Medicinal Plants Used for Malaria Treatment in Gamba Village, North Region of Cameroon: Ethnopharmacological Survey; *In* Vivo Antimalarial Activity of Aqueous Extracts of *Khaya Senegalensis Bark.*

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Abstract

Background: In traditional medicine, the floral diversity permits the inhabitants of North Cameroon to use a great number of plants to fight against Malaria. The aim of this study was to identify plants used in traditional medicine to treat malaria, and to verify the scientific basis for the use of one of these plants in the locality of Gamba.

Methods: An Ethnopharmacological survey was carried out on 15 traditional healers. We collected data on use of medicinal plants using questionnaires. Then *in-vivo* antimalarial activity of the decoctioned and macerated aqueous extracts of *khaya senegalensis* trunk bark was evaluated. The 4-day suppressive peters test was realised on *mus musculus swiss* albino mice. On day one, mice were infected with 10^7 *plasmodium berghei* parasitized red blood cells through intra-peritoneal inoculation. 2 hours after infestation, mice in batches of 6 were treated orally at a dose of 75, 150.300 mg/Kg for macerated aqueous extract and 65, 120.260 mg/Kg for decoctioned extract daily during 3 days at an administration volume of 10 ml/Kg. An extract was considered (% reduction): Highly active (between 100-90 %); moderate (between 90-50 %); weak (between 50-10 %); Inactive (between 0 %). P-values <0.05 were considered statistically significant.

Results: A total of 18 plant species belonging to 12 families were identified for the preparation of 12 recipes. The decocted aqueous extract of *khaya senegalensis* showed moderate anti-plasmodial activity (% reduction = 52.46%) at the highest dose of 260 mg/kg with p<0.001 compared to the positive control group. The aqueous macerate at doses of 150 and 300mg/kg gave respectively a percentage reduction of parasitaemia of 59.42% and 71.80% and also showed moderate anti-plasmodial activity; with p<0.001 between the different extracts and the positive control (99.18%).

Conclusion: In conclusion, extracts of *khaya senegalensis* showed moderate anti-plasmodial activity. It would therefore be necessary to evaluate the anti-malarial activity *in-vivo* and the toxicity of the aqueous extracts macerated using other solvents and also test the other plants listed.

Introduction

Malaria is a parasitosis affecting humans, rodents and monkeys. It is a hemopathy due to a haematozoan of the genus *Plasmodium sp*., transmitted by mosquitoes of the genus *Anopheles*. There are five species responsible for this disease in humans: *P. vivax*, *P. ovale*, *P. malariae*, *P. falciparum* and *P. knowlesii*, but the most harmful and widespread remains *Plasmodium falciparum* [1, 2]. This disease mainly affects populations living in endemic areas (intertropical zones) and remains the world's leading parasitic endemic. Synthetic antimalarial drugs (nivaquine, flavoquine, mefloquine, artesunate etc.) have expanded the possibilities offered by quinine and artemisinin, natural antimalarial drugs and insecticides [3]. These antimalarial drugs raised hopes that malaria would be eradicated. Unfortunately, the germs of malaria are still far from being defeated, malaria is on the rise. According to the WHO 2020 report, the number of malaria cases is estimated at 229 million in 2019. The african region alone 94% of cases[4].In 2019, Cameroon has 2,628,191 confirmed cases of malaria with a percentage of deaths of 18.3%[5]. The principal problem with the treatment using these classical synthetic drugs is that of plasmodium drug resistance. Moreover, the female Anopheles mosquitoes, the vectors that carry the parasites are now resistant to insecticides and the parasites themselves are increasingly less sensitive to the usual drugs. [6, 7]. It is therefore urgent to research alternative therapies. One of the solutions to these problems is to valorise anti-malarial medicinal plants and traditional know-how and knowledge through an ethno-pharmacological approach. Despite the scientific advances made by modern medicine, 80% of the African population still use traditional medicine in primary health care [8]. The flora in the locality of Gamba, like everywhere else in the Northern region of Cameroon is rich and varied [9]. This richness and diversity in flora enables the inhabitants of this locality to use a large number of plants to fight against diseases such as malaria. This study therefore, which aimed at valorizing African medicinal plants and the know-how of herbal therapists, had as main objective, cataloguing the anti-malarial recipes made from medicinal plants in the locality of Gamba and evaluate the scientific basis of the use of the most cited plants in order to develop an

improved traditional medicine that is effective, safe and accessible to low-income families. Specifically, we sought to carry-out an ethnopharmacological survey, with the aim of making an inventory of anti-malarial medicinal plants used by phytotherapists and to assess the scientific basis of the use of one of the plants through the evaluation of the anti-malarial activity *in vivo* using the murine model *Plasmodium berghei / Swiss white mouse* of *Mus musculus* type.

Material And Methods

Ethnopharmacological survey

Plant samples were collected during an ethnopharmacological survey from August 1st to September 2nd 2017 from 15 traditional doctors in the locality of Gamba (Fig. 1). With the help of a botanist technician, the species collected were identified using the national herbarium of Cameroon.

Antimalarial activity

Studied Plants

The barks of *Khaya senegalensis* stems were collected in GAMBA, a village located along the national road $n^0$1in the department of Mayo-Rey, North region of Cameroon and identified by a plant taxonomist. *Khaya senegalensis* specimens are deposited under N◦ 49 688 at the National Herbarium of Cameroon (Yaoundé).

Preparation of *Khaya senegalensis* extracts

The fresh bark of *Khaya senegalensis* was dried at room temperature away from sunlight and moisture. Decoctions were prepared by boiling 60 g of *Khaya senegalensis* bark powder in 350 ml of water for 15 minutes. For maceration, 60 g of *Khaya senegalensis* bark powder was extracted in 350 ml of cold distilled water for 24 hours, then filtered using a Wattman Nº 1 filter paper, the decoction and maceration were evaporated in an oven at 40°C and 6g of a brown colored solid was obtained. The yields of the decocted (black powder) and macerated (brown powder) were 11.6% and 10% respectively.

Experimental animals

The animal species chosen for this study were naive female white *mus musculus swiss* albino mice aged 8–12 weeks and weighing between 18–26 grams. They were purchased from the National Veterinary Laboratory of Garoua, North Cameroon, then bred in a pet shop and maintained in a light/dark cycle of 12 hours at room temperature with access to food and water. All animals were fasted prior to all tests and were randomly assigned to 5 experimental groups, each of 6 mice.

In vivo anti-plasmodial efficacy assessment

A strain of *Plasmodium berghei* was used to evaluate the antimalarial activity in vivo. On the day of the test, donor mice previously infected with *Plasmodium berghei* were anaesthetized by injection of 100 µL of a mixture of Diazepam550/Ketamine (50mg/ml). The infected blood (with ~ 30%-50% parasitaemia) was then drawn by cardiac puncture from the right atrium and collected in tubes containing an anticoagulant (EDTA). The collected parasitized blood was diluted in physiological water (Sodium Chloride 0.9%) such that 200 µl of blood contained 10^7 infected red blood cells.

Assessment of in vivo antiplasmodial activity

Mice who had previously undergone overnight fasting (48 mice), were weighed and divided into 8 batches of 6 mice each. Two hours after infection with 0.2 ml of blood containing 10^7 intraperitoneally parasitized red blood cells, the first 3 batches received doses of 75, 150, and 300 mg/kg/day respectively of the macerated extract, and the 3 other batches received 65, 130, 260 mg/kg/day respectively of the decocted extract for 4 consecutive days, while the remaining 2 batches received respectively quinine at 10 mg/kg/day (positive control group) and 10 ml/kg of distilled water (negative control group) for 4 consecutive days (D0-D4) using an oral feeding tube. On the fifth day (D5), the mice were weighed and thin blood smears made from blood taken from their tails were fixed using methanol, stained with 10% Giemsa and read with an optical microscope using the X100 objective. Parasitaemia was evaluated using the equation [10]:

$$Parasitemia(\%) = \frac{Number\ of\ parasittized\ red\ blood\ cells}{Total\ number\ of\ red\ blood\ cells\ examined} \times 100$$

The percentage reduction in parasitaemia was used to assess antimalarial activity and determined according to the following equation [10] :

$$\%\ \mathbf{reduction} = \frac{C - T}{C} \times 100$$

Where, **C** : is the average percent parasitemia in the control group ; **T** : the average percent parasitemia in the treated group.

The scale of appreciation of the anti-malarial activity of Rasoanaivo plant extracts made it possible to determine the parasitological effectiveness of our extracts [11]. For an extract tested at a dose ≤ 300 mg/kg, its activity was considered: Highly active (% reduction was found between 100 and 90 %) ; moderate (% reduction was found between 90 and 50 % ; weak (% reduction was found between 50 and 10 %.); Inactive (% reduction was 0 %.).

Statistical analysis

Sphinx 2-V5 software was used to prepare the questionnaire and analyze the data collected from the traditional practitioners. Stat graphics® software was used to perform the one-factor analysis of variance (ANOVA). Fischer's test was used to compare the results of the antimalarial test and p-values < 0.05 were considered statistically significant.

Results

Ethnopharmacological study:

A total of 18 plant species belonging to 12 families were recorded during this study. The importance of the plants was materialized by their citation frequencies (CF). The most frequently cited species are: *Azadirachta indica* (CF = 87%), *Khaya senegalensis*, *Eucalyptus globulus*, *Nauclea latifolia* with CF = 60% each (Table 1)

In vivo antiplasmodial activity

Effect of the decocted aqueous extract on mouse parasitemia:

The mean parasitemia values determined in the treated groups ranged from 19.50 to 26.56% (Table 2). There was a statistically significant difference ($p < 0.05$) between the different extracts and the negative control 40.67% ($p < 0,01$).

Effect of the macerated aqueous extract on parasitemia in mice:

The mean parasitemia values determined in the treated groups ranged from 16.83 to 24.17% depending on the dose, compared to the negative control values of 40.67%. There was a very significant difference ($p < 0.01$) between the different extracts and the negative control (Table 2).

Table 1
Antimalarial medicinal plants from Gamba locality.

Plant Families	Plant Species	Local name	frequency of citation (%)	Plant part(s)used	Mode of preparation	Application mode	Accession number
Fabaceae	Senna siamea (lam.) Irvin	Acassia	53	leaves	Decoction	oral	HNC.n°25 661
	Senna javanica /cassia javanica l	Gamoye	40	bark	Maceration	oral	HNC.n°45 764
Burseraceae	Boswellia dalziellii hutch.	Nzapi	40	leaves	Decoction	oral	HNC.n°39 928
	Boswellia papyrifera robbr. Ex colebr.	Nzap	47	bark	Decoction	oral	HNC.n°39 949
Caealpiniaceae	senna alata (l.) Roxb.	Kenkelibaa	20	Whole plant	Decoction	bath + oral	HNC.n°57 704
	Senna occidentalis (l.) Link	Faux kenkeliba	27	Whole plant	Decoction	bath + oral	HNC.n° 7 848
Rubiaceae	Nauclea latifolia sm.	Demhock	60	roots	Decoction	oral	HNC.n°20 144
Limiaceae	Ocimum basilicum l	Baselic	20	Whole plant	Decoction	oral	HNC.n°42 757
	Ocimum gratissimum l.	Ikaa	20	Whole plant	Decoction	oral	HNC.n°49 083
Asteraceae	Vernonia guineensis bak	Kougue	20	root	Decoction	anal	HNC.n°24 247
Meliaceae	Khaya senegalensis	Staapo	60	bark	Decoction ou maceration	oral	HNC.n°49 688
	Azadirachta indica a. Juss/neem	Neem	87	leaves	Decoction	oral	HNC.n° 4 447
	Eucalyptus globulus	Eucalyptus	60	leaves	Decoction	oral	HNC.n° 4 077
Zingberceae	Zingiber officinale rosc	Djidja	20	Whole plant	Decoction	oral	HNC.n°43 146
Caricaceae	Carica papaya l.]	Doukoudje	33	leaves	Infusion	oral	Hnc.n°18 647
Myrtaceae	Psidium guajava l	Guayave	27	leaves	Decoction	oral	Hnc.n°65 619

Plant Families	*Plant Species*	*Local name*	*frequency of citation (%)*	*Plant part(s)used*	*Mode of preparation*	*Application mode*	*Accession number*
Mimosaceae	*Entada africana guill. & perr.*	*Ewandoue*	*47*	*leaves*	*Infusion*	*oral*	*HNC.n°49 693*
Euphorbiacae	*Manihot esculenta crantz*	*Mbaye*	*13*	*leaves*	*Decoction*	*bath*	*HNC.n°18 619*

Table 2
Effects of *Khaya Senegalensis* extracts on *Plasmodium berghei* parasitemia.

Treatment groups	Dose (mg/Kg/day)	Mean Parasitemia(%) ± SD
Maceration	75	24.17 ± 1.17 *a
	150	16.83 ± 1.83 * b
	300	12.17 ± 2.04 *c
Distilled water	10ml/Kg	40.67 ± 3.33 *d
Quinine	10	0.33 ± 0.52 *
Decoction	65	26.50 ± 2.16 *a
	130	21.00 ± 1.67 *b
	260	19.50 ± 1.64 *b
Distilled water	10ml/Kg	40.67 ± 3.33 *c
Quinine	10	0.33 ±0.52 *

* indicates a statistically significant difference. The different letters (a-c) highlight the significant differences between the groups.

Effect of treatment with macerated and decocted aqueous extract on the percentage reduction of parasitaemia

Generally, tests carried out in vivo with the aqueous extracts showed a reduction in parasitaemia proportional to the doses administered. The aqueous macerate at doses of 75, 150 and 300mg/kg gave respectively a percentage reduction of parasitemia of 39.74%, 59.42%, and 71.80% (Fig. 3). There was a significant difference ($p < 0.001$) between the different extracts and the positive control (99.18%). Quinine showed a significant reduction of parasitemia 1.4 times higher than the macerated extract at the 300mg/kg dose. The percentages of parasitemia reduction with the decocted aqueous extracts were 34.84, 48.36 and 52.46% respectively at the doses of 65, 130 and 260 mg/kg body weight of the animals although not significant at the two highest doses ($P < 0.05$) (Fig. 2). Quinine showed a reduction in parasitemia approximately two-times higher than the decocted extract at 260 mg/kg dose.

Discussion

A total of 18 medicinal plants belonging to 12 families have been registered. A general review of the literature on these medicinal plants showed that they are also used in many African countries in the treatment of malaria, such as in Ghana: *Carica papaya, Khaya senegalensis*, *Nauclea latifolia, Azadirachta indica, Psidium guajava* [12]; in Ivory coast: *Ocimum gratissum, Entada Africana, Vernonia guineens* [13, 14]; in Uganda : *Carica papaya; Boswellia papyrifera, vernonia guineensis* [15]; and in Nigeria: *Boswellia dalziellii, Eucalyptus globulus, Senna siamea* [16]. This consensus among users in different countries reflects the importance of medicinal plants to African populations, and the fact that these same plants are used by different communities for the same purpose could possibly indicate their effectiveness. Previous laboratory studies provide evidence to support the anti-malarial activity of many plant species harvested in the locality of Gamba as shown in Appendix 1 which presents the antiplasmodial activity and phytochemical characteristics that confirm their traditional use.

In general, *in vivo* antimalarial activity tests in mice infected with *P. berghei* showed a dose-dependent reduction in parasitemia in mice parasitized with the tested extracts and quinine.

Compared to the Rosanaivo scale, the decocted aqueous extract which gave percentage reductions of 34.84%, 48.36% respectively at doses of 65 and 130 mg/kg body weight had a low activity, while at 260 mg/kg the extract had a moderate activity (52.46%). The antiplasmodial activity of the macerated extract (39.74%) at the 75mg/kg dose reflected a low antiplasmodial activity, compared to the other two doses of 150 and 300 mg/kg, the reduction in parasitemia was 59.41% and 71.79% respectively reflecting a moderate antiplasmodial activity about twice as high as the decocted extract at the 260 mg/kg dose.

At the administration dose of 300 mg/kg, the parasite inhibition by the aqueous macerate was 71.80% whereas at the dose of 10 mg/kg, quinine resulted in 99.18% parasite inhibition. The parasite inhibition of quinine could probably be matched by doubling the dosage and/or optimizing the extraction. The macerate showed better parasitic inhibition than the decocted one. This means that the aqueous decoction was less active than the macerate. This could be related to the boiling temperature, which may have destroyed certain bioactive chemical compounds [17].

The antimalarial drug of reference remains largely more effective than the macerated extract. This is easily understandable when we know that quinine (a fast-acting schizonticide) is a pure molecule [18], while the aqueous macerate is an agglomerate of chemical molecules that can act synergistically or develop antagonism. An isolation of the active molecules responsible for the anti-malarial activity, would allow a much more reliable comparative study to be made. At this stage of the study, it would be difficult to make any structure-activity relationship but we can say that the activity observed could be due to all the chemical groups identified in our extracts according to the literature. Indeed certain phytochemical studies carried out on Khaya senegalensis bark have revealed the presence of saponins, tannins, flavonoids, terpenoids, alkaloids, etc[19, 20]. Studies have shown that the alkaloids and terpenoids of the plants would have an activity on plasmodium falciparum by shizonicidal action. A blood schizonticide is an active product against asexual forms of the blood (cause of clinical manifestations) and cures malaria. Alkaloids are believed to inhibit the polymerization of the haemoglobin heme and thus prevent the reproduction of plasmodium. And terpenoids block an enzyme ,Ca++-ATPase which allows the parasite to pump calcium and thus prevent it from developing. [21]. The limoïdes which are terpenoids were indeed highlighted in this plant. [22]. A study showed that limoids from the meliacae family had moderate activity on Plasmodium berghei [23].

On the other hand, only one *in vitro* study on khaya senegalensis was found to confer good antiplasmodial activity on the chloroquino-resistant strain of Plasmodium falciparum with an IC50 of 5.5 µg/ml [24]. Moderate *in vivo* activity may also be due to low oral bioavailability of certain chemical molecules. With these results, *Khaya senegalensis* cannot exert its activity only by direct action against parasites, the beneficial therapeutic effects claimed by patients could also be due to the anti-inflammatory and immunomodulating activities described for this plant [25, 26].

Conclusions

It appeared from this study that the locality of Gamba has an interesting floristic biodiversity in terms of antimalarial plants. The plants listed in this study constitute a panel that can serve as a starting point for biological screening in the laboratory. The macerated aqueous extract of *Khaya senegalensis* bark showed the highest antiplasmodial activity compared to the decocted aqueous extract. However, this activity remained moderate. These results allowed us to conclude that although presenting a moderate activity on *Plasmodium Berghei in vivo* and a good *in vitro* activity, *Khaya senegalensis* had a possible antiplasmodial activity. It would therefore be necessary to evaluate the *in vivo* antimalarial activity of *Khaya senegalensis* bark using other extractive solvents and to evaluate the *in vivo* antimalarial activity and toxicity of other listed plants.

Abbreviations

CF: citation frequencies

CP: Positive control.

D: days

EDTA: Ethylene Diamine Tetra-acetic Acid

HNC: National Herbarium of Cameroon

P: Plasmodium

WHO: World Health Organization

Declarations

Ethics approval and consent to participate:

Although our work did not involve human subjects, we followed all the rules laid down by the regulations in force concerning work involving animals at the University of Ngaoundere.

Consent for publication:

Not Applicable

Availability of data and materials:

Not Applicable

Conflict of interests:

The authors report no competing of interest in this work.

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Authors' Contributions:

Davy-Hyacinthe Anguechia Gouissi, Roselyne Teponging Nzangue were responsible for the conception, integrity and reliability of the study. Davy-Hyacinthe Anguechia Gouissi, Josue Haskandi Kalaza, Siméon Pierre Fodouop Chegaing, contributed in the write up and data analysis. All authors took part in the acquisition and analysis of data or interpretation of results, and also examined and approved the final version of the write up.

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References

1. Hayakawa T, Culleton R, Otani H, Horii T, Tanabe K. Big Bang in the Evolution of Extant Malaria Parasites. Mol Biol Evol. 1 oct 2008;25(10):2233-9.
2. Pérez-Tris J, Hasselquist D, Hellgren O, Krizanauskiene A, Waldenström J, Bensch S. What are malaria parasites? Trends Parasitol. 1 mai 2005;21(5):209-11.
3. Kumar A, Paliwal D, Saini D, Thakur A, Aggarwal S, Kaushik D. A comprehensive review on synthetic approach for antimalarial agents. Eur J Med Chem. 6 oct 2014;85:147-78.
4. Rapport 2020 sur le paludisme dans le monde - Messages généraux - World [Internet]. ReliefWeb. [cité 2 févr 2021]. Disponible sur: https://reliefweb.int/report/world/rapport-2020-sur-le-paludisme-dans-le-monde-messages-g-n-raux
5. PNLP | Cameroun – Programme National de Lutte contre le Paludisme [Internet]. [cité 18 janv 2021]. Disponible sur: https://pnlp.cm/
6. Ranson H, Abdallah H, Badolo A, Guelbeogo WM, Kerah-Hinzoumbé C, Yangalbé-Kalnoné E, et al. Insecticide resistance in Anopheles gambiae: data from the first year of a multi-country study highlight the extent of the problem. Malar J. 17 déc 2009;8:299.
7. Sidhu ABS, Valderramos SG, Fidock DA. pfmdr1 mutations contribute to quinine resistance and enhance mefloquine and artemisinin sensitivity in Plasmodium falciparum. Mol Microbiol. 1 août 2005;57(4):913-26.
8. Makita-Ikouaya E, Milleliri J-M, Rudant J-P. Place de la médecine traditionnelle dans le système de soins des villes d'Afrique subsaharienne : le cas de Libreville au Gabon. Cah Détudes Rech Francoph Santé. 1 oct 2010;20(4):179-88.
9. Scholte P, Kirda P, Adam S, Kadiri B. Floodplain rehabilitation in North Cameroon: Impact on vegetation dynamics. Appl Veg Sci. 2008;3(1):33-42.
10. Zucker JR, Campbell CC. Malaria. Principles of prevention and treatment. Infect Dis Clin North Am. sept 1993;7(3):547-67.
11. Rasoanaivo P, Deharo E, Ratsimamanga-Urveg S, Frappier F. Guidelines for the nonclinical evaluation of the efficacy of traditional antimalarials. In: Willcox M, Bodeker G, Rasoanaivo P, éditeurs. Traditional medicinal plants and malaria [Internet]. Boca Raton: CRC; 2004 [cité 16 juin 2018]. p. 255-70. (Traditional Herbal Medicines for Modern Times). Disponible sur: http://www.documentation.ird.fr/hor/fdi:010042409
12. Asase A, Akwetey GA, Achel DG. Ethnopharmacological use of herbal remedies for the treatment of malaria in the Dangme West District of Ghana. J Ethnopharmacol. 16 juin 2010;129(3):367-76.
13. Bla KB, Trebissou JND, Bidie AP, Assi YJ, Zihiri-Guede N, Djaman AJ. Étude ethnopharmacologique des plantes antipaludiques utilisées chez les Baoulé- N'Gban de Toumodi dans le Centre de la Côte d'Ivoire. J Appl Biosci. 1 janv 2015;85(1):7775– 7783.
14. Kamanzi Atindehou K, Schmid C, Brun R, Koné MW, Traore D. Antitrypanosomal and antiplasmodial activity of medicinal plants from Côte d'Ivoire. J Ethnopharmacol. 1 févr 2004;90(2):221-7.

15. Stangeland T, Alele PE, Katuura E, Lye KA. Plants used to treat malaria in Nyakayojo sub-county, western Uganda. J Ethnopharmacol. 1 sept 2011;137(1):154-66.
16. Adebayo JO, Krettli AU. Potential antimalarials from Nigerian plants: A review. J Ethnopharmacol. 27 janv 2011;133(2):289-302.
17. A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Med Aromat Plants [Internet]. 2015 [cité 6 nov 2020];04(03). Disponible sur: http://www.omicsgroup.org/journals/a-review-on-the-extraction-methods-use-in-medicinal-plants-principle-strength-and-limitation-2167-0412-1000196.php?aid=58448
18. Genest G, Thomson DMP. Fixed drug eruption to quinine: a case report and review of the literature. J Allergy Clin Immunol Pract. août 2014;2(4):469-70.
19. Ayo RG, Audu OT, Amupitan JO. Physico-chemical characterization and cytotoxicity studies of seed extracts of *Khaya senegalensis* (Desr.) A. Juss. Afr J Biotechnol [Internet]. 2007 [cité 6 nov 2020];6(7). Disponible sur: https://www.ajol.info/index.php/ajb/article/view/56940
20. Ugoh SC, Agarry OO, Garba SA. Studies on the antibacterial activity of Khaya senegalensis [(Desr.) A. Juss)] stem bark extract on Salmonella enterica subsp. enterica serovar Typhi [(ex Kauffmann and Edwards) Le Minor and Popoff]. Asian Pac J Trop Biomed. 1 mai 2014;4:S279-83.
21. Foote SJ, Cowman AF. The mode of action and the mechanism of resistance to antimalarial drugs. Acta Trop. 1 mars 1994;56(2):157-71.
22. Khalid SA, Friedrichsen GM, Kharazmi A, Theander TG, Olsen CE, Brøgger Christensen S. limonoids from Khaya senegalensis. Phytochemistry. 20 nov 1998;49(6):1769-72.
23. Bray DH, Warhurst DC, Connolly JD, O'Neill MJ, Phillipson JD. Plants as sources of antimalarial drugs. Part 7. Activity of some species of meliaceae plants and their constituent limonoids. Phytother Res. 1 févr 1990;4(1):29-35.
24. El Tahir A, Satti GMH, Khalid SA. Antiplasmodial activity of selected Sudanese medicinal plants with emphasis on Maytenus senegalensis (Lam.) Exell. J Ethnopharmacol. 1 mars 1999;64(3):227-33.
25. Koko WS, Mesaik MA, Yousaf S, Galal M, Choudhary MI. In vitro immunomodulating properties of selected Sudanese medicinal plants. J Ethnopharmacol. 19 juin 2008;118(1):26-34.
26. Thioune O, Pousset JL, Lo I. [Anti-inflammatory activity of the bark of Khaya senegalensis (A Juss). Preliminary research of structure/activity relationship]. Dakar Med. 1999;44(1):12-5.
27. Ajaiyeoba EO, Ashidi JS, Okpako LC, Houghton PJ, Wright CW. Antiplasmodial compounds from Cassia siamea stem bark extract. Phytother Res. 1 févr 2008;22(2):254-5.
28. Bukar A, Mukhtar M, Hassan A. Phytochemical screening and antibacterial activity of leaf extracts of Senna siamea (LAM) on Pseudomonas aeruginosa. Bayero J Pure Appl Sci. 1 janv 2009;2(1):139-42.
29. Clarkson C, Maharaj VJ, Crouch NR, Grace OM, Pillay P, Matsabisa MG, et al. In vitro antiplasmodial activity of medicinal plants native to or naturalised in South Africa. J Ethnopharmacol. 1 juin 2004;92(2):177-91.
30. K. P C. Cassia Javanica Linn: A Review on Its Phytochemical and Pharmacological Profile. J Biomed Pharm Res [Internet]. 9 févr 2013 [cité 29 nov 2017];2(01). Disponible sur: http://jbpr.in/index.php/jbpr/article/view/84
31. Camarda L, Dayton T, Di Stefano V, Pitonzo R, Schillaci D. Chemical Composition and Antimicrobial Activity of Some Oleogum Resin Essential Oils from Boswellia SPP. (Burseraceae). Ann Chim. 1 août 2007;97(9):837-44.
32. Zirihi GN, Mambu L, Guédé-Guina F, Bodo B, Grellier P. In vitro antiplasmodial activity and cytotoxicity of 33 West African plants used for treatment of malaria. J Ethnopharmacol. 26 avr 2005;98(3):281-5.
33. Sule WF, Okonko IO, Joseph TA, Ojezele MO, Nwanze JC, Alli JA, et al. In vitro antifungal activity of Senna alata Linn. crude leaf extract. Res J Biol Sci. 2010;5(3):275-84.
34. Yadav JP, Arya V, Yadav S, Panghal M, Kumar S, Dhankhar S. Cassia occidentalis L.: A review on its ethnobotany, phytochemical and pharmacological profile. Fitoterapia. 1 juin 2010;81(4):223-30.

35. Adebajo AC, Odediran SA, Aliyu FA, Nwafor PA, Nwoko NT, Umana US. In Vivo Antiplasmodial Potentials of the Combinations of Four Nigerian Antimalarial Plants. Molecules. 26 août 2014;19(9):13136-46.
36. Deeni YY, Hussain HSN. Screening for antimicrobial activity and for alkaloids of Nauclea latifolia. J Ethnopharmacol. 1 oct 1991;35(1):91-6.
37. Benoit-Vical F, Valentin A, Cournac V, Pélissier Y, Mallié M, Bastide J-M. In vitro antiplasmodial activity of stem and root extracts of Nauclea latifolia S.M. (Rubiaceae). J Ethnopharmacol. 1 juill 1998;61(3):173-8.
38. Bilal A, Jahan N, Ahmed A, Bilal SN, Habib S, Hajra S. Phytochemical and pharmacological studies on Ocimum basilicum Linn-A review. Int J Curr Res Rev. 2012;4(23).
39. Akono Ntonga P, Baldovini N, Mouray E, Mambu L, Belong P, Grellier P. Activity of *Ocimum basilicum* , *Ocimum canum* , and *Cymbopogon citratus* essential oils against *Plasmodium falciparum* and mature-stage larvae of *Anopheles funestus* s.s. Parasite. 2014;21:33.
40. Tchoumbougnang F, Zollo PH, Dagne E, Mekonnen Y. *In Vivo* Antimalarial Activity of Essential Oils from *Cymbopogon citratus* and *Ocimum gratissimum* on Mice Infected with *Plasmodium berghei*. Planta Med. janv 2005;71(1):20-3.
41. Nweze EI, Eze EE. Justification for the use of Ocimum gratissimum L in herbal medicine and its interaction with disc antibiotics. BMC Complement Altern Med [Internet]. déc 2009 [cité 29 nov 2017];9(1). Disponible sur: http://bmccomplementalternmed.biomedcentral.com/articles/10.1186/1472-6882-9-37
42. Toyang NJ, Krause MA, Fairhurst RM, Tane P, Bryant J, Verpoorte R. Antiplasmodial activity of sesquiterpene lactones and a sucrose ester from Vernonia guineensis Benth. (Asteraceae). J Ethnopharmacol. 3 juin 2013;147(3):618-21.
43. Ugoh SC, Agarry OO, Garba SA. Studies on the antibacterial activity of Khaya senegalensis [(Desr.) A. Juss)] stem bark extract on Salmonella enterica subsp. enterica serovar Typhi [(ex Kauffmann and Edwards) Le Minor and Popoff]. Asian Pac J Trop Biomed. 1 mai 2014;4(Supplement 1):S279-83.
44. Njayou FN, Aboudi ECE, Tandjang MK, Tchana AK, Ngadjui BT, Moundipa PF. Hepatoprotective and antioxidant activities of stem bark extract of Khaya grandifoliola (Welw) C. DC and Entada africana Guill. et Perr. J Nat Prod. 2013;6:73–80.
45. Prawat H, Mahidol C, Ruchirawat S, Prawat U, Tuntiwachwuttikul P, Tooptakong U, et al. Cyanogenic and non-cyanogenic glycosides from Manihot esculenta. Phytochemistry. 1 nov 1995;40(4):1167-73.
46. Anagu OL, Attama AA, Okore VC, Gugu HT, Ngene AA, Esimone CO. Azadirachta indica extract-artesunic acid combination produces an increased cure rate of Plasmodium berghei-infected mice. Pharm Biol. juill 2014;52(7):883-9.
47. Sujarwo W, Keim AP, Caneva G, Toniolo C, Nicoletti M. Ethnobotanical uses of neem (Azadirachta indica A.Juss.; Meliaceae) leaves in Bali (Indonesia) and the Indian subcontinent in relation with historical background and phytochemical properties. J Ethnopharmacol. 2 août 2016;189:186-93.
48. Zofou D, Tene M, Ngemenya MN, Tane P, Titanji VPK. In Vitro Antiplasmodial Activity and Cytotoxicity of Extracts of Selected Medicinal Plants Used by Traditional Healers of Western Cameroon [Internet]. Malaria Research and Treatment. 2011 [cité 29 nov 2017]. Disponible sur: https://www.hindawi.com/journals/mrt/2011/561342/abs/
49. Pereira SI, Freire CSR, Neto CP, Silvestre AJD, Silva AMS. Chemical composition of the essential oil distilled from the fruits of Eucalyptus globulus grown in Portugal. Flavour Fragr J. 1 juill 2005;20(4):407-9.
50. Ahmad I, Zahin M, Aqil F, Hasan S, Khan MSA, Owais M. Bioactive compounds from Punica granatum, Curcuma longa and Zingiber officinale and their therapeutic potential. Drugs Future. 2008;33(4):329.
51. Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): A review of recent research. Food Chem Toxicol. 1 févr 2008;46(2):409-20.

52. Kovendan K, Murugan K, Panneerselvam C, Aarthi N, Kumar PM, Subramaniam J, et al. Antimalarial activity of Carica papaya (Family: Caricaceae) leaf extract against Plasmodium falciparum. Asian Pac J Trop Dis. 1 janv 2012;2(Supplement 1):S306-11.
53. Schweiggert RM, Steingass CB, Mora E, Esquivel P, Carle R. Carotenogenesis and physico-chemical characteristics during maturation of red fleshed papaya fruit (Carica papaya L.). Food Res Int. 1 juin 2011;44(5):1373-80.
54. Gutiérrez RMP, Mitchell S, Solis RV. Psidium guajava: A review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol. avr 2008;117(1):1-27.

Appendix

APPENDIX : Physicochemical and antimalarial properties of plants

Species	physicochemical properties	Antimarial activity
Senna siamea (Lam.) Irvin & Barneby	Triterpenoids, anthraquinones, flavonoïds	*In vitro* antplasmodial activity [27]
	Alkaloïds [28]	
Senna javanica /Cassia javanica L	Anthraquinone, Javanins, quercétins ; alkaloïds	*In vitro* antplasmodial activity [29]
	Quercetin [30]	
Boswellia papyrifera Robbr. ex Colebr.	triterpens : β-amyrin, α-amyrin, β-amyrenon	
	acétate d' ocyle , acide α-boswellic [31]	
Senna alata (L.) Roxb.	tanins, stéroïdes, alkaloïdes, anthraquinones, terpens	*In vitro* antplasmodial activity [32]
	saponines[33]	
Senna occidentalis (L.) Link	chrysophanol saponins, alkaloïds, sterols, triterpenoids,	*In vitro* antplasmodial activity [32]
	, tanins et flavonoïds [34]	
Nauclea latifolia Sm.	Akcaloïds**,** saponins and catechic tannins	*In vivo* antplasmodial activity [35]
	c[36]	
Ocimum basilicum L	Tanins, Phenolic compound , steroïds [38]	*In vitro* antplasmodial activity [39]
Ocimum gratissimum L.	Saponins, flavonoïds,tanins, reducing sugar ,	In vivo antplasmodial activity [40]
	anthroquinone[41]	
vernonia guineensis BAK	sesquiterpene lactones , ester saccharose [42]	antplasmodial activity [42]
Khaya senegalensis A. Juss./Cailcédrat	saponines, tanins, phlobatannins, flavonoïds, terpenoïds	
	alkaloïdes, anthroquinones [43]	

Entada Africana Guill. & Perr.	Flavonoïds, tannins, polyphénols [44]	
Manihot esculenta Crantz	flavonoïds,saponins, lotaustraline, , Glycosids	
	cyanogenic, non-cyanogenic [45]	
Azadirachta indica A. Juss/Neem	Diterpen, triterpens, phénoliques ; Flavonoïds ; Tannins	*In vivo* antplasmodial activity [46]
	Alcaloïdes ; [47]	
Eucalyptus globulus	Sesquiterpènes,tanin, Robustaol A, Robustadial B	*In vitro* antplasmodial activity [48]
	pinène [49]	
Zingiber officinale Rosc	sesquiterpene hydrocarbons , sesquiterpene alcohols	*In vitro* antplasmodial activity [50]
	gingerols and shogaols [51]	
Carica papaya L.]	Anthraquinone; Terpénoïds ; Flavonoïds, Saponins; Tanins	*In vitro* antplasmodial activity [52]
	alkaloïds, cardiac glycosides [53]	
Psidium guajava L	phenolic compounds and flavonoids; triterpenic acids	
	tanin[54]	*In vitro* antplasmodial activity [54]

Figures

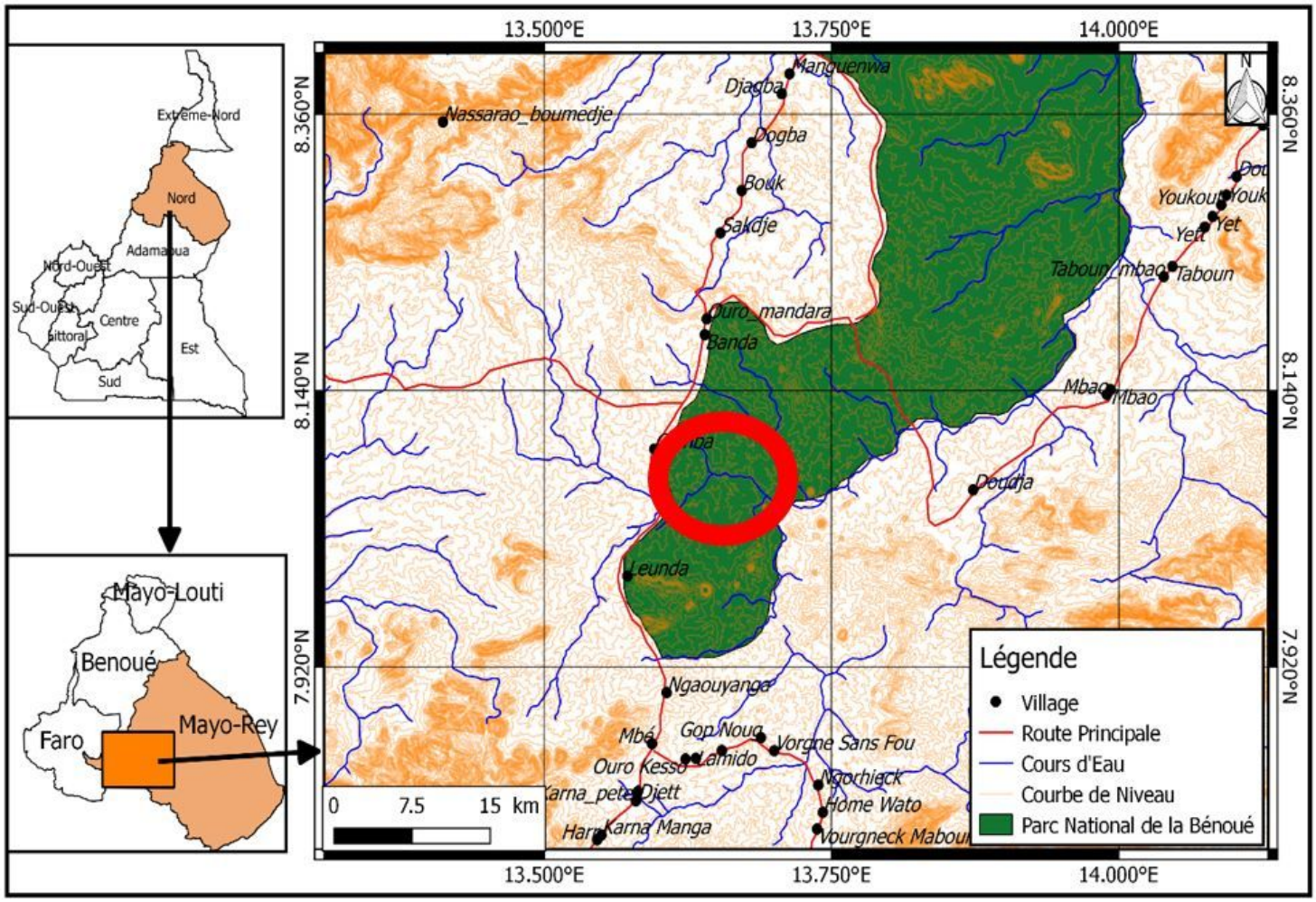

Figure 1

Location map of GAMBA (source: Department of Geoscience and environment, University of Ngaoundere). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

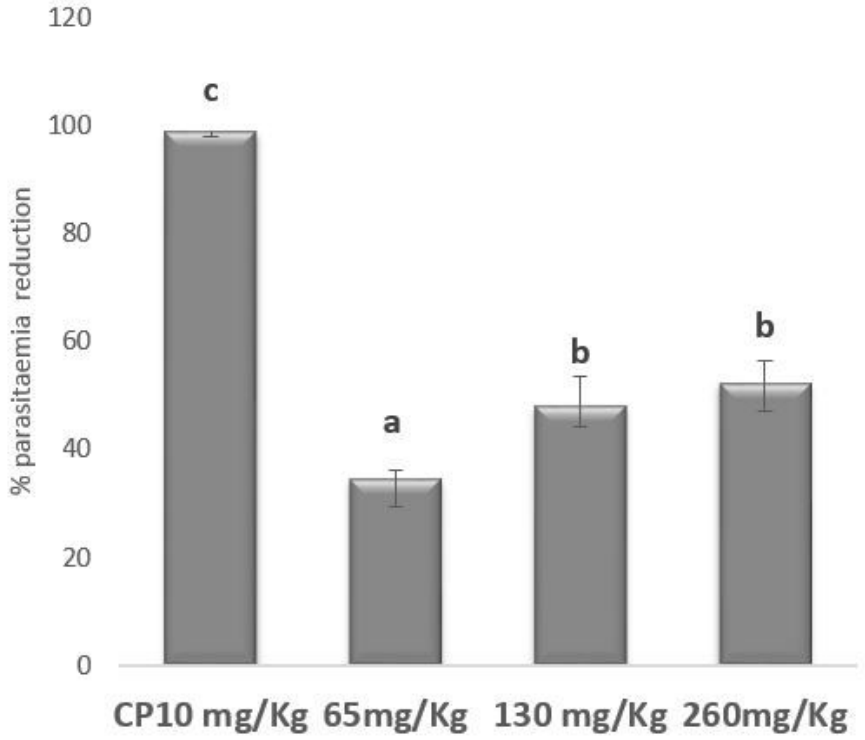

Figure 2

% reduction of parasitaemia aqueous extracts decocted; (The different letters (a-c) highlight the significant differences between the groups.) CP: Positive control.

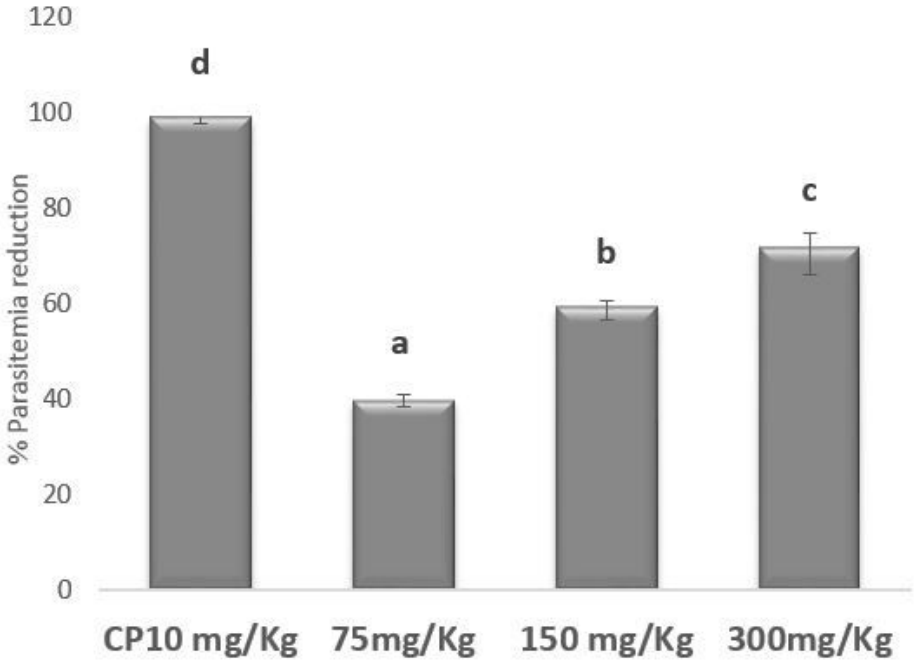

Figure 3

% reduction of parasitaemia macerated aqueous extract (The different letters (a-c) highlight the significant differences between the groups.) CP: Positive control.