Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
https://www.phytojournal.com
JPP 2023; 12(3): 37-42
Received: 11-03-2023
Accepted: 17-04-2023

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Phytochemical profile and antiradical and antidiabetic activities of a plant recipe known to be antidiabetic in traditional Congolese medicine

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Abstract
The aim of this work is to promote traditional Congolese medicine. Thus, a plant recipe known to be anti-diabetic, called "NGOSI" was used for a chemical and biological study. Phytochemical screening and antiradical activity of the recipe were carried out by TLC on the different fractions (chloroformic, methylethylketone and ethanolic) of this recipe. The anti- diabetic activity was evaluated by monitoring the glycaemia of rats made hyperglycaemic by oral glucose at a rate of 3 g/kg, and of rats made diabetic by injection of alloxane. The results obtained confirm the efficacy of the recipe with a percentage reduction in the average blood glucose level of the rats of 68.03% ($p < 0.01$). The screening results showed the presence of several metabolites (terpenes, sterols, flavonoids, saponosides, glycosides and sugars). The screening of the antiradical activity of this recipe was positive on TLC. These results justify the use of this recipe in the traditional treatment of diabetes.

Keywords: Screening, diabetes, recipe, traditional medicine

Introduction
Diabetes is a metabolic disease that manifests itself as chronic hyperglycaemia and is a major public health problem. Today, it is considered one of the five leading causes of death in the world [1]. It is one of the fastest growing pandemics of the century. It is an insidious disease by definition and shows an epidemiological transition is more than worrying. According to WHO figures, 537 million people worldwide have diabetes, with 6.7 million deaths expected in 2021 [2]. In addition, the International Diabetes Federation estimates that 382 million people worldwide have diabetes and this figure is expected to rise to 592 million by 2035. In 2017, it was estimated that one in eleven adults worldwide had diabetes, 50% of whom were undiagnosed but at high risk of developing serious complications and premature death. According to the Congolese Ministry of Health in 2015, the prevalence of diabetes is estimated at 7% and is the leading cause of blindness, chronic end-stage renal disease and lower limb amputations in the Republic of Congo. The various treatments for diabetes consist of controlling blood sugar levels through dietary measures, taking oral antidiabetics for type II diabetics and only insulin therapy for type 1 diabetics [3]. Despite the progress of modern medicine, the various treatments for diabetes are very costly and are becoming less and less effective in the face of the complications that the disease generates. As a result, many diabetics are turning to plant-based treatments. This alternative is not new, as the use of plants for medicinal purposes dates back to prehistoric times and this tradition has been passed on from generation to generation [4]. Today, 80% of the world's population uses traditional medicine according to the WHO. The availability, lower cost and satisfactory results of these plant-based treatments are encouraging some countries, especially African countries, to carry out further studies in order to valorize these different plants. Thanks to the bioactive molecules they contain, these plants can be used to make Improved Traditional Medicines (ITMs). Although there have been important studies on the identification of anti-diabetic species and their chemical composition [5], very few studies have focused exclusively on anti-diabetic plants in general and, more importantly, on the recipes of these plants in the world and in Congo in particular. Of the 37 plants presumed or reputed to be anti-diabetic already inventoried in the Republic of Congo [6], very few have been the subject of scientific investigation. With this in mind, we undertook a chemical and biological study of "NGOSI", which is one of the plant recipes used to treat diabetes in Brazzaville (Republic of Congo).

Material and methods

Plant material

The plant material used in this work consists of the anti-diabetic recipe which is a mixture of six plants (leaves and roots) called "NGOSI". It was developed by the tradithérapeute of CENACLE (Research and treatment Center of Plants Reveal) located in Brazzaville, recognized by the WHO and authorized by the Congolese Ministry of Health under N0 021/2002 MSSAH/DAS/CAS. This aqueous solution (herbal tea) was prepared and purchased directly from CENACLE (figure 1).

Animal material

Male albino rats weighing between 180 and 270 g, bred at the animal house of the Faculty of Science and Technology of the Marien Ngouabi University were used in this study. The pharmacological tests were carried out in the Laboratory of Pharmacodynamics and Experimental Physiopathology (L2PE) where the animals had free access to food and water outside the juvenile periods preceding the experiment (figure 1).

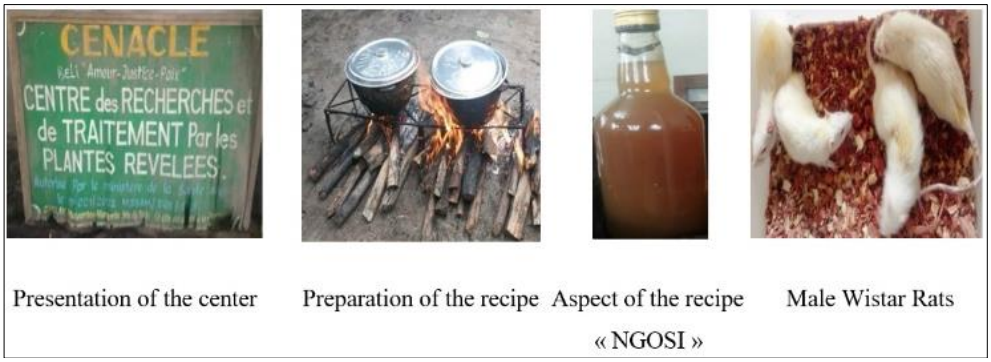


Fig 1: Materials used

Six (6) plants constituting the recipe were mixed and boiled for about fifteen minutes. The resulting solution was then left to cool and filtered. 1 L of this decoctate was concentrated to half strength using a rotary evaporator.

Fractionation of the recipe

Using a separating funnel, 500 mL of the plant recipe concentrate was fractionated successively with chloroform, methylethylketone (MEK) and ethanol. The different fractions obtained were concentrated to dryness and stored in the refrigerator at 4°C for analysis.

Phytochemical screening

Phytochemical screening was performed on TLC plates (60 F254, aluminium support, 20×20) following the methods described in the literature [7]. Different elution systems were used: Hexane/Ethylacetate (7/3; v/v); Chloroform/Acetone/Methanol (5/7/1; v/v/v) for the chloroform and MEK fractions; Ethyl acetate/ Formic acid/ Water (8/1/1 ; v/v/v) for the MEK and ethanolic fractions; Dichloromethane / Acetic Acid / Methanol (9/3/2; v/v/v) and Butanol / Acetic Acid/EthylAcetate/Water (3/2.5/1.5/0.5; v/v/v) for the ethanolic and water fractions. Depending on the type of secondary metabolites to be identified, several specific reagents were used: anisaldehyde, vanillin and sulphuric naphthol for terpenes, sterols, glycosides, sugars and saponins, NEU and AlCl3 for flavonoids, FeCl3 for tannins and phenolic compounds, SbCl3 for saponosides.

Screening for antiradical activity (ARA)

Screening for ARA was performed on TLC according to the method described by Cavin in 1999. Plates were developed in two elution systems respectively, namely: Hexane/ethylacetate (7/3; v/v) for the chloroformic fraction; Dichloromethane/acetic acid/methanol (9/3/2; v/v/v) for the ethanolic fraction. After drying, the TLC plates were sprayed with a 2 mg/mL ethanolic solution of DPPH. Constituents with free radical scavenging activity appear as yellow-white spots on a purple background [8].

Anti-hyperglycaemic activity of the recipe

This activity consists of administering the plant recipe extract to normoglycaemic animals one hour before the 10% glucose overload (3 g/kg) and then monitoring blood glucose levels for at least 3-4 hours after the overload [9]. Thus, four (4) group of five (5) rats each were formed:

- The group 1 receiving the distilled water 10 mL/ kg ;
- The group 2 receiving the reference product (Glibenclamide 5 mg/ kg);
- The group 3 and 4 receiving the recipe at two different doses.

After 18h of fasting with free access to tap water, the animals received at:

- t_{-1h}, distilled water, Glibenclamide and the extracts at different doses ;
- t_0, the glucose overload. Then the blood glucose monitoring was performed for 3 h ;

Blood glucose measurements were taken at $t_{1/2h}$; t_{1h}; t_{2h} and t_{3h} after glucose overload.

Induction of diabetes

Diabetes mellitus similar to type II diabetes was induced by intraperitoneal injection of 75 mg/kg body weight of Alloxane into fasted male rats for 16-18 hours. After injection, the rats were returned to the cages with free access to food and a 5% glucose solution to drink overnight to avoid hypoglycaemic shock. Food and water consumption of the animals was monitored daily. Three days after induction, a blood glucose check was performed to select animals with blood glucose levels above 1.26 g/L for testing [10].

Antidiabetic activity

This activity consists of administering the plant recipe to animals made diabetic. Thus, four (4) group of 5 animals each were constituted:

- The group 1 receiving distilled water (10 mL/kg);

- The group 2 receiving the reference product, Glibenclamide (5 mg/ kg);
- The group 3 and 4 receiving the recipe at two different doses (0.0075 mL/g and 0.01 mL/g)

After 18 h of fasting, with free access to tap water, the animals received distilled water, Glibenclamide and the extracts at different doses. Glycemic monitoring was done every 1 h for 6 h on animals.

Results and discussion

Phytochemical screening

The phytochemical screening carried out on the recipe showed (figure 2):

- In the chloroform fraction, a richness in terpenes and sterols by the presence of purple, blue, green, yellow, brown and red spots (chromatogram 1, 2) ;
- In the MEK fraction, a diversification of flavonoid aglycones, flavonoid glycosides characterized by the presence of yellow, blue, yellow-orange spots (chromatogram 2) ;
- In the ethanolic fraction, a diversification of flavonoids identified by the different yellow, yellow-orange, blue, red and orange spots. Similarly, in this extract, violet, blue, green, yellow, brown and red stains likely to characterize the glycosides (chromatograms 2, 3) ;
- In the aqueous fraction, sugars and saponosides were revealed by the presence of green- blackish and purple spots (chromatograms 4 and 5).

The presence of these different compounds in this recipe justifies its therapeutic effect as these compounds are identified in several plants presumed or known to be anti-diabetic and play an important role in the treatment of diabetes.

Indeed, triterpenes and steroidal glycosides are bioactive compounds present in several plants with known hypoglycaemic activity [11]. Momordicoside, a glycoside isolated from *Momordica Charantia* L., has been shown to improve glucose absorption by increasing insulin secretion [12]. The presence of bioactive compounds such as alkaloids, flavonoids, cardiac glycosides, terpenes, steroids, resins and sulphur compounds such as alline identified in *Allium Sativum* commonly known as "garlic" have shown anti-diabetic activity with the mechanism of controlling insulin excretion from cells, improving glucose tolerance and glycogen synthesis [13-14]. In addition, the identification of allylpropyldisulfide and *S*-methylcysteinesulfoxide in garlic has shown that they can lower blood glucose levels by restoring the insulin response [15]. Apart from their antioxidant powers by excellence [16], flavonoids have many therapeutic virtues and involvement in the reduction of several parameters associated with diabetes. For example, quercetin has the ability to reduce blood glucose levels in diabetic rats [17-19]. They modulate glucose metabolism or insulin sensitivity at different levels by increasing glucose uptake, insulin secretion and inhibition of glucose production [20]. Naringin and hesperidin, two flavonoids that have been shown to reduce GLUT2 protein expressions in the liver [21]. In addition, apigenin is 200 times more potent than metformin, a drug sold in pharmacies as an oral anti-diabetic. At the cellular level, exposure of HepG2 cells to high levels of glucose and apigenin reduces ACC phosphorylation and impairs lipid accumulation [22]. Kaempferol, a flavonoid found in *Ginkgo biloba* L., grapefruit, tea and some edible berries, is able to reduce fasting blood glucose, serum HbA1c levels and increase insulin resistance [23]. Analysis of liver gene expression revealed that Kaempferol reduced the expression of PPAR-γ and SREBP- 1c. As a result, Kaempferol is thought to have anti-obesity and anti-diabetic effects [24]. Glycosides, on the other hand, have a hypoglycemic effect on diabetic patients. The example of charantine isolated from *Momordica charantia* Linn. is one of the cases of these metabolites having an "insulin-like" effect responsible for hypoglycaemic activity, particularly in type II diabetes *in vitro* [25].

Polysaccharides also have antidiabetic potential with various underlying molecular mechanisms to combat diabetic complications. They regulate the main basis for the development of these products is their source, composition and preparation. They have been documented to have potent anti-diabetic activity such as *β-D*-(1-6)-glucan, a sugar that can improve insulin levels and hepatic glycogen accumulation by decreasing blood glucose in streptozotocin (STZ)-induced diabetic mice [26]. The presence of rutin or compounds with the same basic skeletons as rutin in this recipe could further justify the anti-diabetic activity of the flavonoids contained in this "NGOSI" recipe. These results on rutin were elucidated by the work of Kamalakkannan in 2006 who showed that rutin exhibited antihyperglycemic activity in rats made diabetic by streptozotocin [27].

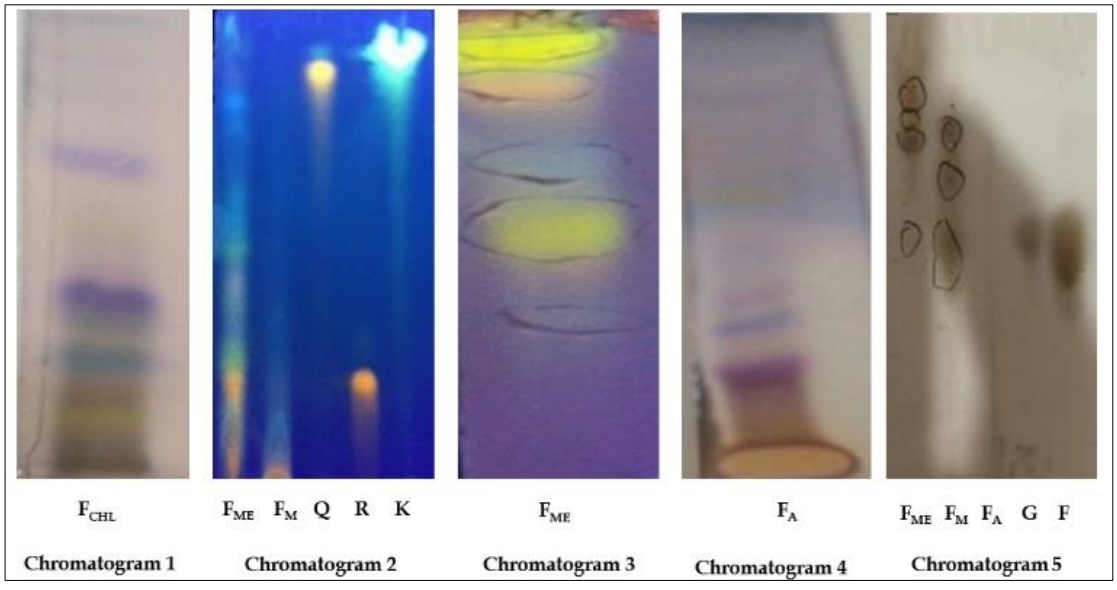


Fig 2: Different chromatographic plates from recipe and different fractions

FCHL: Chloroformic Fraction, FME : MEC Fraction, FM : Methanolic Fraction, FA: Aquoeus Fraction, Q: Quercetin, R : Rutin, K : Kampferol, G : Glucose, F: Fructose		
Chromatograms	**Elution system**	**Developer**
Chromatogram 1	Hexane/Ethylacetate (7/3; v/v)	Sulphuric anisaldehyde
Chromatogram 2	Chloroform/Acetone/Methanol (5/7/1; v/v/v)	NEU
Chromatogram 3	Ethylacetate/Formic acid/Water (8/1/1; v/v/v)	
Chromatogram 4	Dichloromethane/Acetic acid/Methanol (9/3/2; v/v/v).	Sulphuric vanillin
Chromatogram 5	Butanol/Acetic acid /Ethylacetate/Water (3/2.5/1.5/0.5; v/v/v)	SbCl3

TLC screening for antiradical activity (ARA)

The presence of the pale yellow spots on a purple background proved that the recipe contains phytocompounds that can scavenge free radicals (Figure 3). By comparing the chromatographic profiles of the phytochemical screening and the antioxidant activity screening, the correspondence between the active zones and the phytocompounds responsible for this activity was established. The yellow spots would correspond to flavonoids, terpenes and sterols. These The results once again justify the use of the recipe in the treatment of diabetes, as plants with ARA can prevent oxidative stress, which is consequently involved in the *β*-cell dysfunction noticed in diabetics [28].

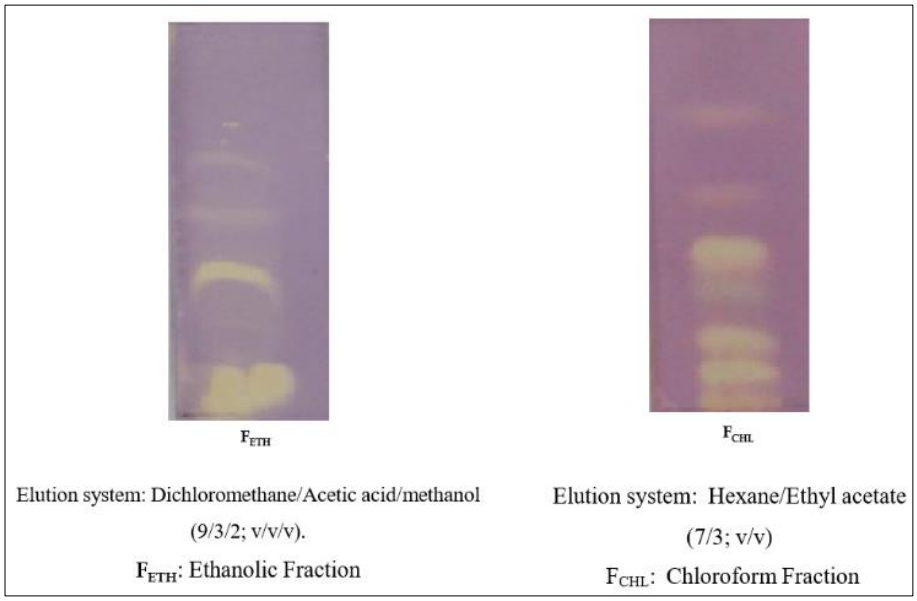
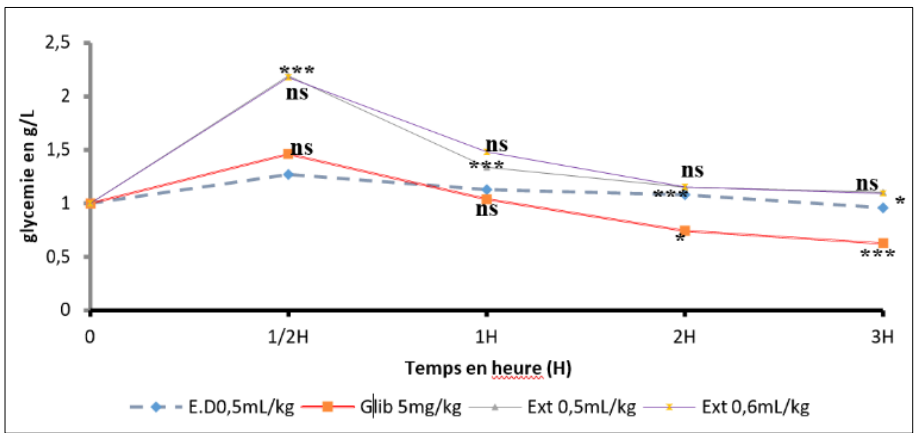


Fig 3: Chromatographic plates of antiradical activity from ethanolic and chloroformic fractions

Effect of the recipe extract on blood glucose levels normal rats undergoing the oral hyperglycaemia test

Analysis of Figure 4, reflecting the oral hyperglycaemia test, reveals hyperglycaemia in rats after 30 min of the glucose overdose. Rats given the extract at different doses show even more pronounced hyperglycemia than the others. However, lower peak blood glucose levels were observed in rats given distilled water (control) and glibenclamide. This implies that the recipe would not prevent the treated animals from having high blood sugar peaks compared to the control group.

After 3 h of the glucose overdose, glibenclamide significantly decreased the blood glucose levels of the rats with a percentage of 37.54%. However, the animals that received the recipe at the different doses did not show any decrease in blood sugar levels, with percentages of 10.68% for the 0.5 mL/100 g dose and 9.18% for the 0.6 mL/100 g dose (body weight) compared to the control lot that received distilled water, which showed a percentage of 4.30%. These results show that the recipe does not have the anti-hyperglycemic effect on normal rats subjected to glucose overdose.



(*) p < 0.05; (**) p < 0.01; (***) p < 0.001: Significant difference of the extract compared to the control; ns : Not significant difference.

Fig 4: Anti-hyperglycaemic effect of the recipe extract Antidiabetic activity

Antidiabetic activity

Table 1 show the blood glucose monitoring of diabetic rats according to the different treatments. After 3 h of treatments, the batch of animals treated with the herbal recipe at the dose of 0.01 mL/g showed a non-significant decrease in blood glucose, i.e. a percentage reduction of 14.01%. The rats treated with glibenclamide showed a significant decrease in blood glucose ($p < 0.01$) and a percentage reduction of 45.35%. At 4 h of the experiment, the 0.01 mL/ g body weight recipe showed a non-significant decrease in blood glucose with a percentage reduction of 30.99% ($p < 0.05$); this decrease became significant with a percentage reduction of 51.41%. After 5 h, glibenclamide remains more significant ($p < 0.001$) with a percentage reduction of 70.32%.

However, after 6 h, glibenclamide remains effective ($p < 0.01$) with a percentage reduction of 76.42%. The extract confirms its effectiveness by showing a significant decrease ($p < 0.01$) and a percentage reduction of 68.03%.

These results are in agreement with those of some studies carried out on plants presumed or reputed to be part of the Congolese pharmacopoeia, which have shown their efficacy in tests on rats. This is the case of AMPA Raoul's work in 2013 on the leaves of *Trilepisium madagascariense*, one of the plants used in traditional medicine in Congo. These results showed a significant reduction in blood sugar levels in rats made diabetic by streptozotocin [9]. All these results justify the use of the plant recipe in the traditional management of type II diabetics in Congo.

Table 1: Glycemic monitoring of diabetic rats according to different treatments

Treatments	Average blood glucose values in g/L and percentage reduction in blood glucose						
	0	**1H**	**2H**	**3H**	**4H**	**56**	**6H**
distilled water	1,76 ± 0,17	3,34 ± 0,47	3,91 ± 0,73	3,97 ± 0,17	3,69 ± 0,78	3,63 ±0,80	3,57 ± 0,82
0,5 mL/100 g	/	(- 89,77%)	(- 122,15%)	(- 125,56%)	(- 110,03%)	(-106,43%)	(-102,84%)
Glibenclamide	5,08 ± 0,28	4,37 ± 0,35	3,44±0,13	2,77 ± 0,18	1,97 ± 0,15	1,51 ± 0,27	1,19 ± 0,35
5 mg/kg	/	(13,985%) ns	(32,24%) **	(45,37%) **	61,06%) ***	70,32%) ***	(76,42%) **
recipe	4,47 ± 0,55	5,08 ± 0,38	4,48 ± 0,31	3,87 ± 0,40	3,08 ± 0,42	2,17± 0,44	1,43±0,30
1 mL/100 g	/	(-13,56%) ns	(-0,29%) ns	(14,01%) ns	(30,99%) ns	(51,41%) *	(68,03%) **

(*) $p < 0.05$; (**) $p < 0.01$; (***) $p < 0.001$: Significant difference of the extract compared to the control; ns: Non significant difference.

Conclusion

The present study aimed to valorize a plant-based recipe used in the treatment of diabetes in traditional Congolese medicine. The results of the phytochemical screening and the evaluation of the antiradical and antidiabetic activities showed that the recipe is rich in secondary metabolites with antiradical power and significantly reduces blood sugar levels in diabetic rats. In view of these results, this traditional recipe can be considered as a serious alternative to modern medicine and should be strongly recommended to the Congolese population. This work makes a phytochemical contribution to the knowledge of the plant recipe, thus allowing a better understanding of the pharmacodynamics properties of this extract. It would therefore be interesting to exploit this extract to evaluate its toxicity and to search for the active principles responsible for its pharmacological properties.

Acknowledgement

Our thanks go to the traditionnel practics and his team for the preparation and availability of the recipe.

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