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ANTIPYRETIC ACTIVITY OF AQUEOUS EXTRACT OF CROSSOPTERYX FEBRIFUGA STEM BARKS IN WISTAR RATS

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ABSTRACT

Crossopteryx febrifuga is used in Ivorian traditional medicine by populations of Pakouabo village to treat fever. The present study was designed to evaluate the antipyretic activity of an aqueous extract of the stem barks of *Crossopteryx febrifuga* in wistar rats. The antipyretic activity of *Crossopteryx febrifuga* was evaluated by brewer's yeast-induced pyrexia in rats in comparison to paracetamol (100 mg/kg body weight). The extract of this plant did not show an hypothermic effect. A very marked antipyretic activity with a percent inhibition of pyrexia of more than 50% was obtained with the extract of *Crossopteryx febrifuga* at the concentration of 25 mg/kg and 50 mg/kg. The antipyretic activity of this aqueous extract at a dose of 50 mg/kg was identical to that of paracetamol (100 mg/kg). Phytochemical characterization revealed the presence of sterols, polyterpens, polyphenols, flavonoids, saponosides and catechin tannins. These findings suggest the aqueous extract from stem barks of *Crossopteryx febrifuga* presents significant antipyretic activity on hyperthermia in rats.

KEYWORDS: Extract, brewer's yeast, hyperthermia, hypothermic.

INTRODUCTION

In West Africa, as in all developing countries, plants are commonly used in the culinary, cosmetic and therapeutic fields. According to the World Health Organization (WHO), more than 80% of the African population use plants for their health.[1] This increasing interest of the populations for the plants has its origin in the ancestral practices.[2] Considering the place of traditional medicine in African countries, governments need to develop regional strategies on traditional medicine to undertake scientific work on the efficacy, safety and toxicity of medicinal plants; and to promote their optimal uses in health care delivery systems.[1]

In Côte d'Ivoire, initiatives have been taken to contribute to the development of plants used in the treatment of infectious diseases in traditional environments. These pathologies include bacterial, fungal, parasitic and viral infections that are most often associated with pyrexia or hyperthermia commonly known as fever.[3] In children, fevers cause dramatic situations ranging from convulsions to loss of consciousness and even death. These situations are most often experienced by people in the most remote areas where access to primary health care is almost non-existent. Faced with this situation, local people use plant species to treat their fever. In Côte d'Ivoire, ethnobotanical and ethnopharmacological surveys have identified plant species with anti-inflammatory and antipyretic properties (against fever).[4] These species include *Alchornea cordifolia*, *Dicliptera verticillata* and *Crossopteryx febrifuga*,[5,6] *Crossopteryx febrifuga* (Afzel, ex G. Don) Benth is a plant commonly used in the treatment of many pathologies such as antimicrobial[7], gastroprotective[8], antiparasitic[9,10] and antitussives.[11]

The general objective of this study was to evaluate the antipyretic activity of an aqueous extract of the stem barks of *Crossopteryx febrifuga* in the way to provide scientific evidence to the ethnobotanical use of this plant in the treatment of pyrexia.

MATERIAL AND METHODS

Plant material

Stem barks of *Crossopteryx febrifuga* (Afzel, ex G. Don) Benth were collected from Pakouabo (Bouaflé, Côte d'Ivoire). It was identified and authenticated by National Floristic Center (NFC) of Abidjan to the specimen number 7946 collected by Professor Aké-Assi in March, 5th 1965.

Animals

Sixty (60) Wistar rats (*Rattus norgevicus*) (180-250 g) were used for the study of antipyretic activity. The rats were supplied by the pet shop of the laboratory of Pharmacology of UFR Pharmaceutical and Biological Sciences of Felix Houphouet-Boigny University. The rats were housed under standard conditions of temperature 24 ± 1°C with 75% humidity and light (approximately 12/24 light-dark cycle). All experiments performed on the laboratory animals in this study followed the standard operation procedures.

Ethnopharmacological survey

Twenty-five (25) people recognized for their knowledge on medicinal plants in Pakouabo village were interviewed about *Crossopteryx febrifuga* used by populations of this village for the management of diseases. The vernacular names of the plant, the plant parts and the modes of preparation of recipes were recorded.

Preparation of Crossopteryx febrifuga stem barks aqueous extract

Stem barks of *Crossopteryx febrifuga* plant material were dried in a dark ventilated room for 10 days. These parts were ground to fine powder using Restsch GM 300 ™ grinder mill. Extraction was carried out by cold maceration of 100 g of fine powder with 1000 ml of distilled water for 24 hours. The macerate was successively filtered through fabric, hydrophilic cotton and finally Whatman paper. Subsequently, the filtrate was evaporated dried in a Memmert ™ brand oven at 45°C for 3 days and the dark brown dried solids were stored in a refrigerator at 4°C for the pharmacological study.

Effect of *Crossopteryx febrifuga* on basal temperature of rats (Hypothermic effect)

Initial rectal temperatures of the rats were taken at the time T0h corresponding to the time after 16 hours of fasting. These temperatures made it possible to constitute 2 groups of 6 rats each homogeneous in temperature. Experimental group 1 was received orally administration aqueous extract of *C. febrifuga* at 100 mg/kg and control group 2 received 0.09% NaCl. The rectal temperatures were then noted at 1 h (T1h), 2h (T2h), 3h (T3h) and at 4 h (T4h) using a digital thermometer TMP 812 RS ™ (Panlab).[12]

Evaluation of antipyretic activity of *Crossopteryx febrifuga* stem barks aqueous extract

After weighing the rats and before any administration, the basal rectal temperature of each rat was taken (initial temperature T-16h) using a digital thermometer TMP 812 RS ™ (Panlab). Rats were immediately administered subcutaneously in the dorsolateral region, an aqueous

suspension of 20% brewer's yeast at 1 ml per 100 g body weight. Then, the rats were fasted for food (free access to water). Sixteen hours (16h) later, rectal temperatures were again measured (T0h). Seven (07) homogenous groups of 6 rats each were made with the rats which showed an increase of at least 0.6°C in their rectal temperature. Homogeneity was obtained using the level of variation of hyperthermia. By orally administration, group 1 received 0.09% Nacl; group 2 received Paracetamol 100 mg/kg (reference Standard drug) while groups 3, 4, 5, 6, and 7 received doses of the aqueous extract at 12.5; 25; 50; 100 and 200 mg/kg body weight respectively. The evolution of the rectal temperature was monitored every hour for four (4) hours.[13]

Determination of percentage reduction of hyperthermia

Antipyretic activity was measured by calculating the percentage reduction in hyperthermia at n hours after administration of the substances (Nacl, Paracetamol and Extract) according to the formula below.[13,14]

$$\% \text{ Reduction n hour} = \frac{\Delta T0 - \Delta Tn}{\Delta T0} \text{ x } 100$$

$\Delta T_0 = T_{0h} - T_{-16h}$ is the change in mean rectal temperature before antipyretic treatment.

$\Delta T_n = T_{nh} - T_{-16h}$ is the variation of the mean rectal temperature of the group at n hour after antipyretic treatment.

T_{nh} means the average temperature of the group at n hours after antipyretic treatment.

T_{0h} refers to the temperature recorded 16 hours after injection of brewer's yeast.

T_{-16h} refers to the initial or basal temperature recorded before injection of brewer's yeast.

Phytochemical screening of *C. febrifuga* aqueous extract

Characterization of the secondary metabolites in the aqueous extract of this plant was carried out by performing color and precipitation tests in tubes as described by some authors.[15;16;17] Secondary metabolites tested for include: sterols and polyterpens, polyphenols, flavonoids, tannins, quinones, alkaloids and saponosides.

Statistical analysis

Percentages reduction of hyperthermia were expressed as mean ± S.E.M. The significance of difference between the controls and treated groups were determined using ANOVA test. $P<0.05$ were considered to be statistically significant.

RESULTS

Ethnopharmacological survey

At the end of the investigation, the vernacular names in Côte d'Ivoire of *Crossopteryx febrifuga* (Afzel, ex G. Don) Benth were Kloklo-waka (Baoulé) and Kinguéhoun or Linguéhoun (Malinké). In the Pakouabo village, the stem barks of this plant were used in decoction in the treatment of fever, cough and oral infections.

Effect of *Crossopteryx febrifuga* on basal temperature of rats

The hypothermic effect study of the aqueous stem barks extract of this plant showed that the rectal temperature variations recorded at the extract dose of 100 mg/kg body weight look similar to that of the control (0.09% NaCl) around 37°C and this concentration didn't show a significant decrease of the basal temperature in the rats (Fig. 1).

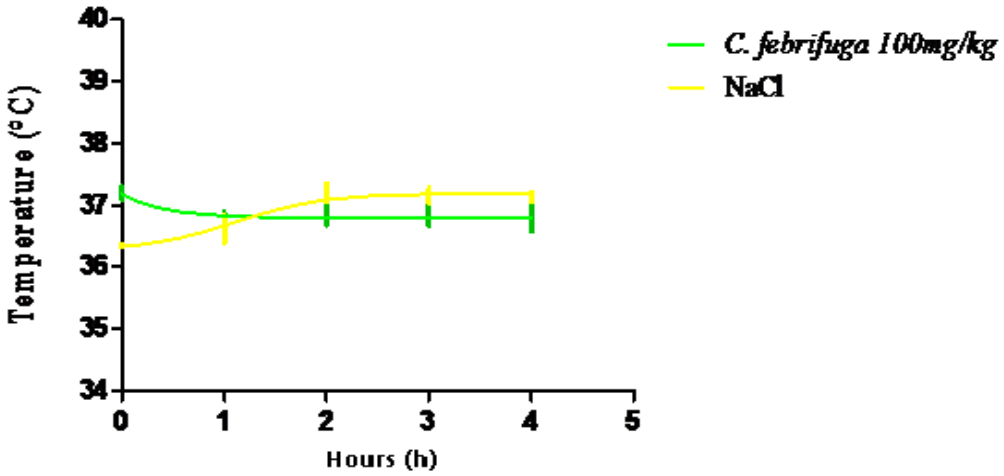

Fig. 1: Effect of *Crossopteryx febrifuga* on basal temperature basale.

Antipyretic activity of *Crossopteryx febrifuga* aqueous extract

In Fig. 2, temperature peaks were observed at T0 for each of the batches of rats. Subsequently, from T0 to T4, with the exception of group1 receiving Nacl for which the temperatures remained constant around 38.4°C, all other rat batches experienced a decrease in rectal temperature with curves with decreasing speed. The decrease in temperature was more noticeable in batches of rats fed *C. febrifuga* extract at doses of 25 mg/kg and 50 mg/kg body weight. The curves of the extracts at these doses were similar to those of paracetamol at 100 mg/kg. However, from T3, temperatures at 25 mg/kg increased slightly as those recorded with paracetamol while these temperatures remained constant at 50 mg/kg.

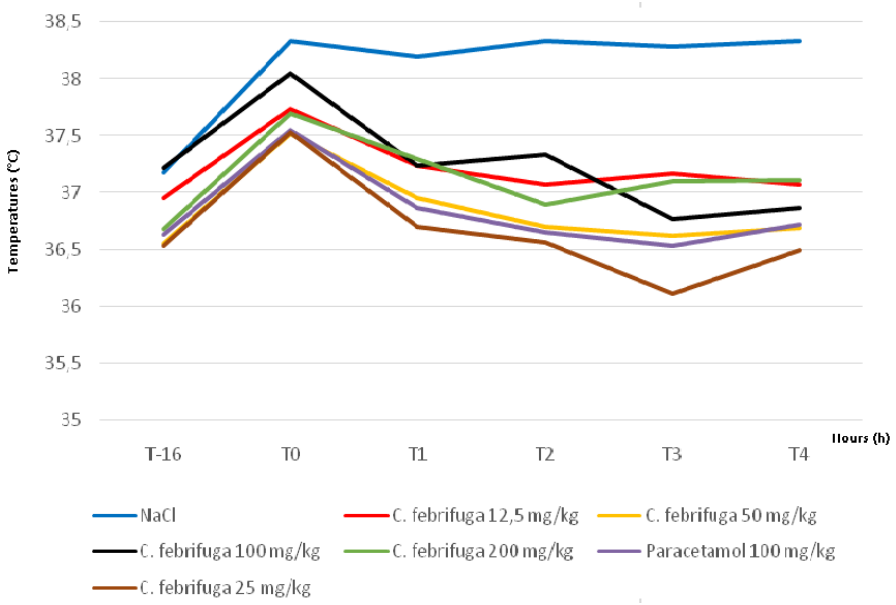

Fig. 2: Effect of *Crossopteryx febrifuga* on hyperthermia in rats.

The percent reduction in hyperthermia after oral administration of the substances (Nacl, Paracetamol and aqueous extract at different doses) was calculated and shown in Fig. 3.

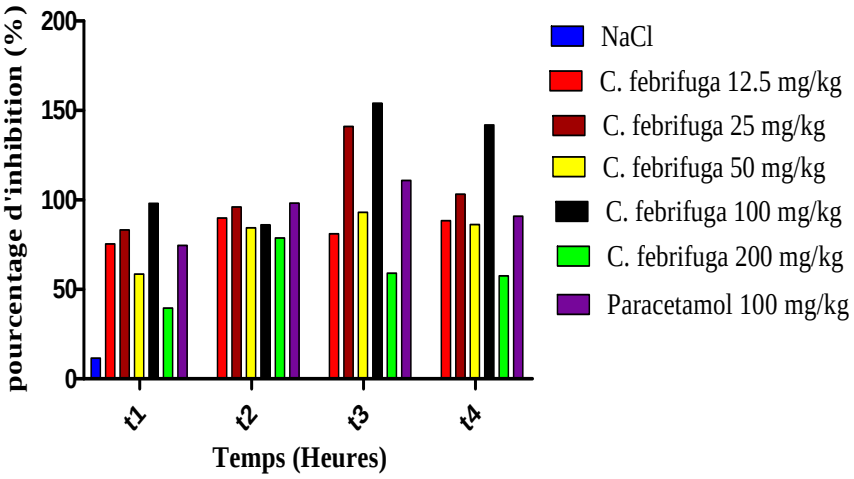

Fig. 3: Percentage reduction of hyperthermia with *Crossopteryx febrifuga* stem barks.

From t1 to t4, the percentages of inhibition of hyperthermia with the different substances were all positive. At t1, the highest inhibition percentages relative to paracetamol were observed with the extract at doses of 12.5 mg/kg, 25 mg/kg and 100 mg/kg. At t2, only the percent inhibition of the extract at 25 mg/kg was identical to that of paracetamol. At t3, the highest percent inhibition was achieved with the extract of *C. febrifuga* at 25 mg/kg and 100

mg/kg with respect to paracetamol, and at t4 there was a decrease in percentages inhibition of hyperthermia at these doses but these percentages remained higher than that of paracetamol. From t2 to t4, the percent inhibition at 50 mg/kg of the extract remained almost constant.

Statistical analysis

The statistical analysis focused on the variations in rat rectal temperature and the results were recorded in Table 1.

Table 1: **Values of temperatures obtained for the study of the antipyretic effect.**

	T=1h	T=2h	T=3h	T=4h
NaCl	38.2± 0.21	38.33±0.17	38.28±0.21	38.33±0.12
C. febrifuga **12.5 mg/kg**	37,23 ± 0,28 ***	37,06± 0,27***	37,16±0,30	37,06± 0,33 ***
C. febrifuga ***25*** **mg/kg**	36,7± 0,50***	36,56±0,69***	36,11± 1,00***	36,5± 0,66***
C. febrifuga **50 mg/kg**	36,95±0,44 ***	36,7 ±0,32***	36,61± 0,41 ***	36,68±0,29 ***
C. febrifuga **100 mg/kg**	37,23± 0,28 ***	37,33±0,33***	36,76± 0,92 ***	36,86± 0,32 ***
C. febrifuga **200 mg/kg**	37,3±0,42	36,9± 0,45 ***	37,1±0,26	37,11± 0,48 ***
Paracétamol100 mg/kg	36,86±0,40 ***	36,65±0,37 ***	36,53±0,30 ***	36,71±0,31***

ANOVA Test**:** *** Antipyretic effect statistically different at $p<0.05$. The variations in the rectal temperature of the rats are significantly different from the control group (NaCl).

Phytochemical screening

The results on phytochemical characterization are shown in Table 2.

Table 2: Characterization *of C. febrifuga* chemical groups.

Aqueous extract of *C. febrifuga*	**Reactions**
Sterols et polyterpenes	++
Polyphenols	+++
Saponosides	++
Gallic tannins	-
Catechic tannins	+++
Quinones	-
Flavonoïdes	+++
Alkaloïds	-

(-): absence; **(+)**: presence; **(++)**: strong color; **(+++)**: very strong color.

These signs were attributed in comparison with the colorations obtained with the controls.

DISCUSSION

These results revealed the use of *C. febrifuga* by the local population of Pakouabo village in the treatment of fever and various diseases. The study conducted by Dro *et al*. (2013) showed

that *C. febrifuga* is also used by the populations of northern Côte d'Ivoire in the drug preparations of several infections (diarrhea, skin infection, fevers and respiratory problems). Because of its great therapeutic interest, this plant is increasingly rare in Ivorian flora as shown by some authors.[18]

Regarding the pharmacological activity, the results obtained showed that the aqueous extract of *C. febrifuga* has no hypothermic effect at a dose of 100 mg/kg. This result helped to demonstrate that the extract would not act on the thermoregulatory center located in hypothalamus. In contrast, the antipyretic activity observed at doses of 12.5 mg/kg, 25 mg/kg, 50 mg/kg and 100 mg/kg showed that this extract would oppose the rise in basal temperature. This demonstrates that the extract would inhibit the synthesis of the chemical mediators of hyperthermia by reducing cytokine release and prostaglandin 2 biosynthesis.[19,20] Indeed, the hyperthermia induced by the yeast of beer (20%) is due to an inflammatory process which would lead to the biosynthesis of the chemical mediators elaborated starting from the arachidonic acid.[21,22] The decrease in temperature following the administration of the aqueous extract of *C. febrifuga* is probably due to the inhibition of PGE2 biosynthesis. This hypothesis has also been defended in similar work by some authors on *Alchornea cordifolia* and *Crossopteryx febrifuga*.[5,23]

Concentrations of the aqueous extract of *Crossopteryx febrifuga* at 25 mg/kg and 50 mg/kg have an effect almost similar to that of paracetamol at T = 1 hour and T = 2 hours while at 100 mg/kg of this extract, the antipyretic effect is more significant. It also appears that at the dose of 50 mg/kg, the effect of the extract remains constant after 3 hours while that of paracetamol begins to increase. The percentages of inhibition of hyperthermia calculated at the doses of 12.5 mg/kg to 200 mg/kg from 2h are all greater than 50%, this shows the effectiveness of this plant as a plant species antipyretic. These results corroborate those of some authors[23] conducted on a methanolic extract of *C. febrifuga* bark harvested in Nigeria and for which antipyretic activity is dose-dependent. This aqueous extract which is a complex mixture of compounds would be more effective than paracetamol. This effectiveness is linked to a synergistic action of the compounds (sterols, polyterpenes, polyphenols, flavonoids, catechin tannins and saponosides) contained in this extract as shown by the results of the phyochemical screening. Some authors have also found the same constituents in other parts of the plant ie the seed.[24] These compounds are supposed to be at the origin of several pharmacological activities of plant extracts such as anti-inflammatory, analgesic and

antipyretic effects.[25,26] The results obtained justify the use of *C. febrifuga* for the treatment of fever in a traditional environment.

CONCLUSION

The ethnopharmacological survey carried out on *Crossopteryx febrifuga* has shown that this plant is frequently used by the indigenous population of Pakouabo village in the treatment of fever, cough and oral infections. The study shown that at a concentration of 100 mg/kg of body weight, the aqueous extract of this plant has no hypothermic effect. However, a similar antipyretic effect to paracetamol (100 mg) was observed at doses of 25 mg/kg, 50 mg/kg whereas at the concentration of 100 mg/kg of this extract, the antipyretic effect is more significant than that of paracetamol. The use of this plant in traditional environment as febrifuge would be justified. This aqueous extract of this plant contains sterols, polyphenols, flavonoids, saponosides and catechin tannins which would be responsible for the observed pharmacological property.

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