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Anti-inflammatory and Analgesic Activities of the Methanolic Extract and the Residual Fraction of the Stem Bark of *Daniellia oliveri* (Fabaceae)

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Authors' contributions

This work was carried out in collaboration among all authors. Author MT performed investigation, data handling and processing, writing, preparation of original draft of the manuscript. Authors ACC, KTT, AGLB and EWLMBK performed investigation, data handling and processing. Authors NO and MK helped in supervision, acquisition of funding and author RWS helped in Idea conception, supervision, acquisition of funding. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of this study was to evaluate the anti-inflammatory and analgesic activities of *Daniellia oliveri* methanolic extract and its fractions in NMRI mice.
Study Design: *In vivo* acute toxicity, anti-inflammatory and analgesic assays.
Place and Duration of Study: The work was carried out in the Department of Traditional Pharmacopoeia and Pharmacy (MEPHATRA / PH) of the Research Institute for Health Sciences (IRSS) Ouagadougou (Burkina- Faso) between December 2020 and February 2021.
Methodology: The toxicity of the extracts was assessed according to OECD guideline 423 of 2001 at a single dose of 2000 mg / kg body weight. Analgesic effect was evaluated on the number of

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abdominal contortions induced by the intraperitoneal injection of acetic acid and the anti-inflammatory activity using the Carrageenan anti-edematous test was determined according to Winter.
Results: The results of the acute oral toxicity study in mice showed no clinical signs of toxicity at dose of 2000 mg/kg b.w. The lethal dose (LD_{50}) value estimated to 5000 mg/kg. The extracts reduced edema from the first hour, then by the third hour and maximum inhibition was achieved by the fifth hour after the injection of carrageenan. Extract and methanolic fraction at different doses showed significant inhibition of abdominal contortions in mice in a dose dependent manner. At 200mg the analgesic effect of methanolic fraction and crude extract was 53.70±1.29% and 41.38±1.25% respectively. At 400 mg/kg, the methanolic fraction inhibited carragenaan-induced edema by 85.97±5.67%.
Conclusion: *Daniellia oliveri* is an important source of anti-inflammatory and analgesic compounds, justifying the use of this plant in traditional medicine for the treatment of inflammatory diseases.

Keywords: Daniellia oliveri; anti-inflammatory; analgesic; traditional medicine.

1. INTRODUCTION

The inflammatory reaction is the body's response to an attack originating from physical (heat, cold, ionizing radiation, etc.), exogenous or endogenous solid elements (pathogenic microorganisms, insect bite, chemicals) or biological components (immune complexes, cytotoxic antibodies, cytokines, etc.) [1]. The inflammation can be short-lived or long-lasting, and manifests itself with signs such as redness, swelling (edema), heat, and pain. Pain and edema are the signs that prompt many patients to seek medical attention [2]. In all cases the inflammatory process involves inflammatory mediators such as proteins, peptides, glycoproteins, cytokines, compounds resulting from the metabolism of arachidonic acid (prostaglandins, thromboxanes, and leukotrienes); free radicals etc. However, the maintenance of inflammatory mediators following chronic inflammation is linked to certain pathologies such as cancer, diabetes II, and rheumatism [3]. Inflammations can heal on their own or with treatment. Most steroidal and non-steroidal anti-inflammatory drugs used in the treatment of various inflammatory pathologies are very effective but present several unwanted side effects that are mostly gastrointestinal and renal. Generally, adverse effects of anti-inflammatory drugs are more observed with short or long-term treatment and/or with patients at risk [4,5]. To avoid these side effects caused by the available anti-inflammatory drugs, the search for new anti-inflammatory therapeutic agents with less adverse effects seems essential.

Daniellia oliveri, a Sudano-Guinean tree, is indicated in the treatment of diseases such as tuberculosis, pneumonia, hemiplegia, hernias, hiccups, neuralgia, wounds, ulcers, persistent headaches, jaundice, and impotence [6]. In Burkina Faso, *Daniellia oliveri* is used in traditional medicine for the management of pathologies with inflammatory components [6]. However, there is little scientific information on the pharmacological properties of this plant. Indeed, Yaya et al, 2016 demonstrated the anti-inflammatory activity of the leaf aqueous extract of *Daniellia oliveri* [7]. Moreover Onwukaeme ND, 1995 showed the anti-inflammatory and analgesic effects of the stem bark of this plant [8]. In this study, the investigations are focused on demonstrating the anti-edematous and analgesic properties of the methanolic extract and the fraction of the stem barks of *Daniellia oliveri* to provide scientific data for further studies.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Plant material

Daniellia oliveri stem bark was harvested in February 2018 at Ziniaré (Burkina Faso). The plant was identified by Pr Amadé OUEDRAOGO from the Ecology Laboratory of the University Joseph KI-ZERBO (Burkina Faso). A voucher specimen was deposited in the herbarium of the Biodiversity Information Center (CIB) under the identification number 17251. The plant material was dried in laboratory conditions. After drying, the stem bark was crushed and packaged for experimentation.

2.1.2 Animal material

Male and female NMRI breed mice weighing between 18 and 28 g were used in this study. These animals were provided by the animal faculty of University Joseph KI-ZERBO (Burkina Faso). Mice were acclimatized at the pet shop of the Department of Traditional Medicine, Pharmacopeia, and Pharmacy (MEPHATRA / PH), at 20-25 °C, a relative humidity of 75% and a photoperiod of 12/14 hours for two weeks before drug administration. In vivo studies were performed according to current guidelines for the care of laboratory animals and ethical guidelines for assessing experimental pain in conscious animals.

2.2 Methods

2.2.1 Extraction

A methanolic maceration of the stem bark powder of *Daniellia oliveri* was carried out at room temperature for 48 hours. The maceration was filtered and then concentrated in a rotavapor, then frozen and lyophilized for 48 hours. Extracts were hermetically sealed and kept at 4°C for the various tests. The fractionation of the crude extract was done using hexane, dichloromethane, ethyl acetate, methanol and butanol respectively. At the end of the fractionation, all the organic phases were dried and conditioned for phytochemical and biological tests.

2.2.2 Acute general toxicity

The toxicity test was carried out using the "dose adjustment" method of the OECD line 423 [7] and consisted of testing the extract of *Daniellia oliveri* at a single dose of 2000 mg/kg body weight. Two groups of 3 mice received the extracts orally as a single dose of 2000 mg/kg body weight. After oral administration of the extract, animals were observed for 2 hours after which they were fed. They were then observed for 24, 48, 72 hours, one week and two weeks, during which time the signs of toxicity including modification of the coat, tremors, weight, breathing, sensitivity to noise after a metallic shock, stool appearance, mobility and mortality were noted.

2.2.3 Anti-inflammatory activity: Carrageenan anti-edematous test

The method described by Winter [8] was used for the anti-edema effect of *Daniellia oliveri*. Six batches of six mice were fasted for 17 hours before the test. The different batches were treated with the herbal drugs at doses of 50, 100, 200, 400 mg/kg. The reference substance used was acetylsalicylic acid acetylsalicylic acid at a dose of 200 mg/kg. The negative control lot received distilled water. The volume administered was 1 ml/100 g body weight per gavage.

A volume of 0.05 mL of carrageenan (1% suspended in 0.9% NaCl) was injected under the hind paw's plantar fascia, thus causing the appearance of edema in the metatarsal region.

The treated paw volume was measured 1 hour before the injection of carrageenan, 1, 3 and 5 hours after the injection of carrageenan. The variation in the volume of the treated paw made it possible to assess the anti-inflammatory power of any substance. The average volume of edema in the treated paw was calculated from 3 scatter measurements not exceeding 4%. The anti-edema activity was evaluated as a percentage reduction in edema in treated mice compared to the control group according to the following formula:

% Inhibition = (A - B / A) x 100

A represents the average difference of the volume increase in the paw of mice in control group at the times T 01 hour, T 03 hours and T 05 hours.
B represents the average difference of the volume increase in the paw of mice in treated groups.

These averages are plotted on a curve to follow the evolution of the edema for each group. The determination of the percentage of inhibition of edema (IOP) makes it possible to evaluate the anti-inflammatory potential of the plant extracts.

2.2.4 Analgesic activity: Acetic acid test

The non-morphine analgesic effect was evaluated on the number of abdominal contortions induced by the intraperitoneal injection of acetic acid (0.6%), according to the method described by Sawadogo et al. [9]. The mice were fasted 17 hours before the experiment. six batches of six mice were formed. The control batch received distilled water, the other batches received the extracts and reference substance (paracetamol at 200 mg/kg) by oral administration. Different doses of extracts (50, 100, 200, and 400 mg/kg) were administered

orally to mice depending on their body weight. One hour after administering the extracts, animals received acetic acid intraperitoneally at 10 mL/kg. Five minutes after the acetic acid injection, the number of contortions was counted in each mouse for 15 minutes. Analgesic effect was evaluated according to the following formula:

% inhibition = (Wb - Wt / Wb) x 100

Wb represents the average of the number of contortions of mice in control group and
Wt is the average of the number of contortions of mice in treated groups.

2.2.5 Statistical analysis

Statistical analysis was performed using Graph Prism 5 software and One Way ANOVA. "Analysis of variance" followed by Dunnett's multiple comparaison tests were used as statistical processing. The differences are considered significant for p value less than 0.05. Values are expressed as mean ± Standard Error of Mean (SEM) p <0.05 is considered significant compared to the control. (**) = p < 0.01, (***) = p < 0.001, and (****) = p < 0.0001 vs control.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Acute toxicity

The results of the acute oral toxicity study in mice demonstrated no clinical signs of toxicity (decreased sensitivity to the stimulus, decreased mobility) and no death after drug administration at 2000 mg/kg body weight (bw). All animals survived after 14 days of observation. According to the Global Classification and Harmonization System (GHS), the LD_{50} of the methanolic extract of *Daniellia oliveri* is higher than 5000 mg/kg.

3.1.2 Anti-inflammatory effect

The result of anti-inflammatory effect of the methanolic extracts of *Daniellia oliveri* at 50, 100, 200 and 400 mg/kg bw demonstrated significant decrease of the edema volume of treated mice after drug administration from one hour to five hours. The volumes of edema are shown in Figs. 1 and 2 and the percentages of inhibition are recorded in Table 1.

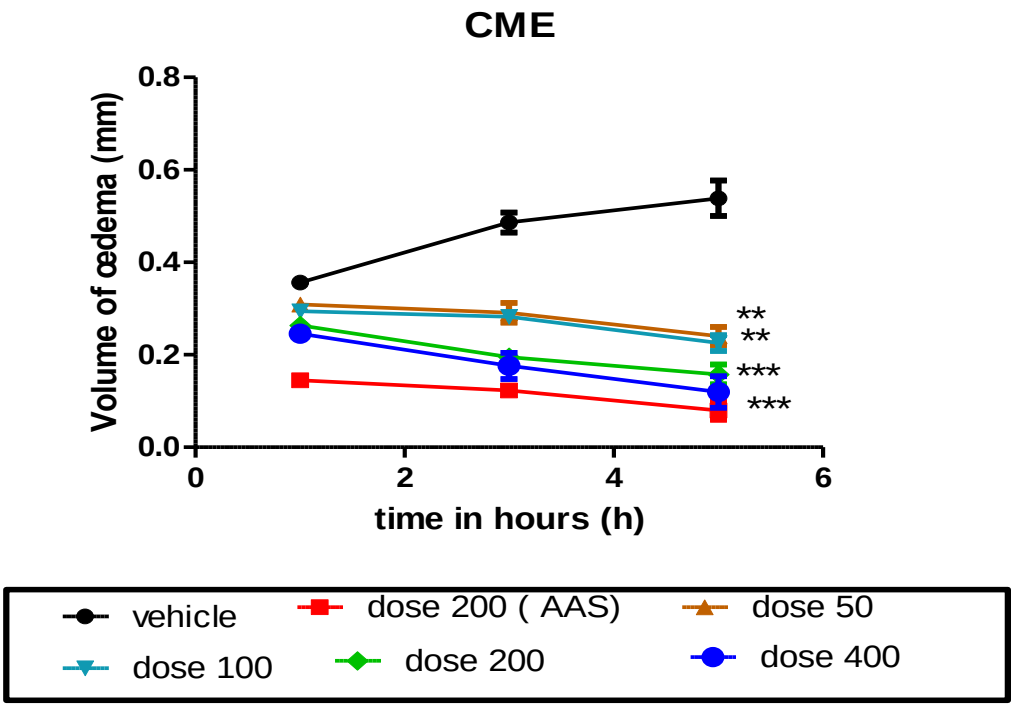

Fig. 1. Effect of acetyl salicylic acid (AAS) and crude methanolic extract (CME) of *Daniellia oliveri*. * P < 0.05; ** p < 0.01; ***p < 0.001 is considered significant compared to the blank control (water). Values are mean ± S.E.M

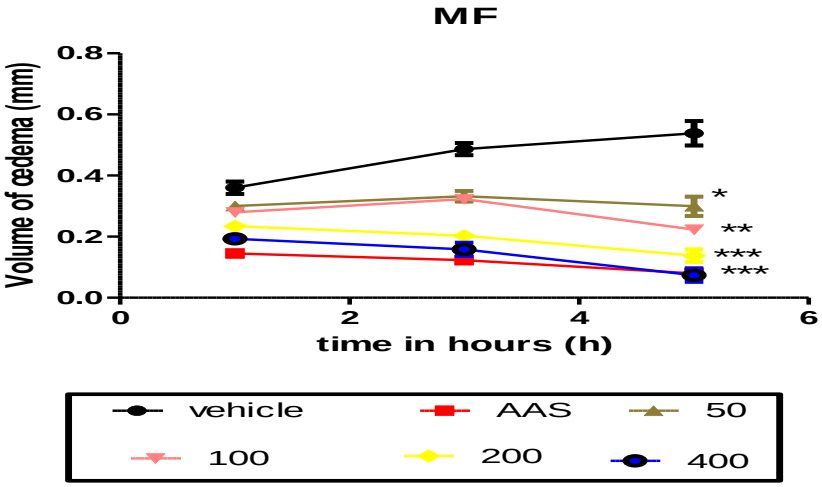

Fig. 2. Effect of acetyl salicylic acid (AAS) and methanolic fraction (MF) of *Daniellia oliveri* * P < 0.05; ** p < 0.01; ***p < 0.001 is considered significant compared vs control. Values are mean ± S.E.M

Table 1. Anti-inflammatory effect of the methanolic extract and methanolic fraction 50% of *Daniellia oliveri*

Sample	Dose (m/ kg)	% Inhibition		
		1h	3h	5h
Crude methanolic extract (CME)	50	13.26 ±0.34***	40.17 ±3.84***	55.23 ±2.5***
	100	17.31 ±1.25***	41.83 ±3.25***	58.10 ±1.01***
	200	25.89 ±1.11***	59.86 ±2.56**	70.69 ±3.88***
	400	31.04 ±3.21***	63.77 ±6.74*	77.81 ±6.87*
Methanolic fraction (MF)	50	15.74 ±1.5***	31.66 ±1.48***	44.00 ±6.78***
	100	21.36 ±0.67***	34.04 ±1.75***	58.42 ±2.46***
	200	41.07 ±3.01***	58.08 ±1.90***	74.12 ±3.38***
	400	45.72 ±3.05***	67.58 ±3.35ns	85.97 ±5.67ns
ASA (Reference)	200	59.28 ±2.92	72.28 ±2.72	87.32 ±2.90ns

*Values are mean ± S.E.M. n = 6. *: P<0.05, **: P<0.01, ***: P<0.001 compared vs control (one way ANOVA analysis followed by Dunnett's test). ns: no significant*

The extracts of *Daniellia oliveri* significantly reduced the edema induced by carrageenan in a dose-dependent manner from the first hour, the anti-edema effect of the extract being greater at the 5th hour.

3.1.3 Analgesic effect

The analgesic effect induced by different doses of *Daniellia oliveri* extracts compared to the paracetamol used as reference drug is reported in Fig. 3.

3.2 Discussion

Daniellia oliveri stem bark can be considered as a low toxicity product by oral route in mice, according to the United Nations Globally Harmonized Classification System and OECD guideline. The LD_{50} of this extract would be higher than 5000 mg/kg. This result gives safe guarantee regarding the oral use of *Daniellia oliveri* stem bark extract. The works of Kabore et al., [10] showed a LD_{50} value of 3500 mg / kg orally administered in mice, with the aqueous extract of *Daniellia oliveri* stem bark and those of Ahmadu et al., [11], a LD_{50} of 4000 mg / kg bw for ethanolic leaf extract in mice by intraperitoneal administration. Although these methods of administration are different, they prove a low toxicity of the *Daniellia oliveri* stem bark extract.

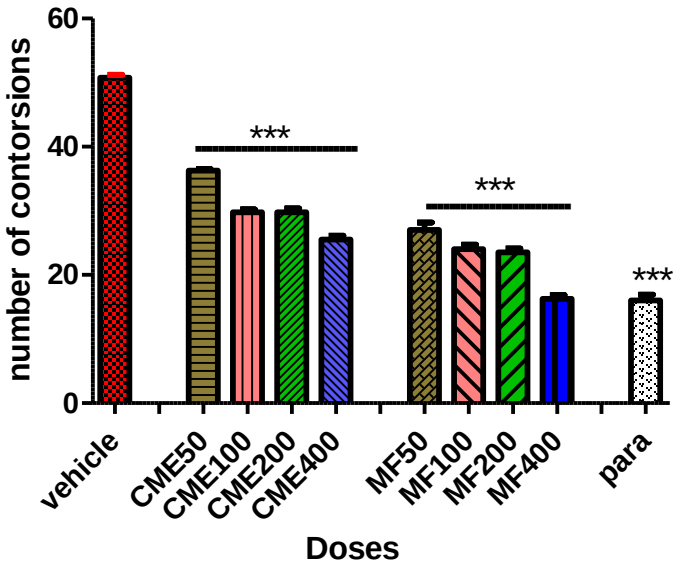

Fig. 3. Variation in the number of contortions of mice with different doses of crude methanolic extract (CME), methanolic fraction (MF) and para (paracetamol) 200 mg/kg* P < 0.05; ** p < 0.01; ***p < 0.001 is considered significant compared to the control

Table 2. Analgesic effect of the stem bark of methanolic extract and methanolic fraction 50% of *Daniellia oliveri*

Samples	Dose (mg/ kg)	% Inhibition
Methanolic extract	50	28.6 ±0.5***
	100	41, 38 ±0.95***
	200	41.38 ±1.25***
	400	49.75 ±1.29***
Methanolic fraction	50	46.8 ± 2.3***
	100	52.70 ± 1.41***
	200	53.70 ±1.29***
	400	67.70 ±0.81 ns
Paracetamol	200	68.5 ±1.58 ns

The injection of carrageenan into the subplanar surface of right hind paw of mice has induced edema which is measurable and whose evolution is determined according to the dose and the time of drug administration. At the 5th hour, the crude methanolic extract and it fraction exhibited significant anti-inflammatory effect in the carrageenan-induced paw edema in mice (Figs. 1 & 2). Carrageenan induced mouse paw edema involves many mediators that induce the inflammatory response in two different phases [1]. An initial phase, which lasts approximately 1 hour 30 min after injection of carrageenan agent attributed to action of mediators such as histamine, serotonin and bradykinin on vascular permeability. A late phase, which is the result of overproduction of prostaglandins in tissues, mediated by cyclo-oxygenase (COX) and which can continue beyond 5 hours after carrageenan injection [12]. The edema induced by carrageenan injection was reduced by crude extract, and methanolic fraction as well as by AAS used as reference substance. At the 5th hour, the crude methanolic extract and its fraction exhibited significant anti-inflammatory effect in the carrageenan-induced paw edema in mice (Figs. 1 & 2). This suggests the possibility of *Daniellia oliveri* extracts to affect the action of prostaglandins or cyclooxygenases (COX 1 and COX 2) responsible for biosynthesis of prostaglandins. Carrageenan-induced edema is sensitive to cyclo-oxygenase (COX) inhibitors and lipoxygenase inhibitors [2]. Therefore, anti-inflammatory effect of *Daniellia oliveri* stem bark may be due to an antagonistic action on biosynthesis of inflammation mediators. Previous

work has revealed the presence of tannins, saponosides, flavonoids and triterpenes / steroids in the methanolic extract of *Daniellia oliveri*. According to Sawadogo et al, Ben A. Chindo [13,14] these components are responsible for the anti-inflammatory properties of plant extracts. Previous works have proven the pharmacological activity of Daniellia oliveri [7,8].

Abdominal contortions caused by intraperitoneal injection of acetic acid is a method used to study peripheral analgesic effect of a substance. The pain induced by the injection of acetic acid is thought to be due to action of local peritoneal receptors as well as release of mediators such as prostaglandins (PGE2α, PGF2α), leukotrienes and cytokines (TNF-α, IL-1β, IL-8) [15]. Both extracts and paracetamol in different doses reduce the number of abdominal contortions (Fig. 3). The extracts reduced contortions in a dose-dependent and significant manner compared to control groups (Fig. 3). The mechanism of the analgesic effect of these extracts may be due to release reduction, histamine, serotonin and prostaglandins, or the direct blocking of receptors of these endogenous mediators [16]. Likewise, chemical compounds such as tannins, saponosides, flavonoids and triterpenes / steroids demonstrated during the chemical screening of *Daniellia oliveri*, extracts could explain analgesic effect of various extracts [17]. According to Sawadogo et al., [13] saponins are well known for their ability to inhibit pain perception. Zeashan Hussain et al. [18]; Ben A Chindo et al. [14] have reported that tannins, saponosides, flavonoids and triterpenes / steroids have analgesic effects.

5. CONCLUSION

Daniellia oliveri stem bark extracts showed anti-inflammatory and analgesic effects. These extracts contain main chemical groups such as tannins, flavonoids, sterols, triterpenes and saponosides which are responsible of the pharmacological activities of this plant. The results of this study constitute a scientific basis for the traditional uses of this plant and the prerequisites for further research and development of anti-inflammatory drugs. The low toxicity of this plant, especially by oral route, is advantage for its traditional and modern use.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL

The *in vivo* testing was carried out in accordance with current laboratory animal care and ethics guidelines for experimental pain research on conscious animals. [19]. Experiments on mice were approved by the local ethic committee through the agreement code CEEA-UJKZ/2020-02 from July 28th, 2020.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Noufou Ouedraogo, Constantin Boladé Atchade, Tata Kadiatou Traore, Laurent G Boly, Esther Kabre WLM, Jules Yoda, Felix B, et al. Anti-Inflammatory Activity of Extracts from Parkia biglobosa (Jacq) R. Br. Ex G. Don. (Fabaceae-Mimosoideae) Trunk Bark. J Pharmacol Toxicol; 2021.
2. Adjaratou Coulibaly, Esther Kabre WLM, Tata Kadiatou Traore, et al. Phytochemical Screening, Anti-inflammatory and Analgesic Activities of Root Barks from Acacia macrostachya Reichenb. Ex DC. (Fabaceae). Annu Res Rev Biol. 2020; 35:76–83.
3. Bartsch H, Nair J. Chronic inflammation and oxidative stress in the genesis and perpetuation of cancer: Role of lipid peroxidation, DNA damage, and repair. Langenbecks Arch Surg. 2006;391:499–510.

4. Noufou Ouedraogo, Marius Lompo, Richard W Sawadogo. Pharmacognosie Étude des activités anti-inflammatoire, analgésique et antipyrétique des décoctés aqueux des feuilles et des racines de Pterocarpus erinaceus. Phytotherapie ; 2012.
5. Yougbare-ziebrou MN, Lompo M, Ouedraogo N, Yaro B, Guissoun IP. Antioxidant, analgesic and anti-inflammatory activities of the leafy stems of *Waltheria indica* L. (Sterculiaceae). J Appl Pharm Sci. 2016;6(02):124–9.
6. Nacoulma O. Plantes médicinales et pratiques médicales traditionnelles au Burkina Faso. Cas Du Plateau Central; 1996.
7. Yaya ST, Claude MJ, Anthelme NS, Flavien T. Anti-inflammatory activity of the aqueous extract of Daniellia oliveri (Fabaceae). Int Arch Integr Med Vol. 2016; 3(2):1–9.
8. Onwukaeme ND. Pharmacological Activities of Extracts. Phytotherapy. 1995; 9:306–8.
9. OCDE. Toxicité orale aiguë - Méthode par classe de toxicité aiguë. Ligne directrice l'ocde pour les essais Prod Chim OCDE 423. 2001;4(423,9):1–14.
10. Winter C, Risley E, GW N. Carrageenin-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proc Soc Exp Biol Med. 1962;111: 544–7.
11. Sawadogo WR, Boly R, Lompo M et al. Anti-inflammatory, analgesic and antipyretic activities of Diclipteraverticillata. Int J Pharmacol. 2006;2(4):435–8.
12. Kabore A, Hamidou T, Traore A. Phytochemical analysis and acute toxicity of two medicinal plants (*Anogeissus leiocarpus* and *Daniellia oliveri*) used in traditional veterinary medicine in Burkina Faso. Arch Appl Sci Res. 2010;2(6):47–52.
13. Ahmadu A, Haruna AK, Garba M, Ehinmidu JO, Sarker SD. Phytochemical and antimicrobial activities of the Daniellia oliveri leaves. Fitoterapia. 2004;75(7–8):729–32.
14. Su S, Hua Y, Wang Y, Gu W, Zhou W, Duan JA, et al. Evaluation of the anti-inflammatory and analgesic properties of individual and combined extracts from *Commiphora myrrha*, and *Boswellia carterii*. J Ethnopharmacol [Internet]. 2012;139(2):649–56.
15. Kumar D. Anti-inflammatory, analgesic, and antioxidant activities of methanolic wood extract of Pterocarpus santalinus L. J Pharmacol Pharmacother. 2011;2(3):200–2.
16. Ladigina EY, LN S, VE O, IA B andina, NI G, AA S, et al. Analyse chimique des plantes médicinales. Édition Moskva Vischaya Chkola. 1983;172.
17. Boye A, Amoateng P, Koffuor GA, Atsu Barku VY, Bawa EM, Anto OE. Antinociceptive and antioxidant activity of an aqueous root bark extract of Daniellia oliveri (Rolfe) Hutch. & Dalziel (Fam: Leguminosae [Fabaceae]) in ICR mice. J Appl Pharm Sci. 2013;3(12):36–45.
18. Hussain Z, Amresh G, Singh CVRS. Antinociceptive Activity of *Amaranthus spinosus* in Experimental Animals. J Ethnopharmacol. 2009;122(3):492 96.

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