2009; Kébièche, 2009; Pandeya et al, 2013**). In addition, other chemical substances such as the saponosids and the alkaloids contained in the aqueous extract of the seeds of *S. camptoneura* can also be responsible of this activity. Former works respectively with the decocted of *Vernonia colorata* leaves and the extracts of *Zizyphus mauritania*, proved that the alkaloids, the flavonoids and the saponosids contain the antidiabetic properties (**Mbodj Ndeye, 2003; Awa, 2003**). It can also be a combined activity of three substances: association flavonoids-alkaloids or flavonoides-terpens like that was observed respectively with the barks and the leaves of *Gnidia glauca* Lin (**Sougataghosh Mehul et al, 2012**) and the leaves of *Lycium shawil* (**Hassan et al, 2011**).

#### 4. CONCLUSION

The results of this study show that the seeds of *S. camptoneura* have a potential antidiabetic of long duration. The dose of 400 mg/kg seems to be more active than those of 200 and 800 mg/kg; this activity is dose-dependent. However, for all the tested doses, the activity of the extract remains significant until the 5<sup>th</sup> hour. The chemical screening revealed the presence of bioactives substances able to decrease the glycemia of the normal and diabetic rats. These results can justify the use of this species in traditional congolese medicine in the treatment of diabetes.

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