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ASSESSMENT OF THE EFFECTS OF AN AQUEOUS TRUNK BARK EXTRACT OF *PARKIA BIGLOBOSA* (MIMOSACEAE) ON BLOOD SUGAR LEVELS IN RATS

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ABSTRACT

The aim of this study is to contribute to the enhancement of the traditional African pharmacopoeia, in view of the establishment of improved traditional medicines. A phytochemical screening and a toxicological study according to the guidelines and the recommendation 423 of the Organization for Economic Co-operation and Development (OECD) as well as Pharmacological tests of the aqueous extract of *Parkia biglobosa* (EAqPB) on blood glucose were performed. All tests substances have been administrated orally. Qualitative phytochemical tests carried out with the aqueous bark trunk extract of *Parkia biglibosa* (Mimosaceae) made it possible to highlight the presence of sterols and polyterpenes, alkaloids, polyphenols, catechin and gallic tannins, flavonoids and saponosides. The acute toxicity study of this extract in mice at doses of 2000 and 5000 mg/kg bw, did not cause any death. The effects of aqueous extract of *Parkia biglibosa* on blood glucose levels in normoglycemic rats showed good hypoglycemic activity at a dose of 1000 mg/kg bw, with a 17.37% reduction of glycemia. After glucose overload, EAqPB exhibited better antihyperglycemic activity in pretreated rats in contrast to glibenclamide, with a 32% reduction percentage compared to the control. EAqPB has hypoglycemic and antihyperglycemic properties that are probably related to the presence of alkaloids, tannins and flavonoids. These compounds, generally recognized for their hypoglycemic and antihyperglycaemic effects, give this extract properties similar to those of certain insulin secretors. These results are therefore favorable for its exploitation for the treatment of diabetes in traditional medicine and provide a scientific basis for its use.

KEYWORDS: *Parkia biglobosa*, Toxicology, Hypoglycemic et Anti-hyperglycemic.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by an abnormal rise in blood sugar. It is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia due to lack of secretion or insulin action or both.[1] According to the WHO,[2] the number of people with diabetes continues to grow alarmingly (108 million in 1980 to 422 million in 2014). Ivory Coast is not immune to this pandemic with a prevalence that rose from 5.7 % before 2000 to 9.6 % in 2010 according to the Obesity and Diabetes Association of Ivory Coast.[3] The management of diabetes is very expensive because of the high cost of treatment. These constraints lead people in developing countries to turn to traditional medicine.[4]

It is with this in mind that we began to study the hypoglycemic and antihyperglycemic effects of an aqueous trunk bark extract of *Parkia biglibosa*, a reputable antidiabetic plant, in the African pharmacopoeia.[5,6,7]

Parkia biglobosa (Mimosaceae), commonly known as the Malinke tongue of Ivory Coast, is a plant used in the treatment of many diseases. It is recommended in the treatment of amebiasis, hookworm, ascariasis, asthma, infertility, peptic ulcers and dental pain.[5] It is used in the treatment of cardiac, renal and hypertension disorders.[8,9]

Our objective for this work is to evaluate the pharmacological effects of an aqueous trunk bark extract of *Parkia biglobosa* (Mimosaceae) on blood glucose levels in rats in order to contribute to the valorization of the use of plants used in medicine for improving the health of populations.

MATERIAL AND METHODS

Vegetal material

The trunk bark of *Parkia biglibosa* (Jacq.) Benth. (Mimosaceae) was collected on August 25, 2017 in Zuénoula, 373 km away from Abidjan, Ivory Coast. The identification was made by Professor ZIRIHI Guédé Noel of the Botanical Laboratory thanks to the herbariums number 10933 of 22 -12-1969, 13329 of 8-02-1976 and 13336 of 9-02-1976 of the National Floristic Center (CNF) of Ivory Coast.

Preparation of the aqueous trunk bark extract of Parkia biglobosa

The bark is cut into pieces, dried at 25 ° C and then ground in a mechanical ball mill.

Fifty grams (50 g) of ground material are mixed with magnetic stirring for 24 hours in 1 liter of distilled water. The macerate is filtered on hydrophilic cotton and "Wattman n02" filter paper. The filtrate obtained was dried in an oven at 60 ° C. A fine brown powder is obtained which is the crude aqueous extract of the trunk bark of *Parkia biglobosa* (EAqPB). The physiological liquid used for the preparation of the different solutions is 0.9% NaCl solution.

Animal material

Female mice of the *Mus musculus* species (Muridae), Swiss strains weighing between 23 and 27 g, were used for the toxicity tests.

Rats (*Rattus norvegicus*) of Wistar strain weighing between 180 and 230 g were used for pharmacological studies on blood glucose. These animals come from the vivarium of the Superior Normal School, Abidjan. They have access to food and water ad libitum. The animals were acclimated under laboratory conditions before the start of the experiment.

Phytochemical study of the trunk bark of Parkia biglobosa

This study was carried out at the Laboratory of Phytochemistry and Medical Materials of the Department of Pharmacognosy of the Faculty of Pharmaceutical and Biological Sciences of Félix Houphouët-Boigny University, Abidjan. It makes it possible to highlight the large chemical groups having a pharmacological interest. It is done by a qualitative method described by Nene Bi et *al.*[10] and Abo.[11]

Study of the acute oral toxicity of the trunk bark of Parkia biglobosa

The acute oral toxicity study is conducted in mice, according to the guidelines of the Organization for Economic Cooperation and Development (OECD 423).[12] The experimental dose of 2000 mg / kg is chosen for the limit test. Each mouse receives 1 ml of a single dose, evaluated in mg / kg body weight (mg/kg bw) of the substance. The mice of the control group each also receive 1 ml of distilled water. Exceptionally, an additional maximum predetermined dose of 5000 mg / kg will be used because the results will be important for the protection of the health of humans and animals in the event that the 2000 mg / kg dose did not cause death. After administration of the extract, the mice are starved for three to four hours. Animals are observed individually at least once during the first 30 minutes and every 24 hours after treatment. Special attention is required during the first four (4) hours and daily

for 14 days after administration of the extracts. The observations relate to changes in hair, eyes and behavior. The 50% lethal dose (LD50) will be determined in case of animal mortality using OECD guidelines 423.[12]

Pharmacological studies

This study evaluated the effects of EAqPB on blood glucose levels in normoglycemic rats and in temporary hyperglycemic rats. The blood glucose is measured using the Accu-Chek blood glucose meter with test strips.

Normoglycemic rats

For this study a total of 24 Wistar weighing rats were used. These animals are divided into 6 lots of 4 rats and fasted for 18 hours. The average weight of each lot is determined. Before administration of test substances, blood glucose is measured in all animals at a time T0. The rats in batch 1 (control group) receive 2 ml of distilled water. The rats of lots 2, 3, 4, 5 and 6 (test lots) receive respectively 2 ml of 200 mg/kg bw, 300 mg/kg bw, 500 mg/kg bw, 1000 mg/kg bw and 2000 mg/kg bw of the aqueous extract. The blood glucose levels of the rats are measured at regular intervals of 30, 60, 90, 120, 150 and 180 minutes after the administration of the test substances.

Temporary hyperglycemic rats

Normal rats are fasted 18 hours before the start of the experiment. Four batches of four (4) rats are formed and the average weight of each lot is determined. These batches of animals are distributed as follows for the hyperglycemia test in its pre-treated rats: Lot 1 (R-T) is the control in which the rats receive 2 ml of distilled water; Lot 2 (R-T +) constitutes the positive control. This is the batch consisting of hyperglycemic control rats. The rats in this batch receive distilled water and, after 30 minutes, 4g / kg of anhydrous glucose; Lot 3 (R-Glib) consists of the rats which receive glibenclamide (oral hypoglycemic sulphonylurea) at a dose of 10^{-2} g/kg bw and 30 minutes thereafter, 4g / kg of anhydrous glucose; Lot 4 (R-EAqPB), where the rats receive 1000 mg/kg bw of EAqPB and, 30 minutes later, 4 g/kg bw of anhydrous glucose; The effects of the aqueous extract of *Parkia biglibosa* on the rats in this experiment series are monitored for 180 minutes. In these rats, blood glucose is measured at 0, 30, 60, 90, 120 and 180 minutes. For the test of post-treated hyperglycemic rats the protocol is the same as that of pre-treated rats except that in this experiment glucose is administered before the test substances.

Statistical analysis

The statistical analysis of the values and the graphical representation of the data were carried out using the Graph PadPrism 7 software (San Diego, California, USA). The statistical difference between the results was achieved through the analysis of variances (ANOVA), followed by the Tukey-Kramer multiple comparison test, with a significance level P <0.05. All values are presented as average ± ESM (Standard Error on Average).

RESULTS

Phytochemical study of the trunk bark of *Parkia biglobosa*

Phytochemical sorting (Table I), made from the aqueous extract of the trunk bark of *Parkia biglobosa*, revealed the presence of sterols, polyterpenes, polyphenols, catechin and gallic tannins, flavonoids, alkaloids and saponosides. In this extract, it is noted the absence of quinone compounds.

Table I: Results of tube reactions for the detection of some secondary metabolites of the aqueous extract of trunk bark of *Parkia biglobosa.*

Chemical Compounds		Reactions / Reagents	Results
Polyphenols		Reaction with ferric chloride	+
Sterols et Polyterpenes		Liebermann-Bouchard's reaction	+
Flavonoids		Reaction to cyanidin	+
Saponosides		Vigorous agitation	+
Quinone Compounds		Reagent from Borntraeger	-
Alcaloids		Dragendorff Reagent	+
		Bouchardât reagent	+
Tannins	**Catechin**	Stiasny Reagent	+
	Galliques	Reaction with ferric chloride	+

(+) positive tests (-) negative tests

Toxicological study of the aqueous extract of the bark of Parkia biglobosa

The gavage administration of dose of 2000 mg / kg bw of the aqueous extract of *Parkia biglobosa* (EAqPB) has not modified in their behavior. However, the maximum dose of 5000 mg/kg bw, administered to the mouse, caused a decrease in motor skills, breathing difficulties and a grouping in a corner of the cage, for 30 minutes after that their behavior is standardized. During14 days of observation, any mortally in mouse was not recorded, for the doses of 2000 and the dose of 5000 mg/kg bw. The 50% lethal dose (LD50) is therefore greater than 5000 mg/kg of bw.

Effects of aqueous extract of Parkia biglobosa bark on blood glucose levels in normoglycemic rats

Figure 1 shows the effects of the increasing doses of EAqPB on the blood glucose levels of the rats. This extract, at doses of 200, 300, 500 and 2000 mg/kg bw, has not significantly modified ($p > 0.05$) the glycemia in the treated animals, compared with controls, after 180 minutes. On the other hand, at the 1000 mg/kg bw dose, EAqPB causes a drop in the glycemia of the treated rats compared with the controls. At this dose, blood glucose level significantly decrease ($p < 0.05$) with reduction rates of 9.6% after twenty (120) minutes and 17.37% ($p < 0.01$) after one hundred and four twenty (180) minutes.

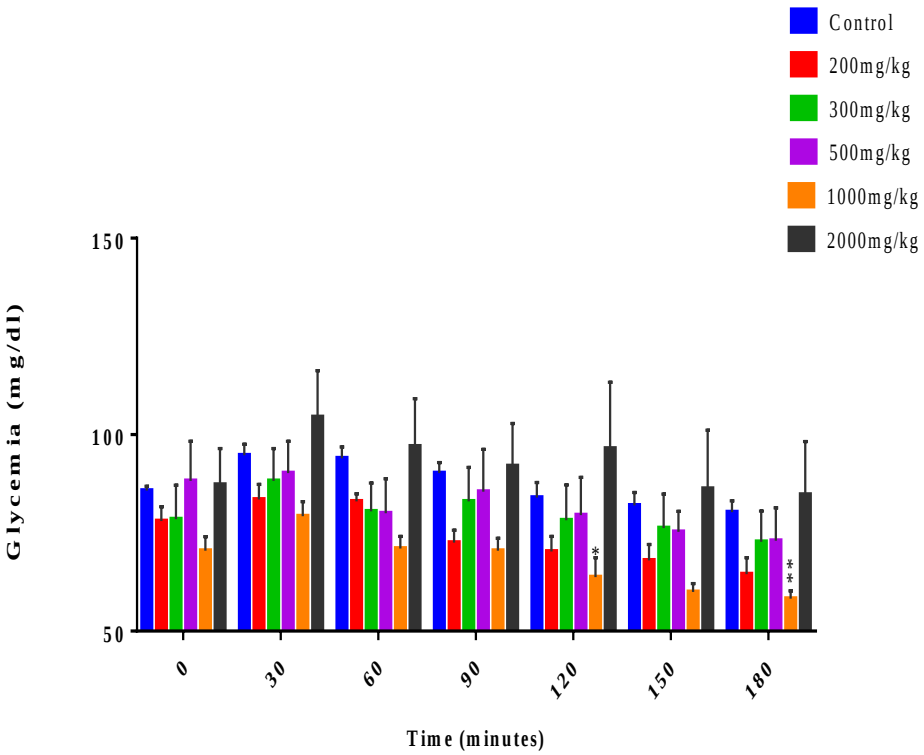

Figure 1: Effects of Parkia biglobosa extract on glycemia of normoglycemic rats over time. (mean ± SEM, * P <0.05, ** P <0.01, n = 4).

Effects of aqueous extract of Parkia biglobosa bark on blood glucose levels in temporary hyperglycemic rats

Figure 2 shows the changes in blood glucose levels of different batches of animals over time. At time T0 (0 min), batches 2, 3 and 4 receive respectively distilled water, glibenclamide and EAqPB. To these 3 batches glucose (4 g/kg bw) was administered at time T30 (30 min). Images of hyperglycemia ($p < 0.001$) were observed 30 min (T60) after administration of the

glucose solution compared to the control. After 3 hours (T180) of experimentation, blood glucose was increased by 19%, 24% and 32%, respectively, in positive control lot in lot positive control lot and in the lots pre-treated respectively with glibenclamide and EAqPB compared to the control.

Figure 3 shows changes in blood glucose levels in post-treated rats. At time T0, lots 2, 3 and 4 receive glucose. At these lots (2, 3 and 4), it was administreted distilled water, glibenclamide and EAqPB are administered 30 minutes after the start of the experiment. After 180 min, EAqPB and glibenclamide reduced hyperglycemia by 22% and 26%, respectively, compared to control.

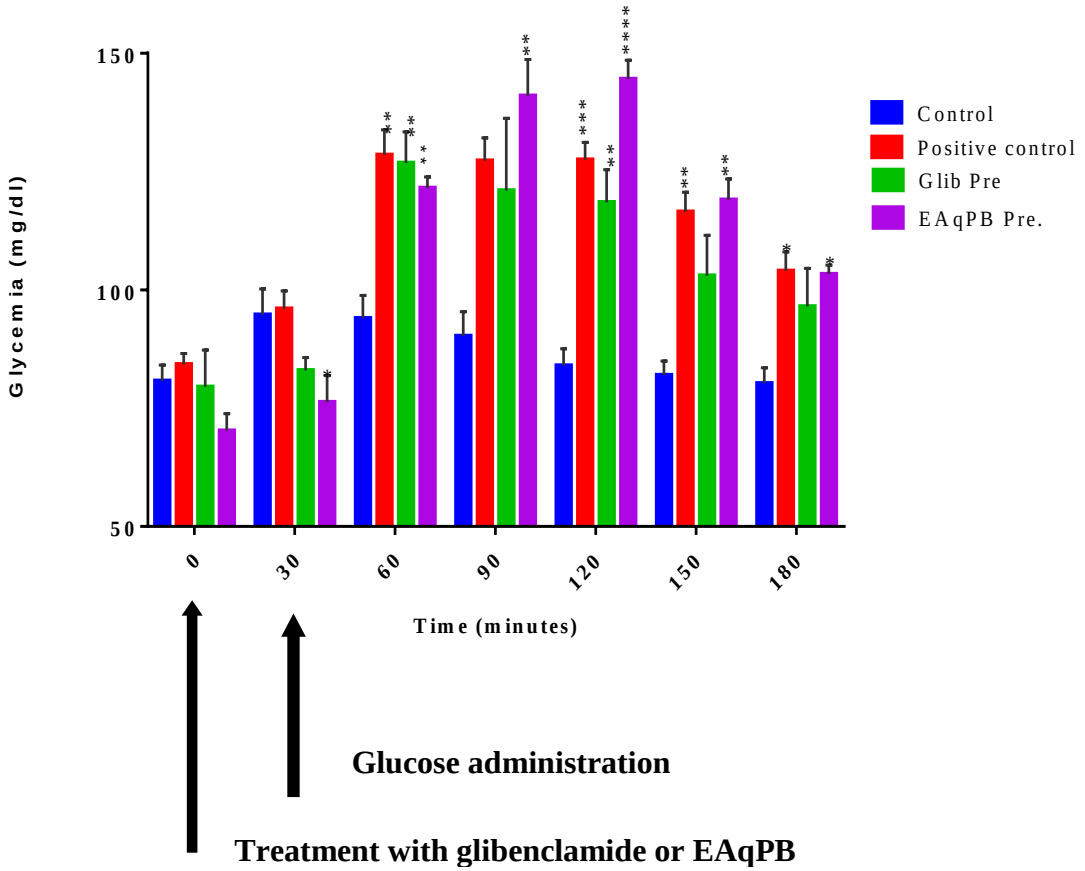

Figure 2: Effects of EAqPB and glibenclamide on the glycemia of hyper-glycemic rats pretreated over time. (Mean ± SEM, * P <0.05, ** P <0.01, *** P <0.001, **** P <0.0001, n = 4). ESM: Standard Error on the Average.

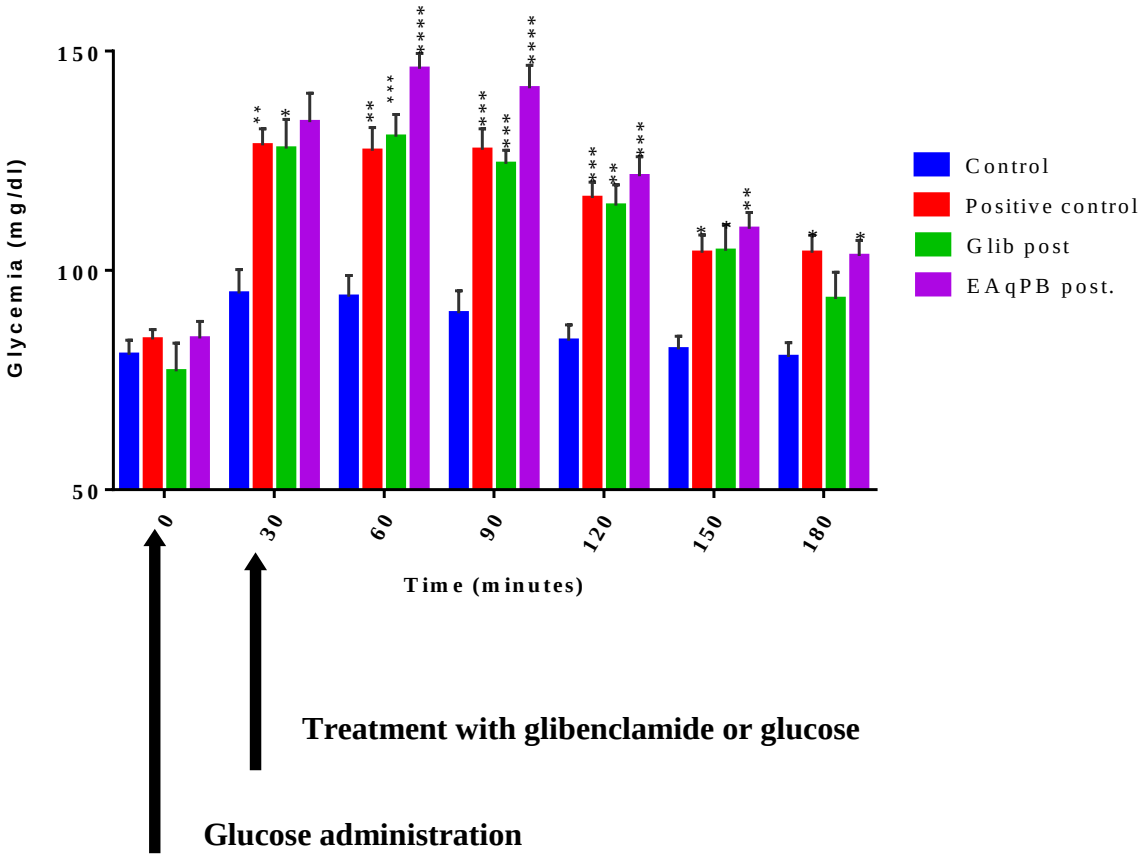

Figure 3: Effects of EAqPB and glibenclamide on glycemia in post-treated hyper glycemic rats over time. (mean ± SEM, * P <0.05, ** P <0.01, *** P <0.001; **** P <0.0001, n = 4). ESM: Standard Error on the Average.

DISCUSSION

Qualitative phytochemical tests, carried out with the aqueous extract of *Parkia biglobosa* bark (Mimosaceae), made it possible to highlight the presence of sterols and polyterpenes, alkaloids, polyphenols, catechin and gallic tannins, flavonoids and saponosides. On the other side, he was noted the absence of quinone compounds in this extract. These results are consistent with those of Milligo et *al.*,[13] Osseni et *al.*,[14] and Kassi et *al.*,[15]

The study of the acute toxicity of *Parkia biglobosa* (EAqPB) in female mice showed that at doses of 2000 and 5000 mg/kg of bw, this extract does not cause any mortality after 14 days of observation. We can therefore conclude that EAqPB is not orally toxic with an LD50 greater than 5000 mg/kg bw.

This absence of toxicity of the aqueous extract of the bark of the trunk of *Parkia biglibosa* is also observed with other plants of the African traditional pharmacopoeia such as the leaves of

Mitragyna inennis (Rubiaceae), the leaves of *Lophira lanceolata* (Ochnaceae), the root bark *Calotropis procera* (Apocynaceae), leaves of *Moringa oleifera* (Moringaceae).[16, 17, 18]

The effects of the *Parkia biglobosa* aqueous extract on blood glucose levels in normoglycemic rats showed that this extract had good hypoglycemic activity at a dose of 1000 mg / kg P with a percentage reduction in blood glucose of 17.37%. However, after glucose overload, EAqPB exhibits better anti-hyperglycaemic activity in pretreated rats, unlike glibenclamide, with a 32% reduction percentage, compared with 24%. Moreover, these two substances exert a non-significant antihyperglycaemic activity, after 180 min, in post-treated hyperglycemic rats, with reductions of 22% for EAqPB and 26% for glibenclamide. These results indicate that EAqPB, just as glibenclamide, in addition to being hypoglycemic, is an antihyperglycemic substance. This extract may prevent the risk of hyperglycemia.

The properties of EAqPB are similar to those of several medicinal plants of the African Pharmacopoeia. Indeed, Odetola et *al.*,[19] Fred-Jaiyesimi and Abo[20] studying the activity of *Parkia biglobosa* seed extract (Mimosaceae) in rats, showed that this extract had an antihyperglycaemic and hypoglycemic effect. Similar results were obtained with extracts of *Rauvolfia vomitoria* (Apocynaceae), *Zizyphus mucronata* (Rhamnaceae), *Pseudarthria hookeri* (Fabaceae), *Annona senegalensis* (Annonaceae) and *Hallea ledermannii* (Rubiaceae) in rats respectively by Leatitia et *al.*,[21] Adama et *al.*,[22] Gohi et *al.*,[23] and Nanti et *al.*,[24]

The total aqueous extract of *Parkia biglibosa* bark is an antidiabetic potential in type 2 diabetics.

This antidiabetic potential would be conferred by the presence of chemical compounds highlighted by phytochemical screening as demonstrated by the work of Guerci et *al.*,[25] Huang et *al.*,[26] and Kebieche.[27]

Indeed, flavonoids are endowed with hypoglycemic and antidiabetic properties according to the work of Huang et *al.*,[26] and Raccah.[28]

In addition, the antidiabetic effect of tannins is attributed to their action on diabetes itself at the cellular level. They promote the action of insulin (by decreasing insulin resistance) and prevent the complications of diabetes by their antioxidant and enzymatic power, also neutralize the effect of free radicals and limit the inflammatory response in different tissue.[29]

As for alkaloids, they exert their hypoglycemic and antihyperglycaemic effects and by inhibiting α-glucosidase.[30, 31]

Note that according to the work of Kim et *al*.,[32] and Sy et *al*.,[33] types of flavonoids and alkaloids probably work in synergy for a significant and lasting hypoglycemic effect.

CONCLUSION

The qualitative phytochemical study carried out with the aqueous trunk bark extract of *Parkia biglobosa* revealed the presence of sterols and polyterpenes, alkaloids, polyphenols, catechin and gallic tannins, flavonoids and saponosides.

Studies on acute oral toxicity have shown that the LD50 of this extract would be greater than 5000 mg/kg bw.

The study of the pharmacological effects of EAqPB on the glycemia of rats has shown that this extract has hypoglycemic effects in normoglycemic rats and better antihyperglycemic activity in pretreated animals.

The secondary metabolites identified would be responsible for the pharmacological effects of this extract which has properties similar to those of certain insulin secretors.

These results are therefore useful for the exploitation of this plant for the treatment of diabetes in traditional medicine and a scientific basic for use.

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