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Hypoglycemic and antihyperglycemic activities of *Bauhinia thonningii* (caesalpiniaceae) fruit in rat wistar

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ABSTRACT

Diabetes is a metabolic disease characterized by chronic hyperglycemia resulting from a defect in the secretion of insulin and / or the action of this hormone. The therapeutic management of this pathology in most developing countries is costly given the low purchasing power of the populations. The traditional African pharmacopoeia offers an alternative to synthetic antidiabetics. The objective of this study is to demonstrate the hypoglycaemic and anti-hyperglycemic properties of Bauhinia thonningii (Caesalpiniaceae) fruits in rats. The aqueous extract of the fruits of this plant was administered orally to different batches of normoglycemic rats and then to hyperglycemic rats at doses of 25, 50, 100 and 150 mg / kg body weight (bw). The results of this study showed that the fruits of Bauhinia thonningi possess hypoglycaemic ($p = 0.0356$) and anti-hyperglycemic ($p < 0.0001$) properties.

1. INTRODUCTION

Diabetes is a chronic metabolic disease characterized by disturbance of the metabolism of carbohydrates, lipids and proteins. It is due to the lack of insulin secretion by the islet cells of Langerhans and / or to the ineffectiveness of its action on the target organs [1]. The number of diabetics around the world has increased from 108 million in 1980 to 422 million in 2014 [2]. In 2000, the global prevalence of diabetes was estimated at 2.8%, which could reach 4.4% by 2030 [3, 4]. It has increased more rapidly in low- and middle-income countries [5]. The prevalence in Côte d'Ivoire is estimated at 4.94% according to the International Diabetes Federation [6]. Diabetes is responsible for 6% of deaths due to noncommunicable diseases (NCDs) [7]. It would be the seventh leading cause of death in the world by 2030 [8]. When treated poorly, diabetes can lead to complications. These complications may be cardiovascular, neurological, nephrological, retinal or renal. Therapeutic management of diabetes is currently based on strict diets, insulin injections and oral antidiabetic drugs [9]. This solution is obviously costly for the sick, given the low purchasing power of the populations in most of the developing countries.

Traditional medicine offers solutions that reach the populations of these countries. Indeed, several medicinal plants are used in the treatment of diabetes mellitus [10-12]. Nevertheless, although these plants are commonly used to treat diabetes, it is clear that their use remains empirical in general. There is therefore a need to carry out scientific work to establish evidence of their therapeutic activity and to identify the compounds that are responsible for these activities.

It is in this context that we are interested in a plant of traditional Ivorian medicine namely *Bauhinia thonningii* (Caesalpiniaceae). This plant is traditionally used by the Ivorian populations to treat diabetes. The objective of this study is to evaluate the activity of *Bauhinia thonningii* (Caesalpiniaceae) fruits on the glycemia of normoglycemic rats and rats subjected to the glucose tolerance test.

2. MATERIAL AND METHODS

Animal equipment: The animal material consists of Wistar strain normoglycemic rats aged 90 days and weighing between 150 and 180 g. These rats were bred at the animal facility of the Ecole Normale Supérieure in Abidjan. The temperature of the breeding room was 25 ° C with 12 hours of light and 12 hours of darkness.

They were fed a diet of wheat breads, peanuts, corn, soybean powder and dried fish in carbohydrate proportions 55%, 33% lipids and 12% protein and free access to water.

Plant material: The plant material used is the fruit of *Bauhinia thonningii* (Caesalpiniaceae). These fruits were bought in Avenue de la Mé near the marketplace in Ajamé (Abidjan). A sample of the fruit was transferred to the National Floristic Center of the University Félix HOUPHOUËT-BOIGNY of Abidjan where it was identified using the analytical flora. The fruits were dried out of the sun at room temperature, about 25 ° C, for one month. They were then pulverized using a Vorwerk Thermomix 3000 mill. The powder obtained was subjected to an aqueous extraction.

Preparation of the aqueous extract: One hundred and fifty (150) grams of vegetable powder was macerated in 1.5 L of distilled water for 1 hour. The macerate was then filtered on Whatman No. 1 paper and then evaporated using a Heidolph type rotary evaporator (Germany). After concentration, the extract obtained was dried in an oven at 50° C. and then weighed to determine the yield.

The extraction yield was calculated by the following formula:

R (%) = M / Mo x 100

M: Mass in grams of the resulting dry extract

M0: Mass in grams of the plant material to be treated.

Phytochemical Screening: Phytochemical analysis of the aqueous extract of *Bauhinia thonningii* (EABt) was carried out according to the methods described by Bekro, Mamyrbekova, Boua, Bi and Ehile [13]. Thus, chemical groups such as tannins, saponins, flavonoids, polyphenols, alkaloids, quinones, terpenes and sterols have been found in the extract of this plant.

Study of Acute Toxicity in Rats: The acute toxicity of the aqueous extract of *B. thonningii* was evaluated in accordance with the guidelines of the Organization for Economic Co-operation and Development 423 [14] for chemical testing. Rats weighing between 95 and 130 g were divided into four different batches of three animals each. The aqueous extract of *B. thonningii* was administered orally (single dose per group) at doses of 300 and 2000 and finally 5000 mg / kg body weight (BW). The control batch received distilled water (10 mL / kg of bw). The animals thus treated were subjected to continuous observation during the 24 hours that followed the treatment and then for 14 days. When zero or one death is observed after two days, three other rats are used in a second step for the confirmatory test. If, after two days, the same results are observed, then the higher dose is used according to the same method. During the two weeks, the number of deaths and the clinical signs observed for each batch were noted. Study of the activity of *Bauhinia thonningii* (AEBt) fruit extract on rat glucose.The blood glucose in rats is measured using an Accu-Cheik Active glucometer and test strips. In this study, the rats were fasted for 12 hours before the experiments. Substances are administered orally.

EABt dose-response effects on blood glucose levels in normoglycemic rats: For this study, 30 rats were used. They were divided into 6 lots of 5 rats.

Lot 1: normoglycemic rats receiving distilled water (10 mL / kg PC) (normal control).

Lot 2: rats treated with glibenclamide (reference substance) at a dose of 10 mg / kg PC (positive control).

Lot 3: rats treated with AEBt at the dose of 25 mg / kg of BW.

Lot 4: rats treated with AEBt at the dose of 50 mg / kg of BW.

Lot 5: rats treated with AEBt at the dose of 100 mg / kg of BW.

Lot 6: rats treated with AEBt at the dose of 150 mg / kg BW.

Blood glucose is first determined just before treatment; this is the initial blood glucose (t0). After the animals are treated, blood glucose is measured every 30 minutes for 2 hours and the percentage change in blood glucose relative to the initial blood glucose is calculated.

Dose-response effects of EABt in the glucose tolerance test on blood glucose in pretreated rats: Hyperglycaemia is caused by oral administration of glucose to rats at a dose of 4 g / kg body weight. For this study, 35 rats were divided into 7 batches of 5 rats.

Lot 1: rats receiving distilled water (10 mL / kg of PC) only (normal control).

Lot 2: rats receiving distilled water (10 ml / kg PC), and 30 minutes after, 4 g / kg of glucose PC (negative control).

Lot 3: rats receiving glibenclamide (10 mg / kg of PC), then 4 g / kg of glucose PC 30 minutes later (positive control).

Lot 4: rats receiving 25 mg / kg of EABt PC, then 4 g / kg of glucose PC 30 minutes later.

Lot 5: rats receiving 50 mg / kg of PC EABt, then 4 g / kg of glucose PC 30 minutes later.

Lot 6: rats receiving 100 mg / kg of EABt PC, then 4 g / kg of glucose PC 30 minutes later.

Lot 7: rats receiving 150 mg / kg of EABt PC, then 4 g / kg of glucose PC 30 minutes later.

The blood glucose levels of the rats in each batch are measured just before the administration of the substances or distilled water and then, after treatment, at intervals of 30 minutes, for 2 hours. The percentage of induction of hyperglycemia and the percentage of reduction of the induced hyperglycemia are then calculated.

$$\text{Rate of blood glucose changes } (\%) = \frac{G_i - G_0}{G_0} \times 100$$

G_0 : Initial blood glucose at time = 0 min and G_i : Blood glucose at time 30 min after.

Expression of results and statistical analysis: Blood glucose values were expressed as mean ± standard error at mean (M ± ESM). Analysis of variance (ANOVA) and the Tukey test for multiple data comparisons were used for statistical analysis using Graph Pad Prism 7.00 (San Diego CA USA). The change in blood glucose was considered significant at the P <0.05 threshold.

3. RESULTS AND DISCUSSION

Phytochemical Screening: The results of the phytochemical characterization revealed that the aqueous extract of the fruits of B. thonningii contained saponins, polyphenols, flavonoids and cathechial tannins. On the other hand, it is devoid of alkaloids and quinones.

Table.1.Chemical composition of the aqueous extract of *B.thonningii* fruits

Chemical groups		Aqueous extract of *B. thonningii* fruits
Saponosides		+
Polyphénols		+
Flavonoïds		-
Sterols et Terpenes		-
Tannins	Catechin	+
	Gallic	-
Alcaloides	Bouchardat	-
	Dragendorf	-
Free and combined Quinones		-

(+): presence of the chemical group highlighted in the extract;
(-): absence of the chemical group highlighted in the extract.

Acute toxicity: Administration of the aqueous extract of the fruit of *B. thonningii* to the respective doses of 300, 2000 and 5000 mg / kg bw resulted in no change in the physical appearance of the rats. Similarly, no mortality was recorded during the two weeks of observation. The lethal dose 50 (LD 50) of this extract is therefore greater than 5000 mg / kg. Test to demonstrate the hypoglycemic effect of the aqueous extract of the fruits of *B. thonningii*. The basal glucose levels of the batches of rats treated with distilled water, glibenclamide and the 100 and 150 mg / kg PC doses of the aqueous extract of B. thonningii decreased gradually during the 2 hours of the experiment except for the doses 25 and 50 mg / kg PC (Figure 1-a). In the batches of rats treated with distilled water, the reduction rate was 3.85% (0.87 ± 0.04 vs 0.91 ± 0.01 g / L) relative to the initial blood glucose.

The reduction in blood glucose is significant at the 150 mg / kg bw dose and glibenclamide level with respective reduction rates of 17.20% (0.72 ± 0.01 vs 0.77 g / L) and 17, 40% (0.59 ± 0.01 vs 0.96 ± 0.01g / L) compared with normal control (Figure 1-b). However, the hypoglycaemic effect was not significant at doses 25, 50 and 100 mg / kg PC of this extract.

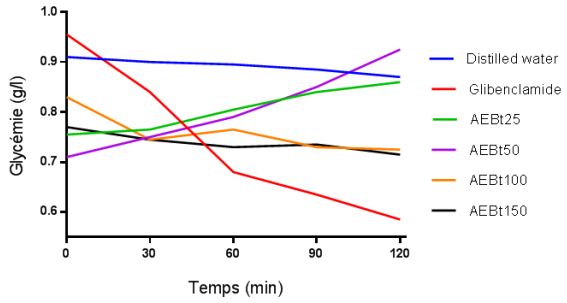

Figure.1a.Hypoglycemic effect of the aqueous extract of *B. thonningii*

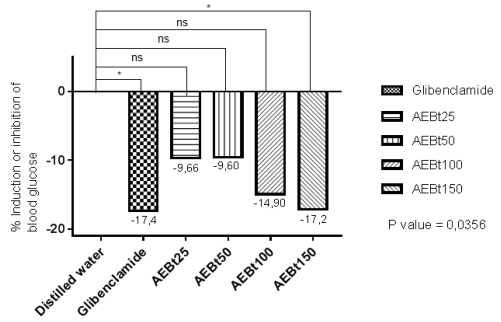

Figure.1b.Hypoglycemic effect of the aqueous extract of *B. thonningii*

Test to demonstrate the anti-hyperglycemic effect of the aqueous extract of *B. thonningii*. Glucose administration at a dose of 4 g / kg bw resulted in a significant increase in blood glucose levels in all pretreated animals relative to the initial blood glucose level (P value <0.0001) (Figure 2-a). The peak of hyperglycemia appeared 30 min after administration of glucose in rats pretreated with the aqueous extract of *B. thonningii* (EABt) at doses of 25, 50 and 100 mg / kg bw and glibenclamide. On the other hand, this peak appeared at the 60th min at the dose of 150 mg / kg bw and with the negative control (glucose) batch.

In rats pretreated with all doses of the aqueous extract of the fruits of B. thonningii, there is a gradual reduction in hyperglycemia. As for the animals in the batch pretreated with glibenclamide, the initial blood glucose is found at the 45th min followed by a marked hypoglycemia from the 90th min to the end of the experiment (Figure 2-a). The antihyperglycaemic effect is more pronounced at a dose of 150 mg / kg bw of *B. thonningii* extract with a 3.93% reduction rate and not significant compared to the normal control (distilled water). However, this effect is lower than that of glibenclamide which is 33.60% (Figure 2-b).

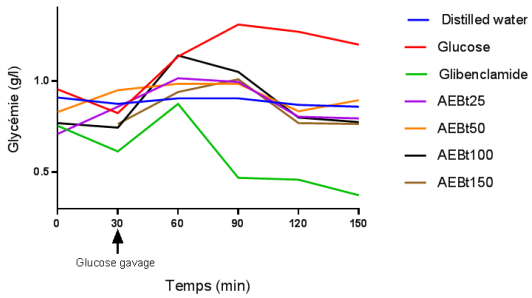

Figure.2a.Glucose tolerance test of the aqueous extract of *B. thonningii*

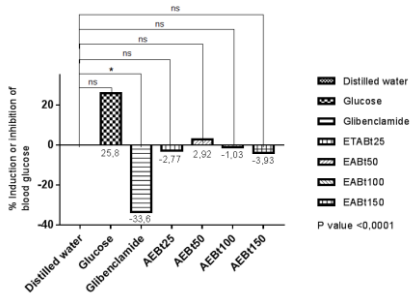

Figure.2b.Glucose tolerance test of the aqueous extract of *B. thonningii*

Discussion: This work is the result of the evaluation of the hypoglycaemic and antihyperglycaemic activity of the fruits of *Bauhinia thonningii* (Caesalpiniaceae) on the glycemia of normoglycemic rats and rats subjected to the glucose tolerance test.

The study of the acute toxicity of the aqueous extract of the fruit of *Bauhinia thonningii* (Caesalpiniaceae) in rats showed that this extract, administered orally, does not cause any mortality for doses up to the dose of 5000 mg / kg. The LD50 is therefore greater than 5000 mg / kg. According to the Globally Harmonized System of Classification of Chemical Substances, *Bauhinia thonningii* aqueous extract is classified as non-toxic or class 5 [15].

The pharmacological study revealed that the aqueous extract of *Bauhinia thonningii* results in a significant hypolgycycemic effect in both normoglycemic (P value = 0.0356) and hyperglycemic (P value <0.0001) rats. The substances contained in *B. thonningii* would be responsible for the pharmacological activities of this extract. Indeed, the triphyochemical results revealed the presence of saponins, polyphenols and catheter tannins in the aqueous extract of the fruits of this plant. Previous studies have led to the hypothesis of a probable link between the effect on blood glucose levels and the phytochemical nature of medicinal plant compounds[16, 17]. Substances such as polyphenols and flavonoids are generally recognized to have hypoglycaemic effects[18-20]. The effect would be comparable to the mechanism of action of the sulfonylureas of which glibenclamide is a part. Indeed, sulphonylurea hypoglycemic agents bind to a specific receptor on the membrane of pancreatic β cells in the vicinity of the dependent potassium channel ATP and cause the latter to close. This will lead to membrane depolarization of the β-cells causing the opening of the voltage-dependent calcium channels and an influx of Ca 2+, thereby triggering by exocytosis the extrusion of the insulin secretion granules [21, 22]. Similarly, Fang, Gao, Yang, Lang, Wang, Yu and Zhu [23] showed that the ethyl acetate fraction of flavonoid-rich E. alatus had stimulating properties on insulin release and was responsible for the hypoglycaemic effects of this enzyme in normoglycemic and antihyperglycemic mice in of mice with type 2 diabetes. Also, other studies such as those carried out by Kambouche, Merah, Derdour, Bellahouel, Bouayed, Dicko, Younos and Soulimani [24] have shown that saponins have an antihyperglycemic effect. However, it would be difficult to approximate the mode of action of the aqueous extract to that of glibenclamide, the reference hypoglycemic product in this study, because of the mixture of compounds which may interfere or have a synergistic action in this extract.

4. CONCLUSION

The results of this study revealed that the aqueous extract of *Bauhinia thonningii* fruits used in traditional Ivorian medicine has hypoglycaemic and antihyperglycaemic properties in rats. The alkaloids, flavonoids and saponins present in this extract would be responsible for these pharmacological activities. Thus, this study justifies the ethnomedicinal use of the fruits of this plant in the treatment of diabetes.

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