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ANTIHYPERGLYCAEMIC ACTIVITY OF SCLEROCARYA BIRREA IN RATS

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ABSTRACT

The trunk bark of *Sclerocarya birrea* (Anacardiaceae) traditionally used for the treatment of diabetes Côte d'Ivoire, have been purchased from herbalists in Abidjan. The decoction of Aqueous extract of *Sclerocarya birrea* (AESB) was administrated orally in the hyperglycemic rats fasting single and repeated taken at the respective doses of 35 mg/kg and 7350mg/kg. Hyperglycemia was induced by oral glucose load with the dose 4g/kg. The result after 2 hours of these EASB doses showed to hyperglycaemic rats greater antihyperglycaemic share of 30% ($p<0,05$; n= 8) in single and 20% in repeat doses. *Sclerocarya birrea* extract at 35mg/kg remained active for 4 times as single administration and after 2 days repeated administration with reductions in blood sugar levels, respectively 40% and 38% in hyperglycaemic rats made In conclusion, the administration of low dose (35 mg/kg) of AESB leading to the hypoglycaemic activity in animals given a glucose load orally. These results confirm the therapeutic indication of *Sclerocarya birrea* concerning its antidiabetic activity in the treatment of diabetes disease in traditional medicine.

KEYWORDS: *Sclerocarya birrea*, Diabetes, Antihyperglycaemic activity.

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of diseases. It's metabolic disorders in which the blood sugar is higher than normal level either because the production of insulin is not enough in type 1 DM or the cells do not properly respond to the insulin in type 2 DM (Lokrou, 2008).

In 2006, according to a report from World Health Organization, about 246 million people have type 2 diabetes. Its incidence is increasing rapidly, and it is expected to increase to more than 365 million by 2030 (Boyle, 2010).

In 2014, 422 million people in the world had diabetes, a prevalence of 8.5% among the adult population (WHO, 2016).

The prevalence of diabetes has been steadily increasing for the past 3 decades and is growing most rapidly in low- and middle-income countries (WHO, 2016).

Diabetes is a chronic disease whose treatment cost is high (Pastakia, 2017). It appears it as a major problem worldwide public health that affects all social strata (Lokrou, 2008). Diabetes and its complications, deaths, and societal costs have a huge and rapidly growing impact on the world.

In Côte d'Ivoire, diabetic's rate diagnosed in the hospital visits varies from 3 % to 7 % (Oga, 2006). But, this prevalence takes into account only the numerous patients who see frequently hospitals.

Throughout the globe, the incidence of type 1 diabetes is increasing at 3% to 5% per year (Atkinson, 2016). A second and more prevalent category, type 2 diabetes, is characterized by a combination of resistance to insulin action and inadequate compensatory insulin secretory response (ADA, 2017).

Type 1 diabetes has been historically, and continues to be, the most common type of diabetes in children and adolescents, although type 2 diabetes is increasingly diagnosed in youth (Dabelea; ADA, 2017).

In developed countries, support diabetes is mainly done in centers legal hospitals while in Africa, 80% of primary care, including people with diabetes (Awah, 2006) are administered outside these centers. Inadequate health opening in Sub-Saharan countries and the high cost of the annual management of the diabetic patient excluding

complications, explain the renewed interest in traditional medicine (Yangni, 2004). So herbal remedies are commonly used in these countries for the treatment of diseases since they are easily accessible and less expensive compared to conventional drugs.

The search for antidiabetic substances of plant origin by in vitro, in vivo and clinical methods for the development of phytomedicines is booming in almost all continents. The extract plants are used to treat diabetes in Africa, America, Asia, Australia and Europe (WHO, 2007).

Thus, the existence of anti-diabetic traditional medicine for the treatment of diabetic condition is confirmed by practitioners and medicines (Yangni, 2004).

Marula trees *synonyms* of *Sclerocarya birrea* is a mesophanerophyte or medium tree 8 to 30 m tall found in the Sudano-Guinean forests and savannas which grows mainly in rocky areas and clayey (Ake-Assi, 2001). It flowers and fruits in full dry season the bark of the *Sclerocarya birrea* are used by traditional healers for their anthelmintic properties (Ake-Assi, 2001).

The objective of this study was to evaluate the antihyperglycaemic activity of an aqueous extract of trunk bark of *Sclerocarya birrea* in Wistar rats from Côte d'Ivoire samples.

MATERALS ET METHODS

Plant material

Plant species

The vegetal material used was fresh trunk bark of *Sclerocarya birrea*. They were collected in the savannah region (North of removes even) conveyed on the urban market in the south (Abidjan) *Sclerocarya birrea* trees is a Sahelian species. In Côte d'Ivoire, it occurs in the Savannah region (Ferkéssédougou and Korhogo). A sample of grass of this plant species discovered by Prof. Aké-Assi on June 30, 1955 in the village of Fongontin is deposited at the Floristic Center and registered under No. 3023 (Ake-Assi, 2001).

Preparation of the aqueous extract

The aqueous extract of Sclerocarya birrea (EASB) was prepared from 300g of trunk bark powder which are introduced into a flask containing 3 liters of distilled water (10% decoction). The decoction was carried out with stirring in a water bath at 100 0 C for 2 hours. After cooling, the decoction was filtered on hydrophilic cotton and Whatman paper N°1. The filtrate obtained was rinsed with a little hot water to obtain 3000 ml and was then concentrated in a rotary evaporator (4000 Laborata Heidsph, France) under vacuum at a temperature of 50 °C. After concentration, the filtrates were taken up with a little distilled water and then lyophilized after 48 hours of freezing. The yield of the extraction was 6.7% because the lyophilization made it possible to obtain a reddish powder of bark of 20.1 g.

Animal equipment

The experiment was performed on 32 Wistar male rats *(Rattus norvegicus)* bred in plastic cages. The animals are kept in pet UFR-Biosciences at room temperature with a stable humidity with a day/night cycle of 12h : 12h. They have free access to water and food.

Experimental method

Distribution of animals

Wistar male rats weighing on average 185 ±10 g were divided 4 groups of 8 which receive two types of specific treatment by oral voice (ov).

Treatment 1: Rats received a single administration of the solutions tested week for 6 weeks,

Treatment 2: It's a reiterated administration in 3 days successive according to this type of administration solutions tested weekly. The treatments were carried out over a period of 42 days.

In these treatments, the rats are distributed:

- lot 1: control rats receiving distilled water;
- lot 2: rats receiving glibenclamide at a dose of 0.2 mg/kg/ov;
- lot 3: hyperglycemic rats treated with EASB of 35 mg/kg/ov;
- lot 4: hyperglycemic rats treated with EASB of 7350 mg/kg/ov.

Induction of oral hyperglycemia

The glucose overload is administered orally to animals after treatment with prepared products (Keita 1998; Ojewole, 2003; King, 2012; Monteomo, 2015) using a stainless steel oesophageal probe. The anhydrous glucose that's used to induce physiological diabetes is at a concentration of 400mg/ml. Each fasting animal received orally, per kg body weight glucose 4g and hyperglycaemic is made to study the antihyperglycaemic activity.

Blood taking

Wistar strain male rats are deprived of food for 14 h prior to the determination of blood glucose. They are then anesthesia in a glass bell containing buffers e cotton soaked in ether. The blood taking were performed on the legs of the animal following a light massage (Weiss, 2000). Once the strip Reactive is inserted into the meter, the latter is activated and a drop of blood is deposited on the appropriate area. The samples were made 1 hour before feeding and then every half hour for 4 hours of treatment, respectively corresponding to the times in minutes : T1 = - 60, T2 = 0, T3 = 30, T4 = 60, T5 = 90, T6 = 120, T7 = 150, T8 = 180, T9 = 210 and T10= 240.

The determination of glucose was made by the principle of a reaction of glucose oxidase using glucose reader One Touch Basic (Lifescan, mulpital, USA) (Rheney, 2000).

Statistical analysis of data

Blood glucose values were expressed as Mean ± Standard deviation (error) at mean. The homogeneity of the blood glucose values in each group was checked by the Student test.

Similarly, the results of the blood glucose levels of the different groups were compared by the previous test. Tα considered risk ($p < 0.05$) determining the criterion of significance, n being the number of experiments (Jordan, 2013).

RESULTATS

Sclerocarya birrea stem-bark aqueous extract resulted in DL50 values of mg/kg.

The effect of the plant extract is obtening by oral pretreatment with AESB (35mg/kg, 7350mg/kg) or Glibenclamide (0,2mg/kg) from -60 min to 240min produced significant reductions in glycemia of rats, compared with distilled water-treated witnesses rats.

The effect of this extract in hyperglycaemic rats begins before the glycemic peak: From 0 to 30 min, a significant increase of 28 ± 7 mg/dl (self 21%; $p < 0,05$) of blood glucose concentrations is denoted with AESB at a dose of 35mg/kg/ov in a single administration. However, with the dose of 7350mg/kg, the glycemia is more increased from 124.5±10 to 176±14mg/dl (35%) in this same time (fig 1).

In rats witnesses, between 0 to 30 min, glucose levels is the most increased from 105 ± 19 to 203 ± 25 mg/dl (48%) ($p < 0.05$; $n = 8$).

Beyond the glycemic peak: 30 minutes to 2 hours, the glucose values are between 140 ± 22 and 108 ± 13 mg/dl, a decrease of blood glucose rate were 30% with AESB dose of 35 mg/kg/ov. AESB of 35, 7350 mg/kg/ov doses and glibenclamide remained active after 4 hours and have led to a decline respectively 40%, 18% and 30% (fig 1).

In repeated dose after 2 days AESB at the dose of 35 mg/kg has reduced blood glucose from 151 ± 15 mg/kg to 116 ± 10 mg/kg (38%). At the dose of 7350 mg/kg of AESB, this head drop was 25% while that related of glibenclamide antihyperglycaemic effect reached 12% (Fig. 2).

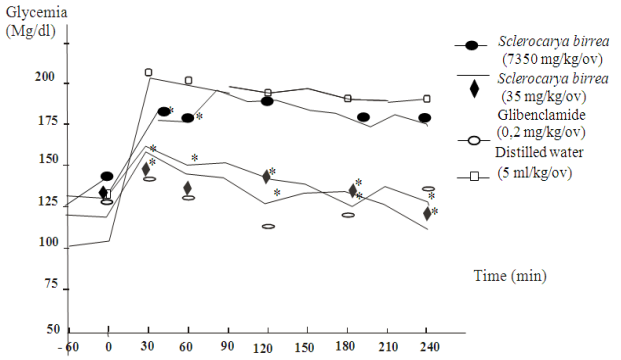

Figure 1: Effect of *Sclerocarya birrea* stem-bark aqueous extract on blood glucose concentrations (mg/dl) of hyperglycaemic rats in a single dose. Each point represents the means of 5 determinations. (*P < 0.05).

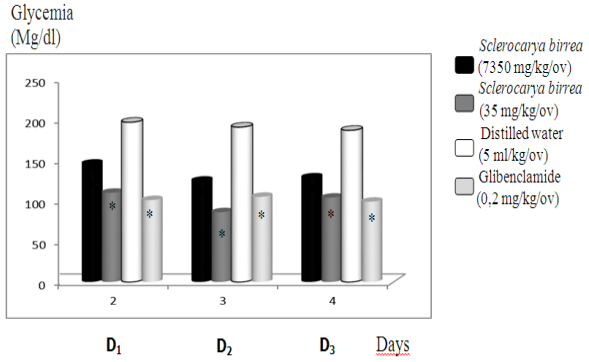

Figure 2: Effect of *Sclerocarya birrea* stem-bark aqueous extract on blood glucose concentrations (mg/dl) of hyperglycaemic rats in reiterated doses. (*P < 0.05).

DISCUSSION

Single-dose administration (35 mg/kg/ov) of the aqueous extract of trunk bark of *Sclerocarya birrea* led to an antihyperglycaemic activity which manifested itself in two stages. Initially from 0 to 30 min, AESB that has little increased glycemic rate prevented and the glycemic peak obtained with the rat hyperglycemic.

In a second step, from 30 min 120 min this aqueous extract resulted in a drop in blood glucose of 30%. The decrease in blood sugar is continued after four hours with maximum significant antihyperglycaemic activity of 40% over a period of 42 days.

Similarly, glibenclamide had an antihyperglycaemic effect of 30% after 4 hours.

Based on the antidiabetic effects obtained, the activity curves biological glibenclamide and EASB 35 mg/kg/ov is similar. However, the AESB had an onset of action lower than glibenclamide or 30min against 120, considered an antidiabetic oral reference. Therefore, AESB can move near first rapid action antidiabetic whose action time is less than 2 hours (Tourniaire, 1994).

From the 4 th hour, hypoglycemia observed with AESB low dose is followed by a return of initial blood glucose values (114.2 ± 9 mg/dl). Thus, its action is not as long as that of glibenclamide which the blood glucose level was 51.4 mg/dl. These two modes of action in fasted rats of the administered products are due to their nature. The first is a total extract tends to normalize blood glucose levels after a certain time while the second is an active ingredient or a molecule. Thus, AESB at a relatively high dose (7350 mg/kg/ov) cannot therefore cause hypoglycemia often encountered during treatment with antidiabetic drugs (Lokrou, 2008).

The dose was 35 mg/kg/ov AESB seems more effective than 7350 mg/kg/ov because it provides respective glycemic rate decreases of 40% and 25% in single dose and reiterated doses. This antihyperglycaemic effect was also found during tests with diabetes are another plant species. This is the infused Western Anarcadium (Anarcadiaceae) administered at doses 175 and 250 mg/kg/ov in a group of 5 Wistar rats made hyperglycaemic by glucose solution (3 g/kg/ov). The results showed and hypoglycaemic effect respectively 24.3% and 43% for the 3rd time in the single taken then in taking repeated the 3rd day (Sokeng 2001). The difference in glycemic previous with our results (40% and 25%) could be explained by the extraction methodology of active chemical groups. Indeed, the decoction is used for trunk bark Sclerocarya birrea (AESB) and while the infusion was used in the case of a Western Anarcadium. In addition, the chemical groups that could be responsible for anti-hyperglycemic activity and identified at AESB are coumarins, terpenoids and flavonoids. Regarding, the Western Anarcadium, chemical composition was dominated by flavonoids (kaempferol, quercetol of rhamnosi) (Sokeng 2001).

In addition, other antihyperglycaemic effects are different from ours studies, using a butanol extract were recorded this time with the parts of Sclerocarya birrea. In these hyperglycaemic rats, it was shown that the effect of this plant was dependent on the dose administered for the extract. Indeed, with 25 and 10 mg/kg doses, orally, glycemic reductions were respectively 25.9 % and 7.6% in the 2 nd hour (Laurens, 1997).

The mechanism of antihyperglycaemic activity can be explained the action of chemical groups assets AESB stimulate the regulation and release of insulin in the pancreas especially in experimental hyperglycemia in our handling for a glucose uptake by the muscles tissue animal. Better, glycosylation (ability to set glucose) can be attributed to flavonoids, phenolic compounds that tend to bind sugars for flavonoides glycosides (Breneton, 2002) Thus, if a glycogenogenesis liver or muscle allows correlated with the activity of insulin that regulates glycogen deposition by stimulating synthase inhibiting gluconeogenesis and glycogen phosphorylase (Tourniaire, 1994).

CONCLUSION

In short, the decrease in blood glucose in rats on an oral glucose confirms that EASB has hypoglycaemic activity with non-significant weight (less than 10%) in 6 weeks of treatment.

The antihyperglycaemic effect of Sclerocarya birrea extract at 35mg/kg demonstrated by means reductions of 40% in single and 38% in reiterated doses would justify its use in traditional medicine.

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