Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)
Copyright©2024; The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited

RESEARCH ARTICLE

ANTI-INFLAMMATORY EFFECTS OF ROOT BARK METHANOLIC EXTRACT OF *BOSWELLIA DALZIELII* IN ALBINO MICE

Jeweldai Vedekoi[1,4]*, Elizé Dadaya[2], Koubé Juliette[3], Edima Carole Hélène[1], Sokeng Dongmo Sélestin[4]

[1]*Department of Biotchnologies and Pharmacognosy, Faculty of Science, University of Ebolowa, Ebolowa, Cameroon.*
[2]*Department of Life Sciences, Higher Teachers Training College, University of Bertoua, Bertoua, Cameroon.*
[3]*Department of pharmaceutical sciences, Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Cameroon.*
[4]*Department of Biological Sciences, Faculty of Science, University of Ngaoundere, Ngaoundere, Cameroon.*

Article Info:

Article History:
Received: 13 May 2024
Reviewed: 16 July 2024
Accepted: 28 August 2024
Published: 15 September 2024

Cite this article:
Vedekoi J, Dadaya E, Juliette K, Hélène EC, Sélestin SD. Anti-inflammatory effects of root bark methanolic extract of *Boswellia dalzielii* in albino mice. Universal Journal of Pharmaceutical Research 2024; 9(4): 32-39.
http://doi.org/10.22270/ujpr.v9i4.1152

***Address for Correspondence:**
Jeweldai Vedekoi, Department of Biotchnologies and Pharmacognosy, Faculty of Science, University of Ebolowa, Ebolowa, Cameroon. Department of Biological Sciences, Faculty of Science, University of Ngaoundere, Ngaoundere, Cameroon. Tel: +237674319326; E-mail: *jeweldai2024@yahoo.com*

Abstract

Background and objective: *Boswellia dalzielii* has been traditionally used in the Far North region (Cameroon) to treat fever, rheumatism, asthma and various inflammatory conditions. This investigation was designed to determine the anti-edematous and antioxidant properties to confirm its storied claims.
Methods: The DPPH radical scavenging and reduced Fe^{3+} to the Fe^{2+} assays were two methods used to evaluate the antioxidant activities. The swelling caused by carrageenan paw and xylene ear edema to cause inflammation were applied to evaluate the anti-inflammatory activities of the extract. The mechanisms of action of the methanol extract were evaluated in the serotonin test. Fever induced by yeast was exploited to value antipyretic activity in albinos animals. Diclofenac, ascorbic acid, and paracetamol were utilized as standard medicaments.
Results: Results published the existence of cardiac glycosides, flavonoid, simple phenols, flavonoids, tannins, coumarins and alkaloids. The results indicated also no acute toxicity and the LD_{50} was above 3000 mg/kg. The methanolic extract exhibited the best activity IC_{50} (178.12 µg/mL) against DPPH radical with, which was comparable with ascorbic acid (179.12 µg/mL) and a strong reducing power with an IC_{50} of about 147.85 µg /mL. In addition, the roots extract of *B. dalzielii* significantly inhibited (p<0.001) the volume of paw edema, ear edema and the fever.
Conclusion: Finally, the present study published clearly that the *B. dalzielii* methanolic extract (BDME) possess important antioxidant and anti-edematous effects. The phytoconstituents found in this methanol extract were responsible for the anti-inflammatory and antioxidant effects.
Keywords: Anti-inflammatory, *B. dalzielii*, Carrageenan, DPPH, FRAP, IC_{50}, LD_{50}.

INTRODUCTION

The reactive oxygen species (ERO) are unstable, very reactive elements and their reaction rate constants are very high, ranging from 10^{-9} to 10^{-6} second[1]. By their particular structure, free radicals tend to attract electrons from other atoms and molecules to gain stability[2]. In fact, free radicals, capable of independent existence (hence the term free), are chemical, atomic or molecular species, characterized by instability and/or strong oxidizing power. In the biotic life, these unpaired electrons (the superoxide anion ($O^{2\cdot-}$), the hydroxyl radical ($^{\cdot}OH$), nitrogen monoxide ($NO^{\cdot}$), the peroxide radical ($ROO^{\cdot}$) and the alkoxyl radical ($RO^{\cdot}$)) are produced continuously by the respiratory chain in order to destroy bacteria within phagocytic cells, to regulate lethal cellular functions, to participate in the functioning of certain enzymes, in the transduction of cellular signals, in the regulation of capillary dilation[3]. However, most of the damage to cellular components and tissue structures results in an expression called oxidative stress caused either by a shortage of available antioxidants or by an overproduction of free radicals[4]. Oxidative stress corresponds to effect to a disturbance of the intracellular oxidative status. In terms of counter-effect, an arsenal of (antioxidants) is being put in place to prevent these harmful oxidizing products[5]. But, the use of synthetic antioxidants provokes the appearance of side effects of uncontrolled, inadequate and abusive use and a potential risk of toxicity to human health such as tetragene, mutagenic and carcinogenic effects. Today, antioxidants from natural

sources are causing renewed interest because of their therapeutic values via the chelation of metals and the scavenger effect, the inhibition of enzymes generating free radicals[6]. The search for natural substances as sources for the production of new anti-inflammatory and antioxidant potion has emerged as an alternative to chemical synthesis molecules. There is assuredly that Africa is fortunate with extensive greenery whose medicinal effects are to be rappe[7].

B. dalzielii belongs to *Burseraceae* family is grows up to 13 meters in height. It is native to the Northern Ivory Coast, Northern Nigeria, Cameroun and Central African Republic and is also plenty in the tropical zones of Africa and Asia. This vegetal is very utilized in traditional medicine: the stem bark extract is employed in North-Central zone of Nigeria to treat brainsickness, to show antiulcer activity and reduced gastrointestinal motility[8]. The fresh bark was caused vomiting and cured of vertiginousness and pulses[9]. The stem bark of *B. dalzielii* was used in the Far North region (Cameroon) folk medicine to manage pyrexia, rheumatism, asthma and arthritis. Moreover, this plant is used as an anti-seizure medication. The pharmacological study was approved that the plant methanol extract has been antioxidant, anti-inflammatory and antipyretics properties using classical experimental models. A phytochemical screening was too appraised.

MATERIALS AND METHODS

Planting material and identification

The *B. dalzielii* root barks belong to Burseraceae family was selected for the study. The herbarium of vegetable material was collected in December, 2021 at Mandaka Village, Far North Region, Cameroon. The fresh material plant was collected from original source after kindly identification and authentication from plant taxonomist, Professor MAPONGMETSEM Pierre-Marie. The voucher specimen was kept in the Cameroon National Herbarium, Yaoundé, Cameroon, (Voucher number 20532/SRF-CAM) was assigned. The collected root barks were cut into small pieces, cleaned up and dry in the shade with regular turning to avoid decaying, until crispy.

Experimental animals

The white animals of both sexes (25-30 grams) wereplaced in the clean polypropylene cages of classic size. The experimental albinos were acclimatized at ambient weather (natural, 22±2ºC temperature, 35–60 % humidity), fed with eat selectively, had free access to drinking fresh water *ad libitum*, and purchased from LANAVET (National Veterinary Laboratory), Garoua, Cameroon. Male and female albinos' mice 2 to 2.5 months old are healthy and not pregnant (female). The mice were acclimated for 2 weeks prior they were subjected to the investigation. This living being deprived of water only during the experiment and fasting for six hours before to commencement of the experiments.

Preparation of the roots bark of *B. dalzielii* methanolic extract (BDME)

For preparing extract, the fresh roots of *B. dalzelii* subjected for air dried, were chopped into small pieces and was finely powdered with pestle and mortar and was mixed with absolute methanol. In brief, 20 g of plant powder were extracted with 200 mL at room temperature under agitation. After the extraction, the mixture filtered with Whatman No. 1 filter paper (Maidstone, UK) and was condense by evaporation at 45°C in a Rotavap (UV-2100 Spectrophotometer) to get solid residue. This viscous mass was then stored in a specimen bottle at room temperature for use throughout the study.

Acute oral toxicity study

The toxic effect was studied in healthy female living being (30-35 g) following the OECD guidelines No 423[10]. The mice were abstained from food for 12 h foregoing to the experiments. These mice were (n=6) were divided into 2 groups of 3 animals each. Mice were administered with single dose of BDME, 3 g/kg, orally; while the negative grouping was obtained normal saline (10 mL/kg) andthe food may be withheld for a further 2–3 hours. The mice were seen perpetually for first seventy-two hours and fifteen consecutive hours of sunlight for their extensive physiological manifestations: signs of toxicity, other parameters (weight gain, food and water consumption) and mortality after which the LD_{50} was calculated.

Qualitative phytochemical determination

Qualitative phytochemical determination of the plant material was tested employing the next chemical compounds and interactant. It was verified the presence or absence of saponin (frothing test), tannins ($FeCl_3$), cardiac glycosides (Salkowski test), flavonoid (NaCl and HCl), phenol ($FeCl_3$ and $K_3Fe(CN)_6$), terpenes/sterols (H_2SO_4), coumarins and alkaloids (Dragendorff). These different groups of chemical compounds have been selected for their importance in the therapy of inflammatory pathologies.

DPPH radical scavenging properties

The antioxidant properties of the BDME and the vitamin C was estimed on the base of the DPPH (1,1-diphenyl-2-picryl-hydrazyl) as previously described with minor modifications. [11]In this method, the different extract solution (100, 200, 400, 600, 800 et 1000 µg/ml) of vegetable methanol extract and vitamin C were added to 2 mL of 10 mg/L. The solution was shuddered and was incubed for 30 min to perform complete reaction. Vitamin C was utilized as reference drug. Finally, the absorbance (Abs) of plant material extract was measured at 517 nm by U.V. spectrophotometer. DPPH radical scavenging activity was calculated as the reduction percentage and was determined by the formula:

$$\% \text{ DPPH} = \frac{\text{Adpph} - \text{As}}{\text{Adpph}} x100$$

Where A_{dpph}= Absorbance of the DPPH solution and A_s = Absorbance of the plant extract.

Ferric reducing antioxidant power (FRAP) activity

The protocol used in the laboratory is founded on the methodology described previously[12]. In brief, 200 µl of BDME at 100, 200, 400, 600, 800 and 1000 µg/ml was

added in 0.5 ml of a 0.2 M phosphate buffer solution (pH 6.6) and 0.5 ml of a 1 % solution potassium ferricyanide $K_3Fe(CN)_6$. The mixture was cover in a bain-marie at 50°C for twenty minutes, and then 0.5 ml of 10% trichloroacetic acid was put in to the reaction medium. The solutions were eccentric at 3000 rpm for 10 min. The fractional share (0.5 ml) of floating was mixed with 1 ml of a liquid of $FeCl_3$ (0.1% ferric chloride) newly formed in distilled water. The optical density of the solution was measured at 700 nm against a white prepared under the same conditions but by substitute the extract with methanol which makes it possible to measure the device.

Carrageenan induced mice paw edema

The hoof of mice was conducted based on a previously described[13].Thirty adult mice of both sexes (25-30 g) were arbitrarily divided into the following 5 groupings of six mice each. Group 1, the negative grouping, was obtained normal saline (10 mL/kg); group 2 was obtained diclofenac sodium (10 mg/kg) and Groups 3, 4 and 5 were given the BDME of 100, 200 and 400 mg/kg, respectively. After 60 min, the edema was caused by injecting 0.1 ml of sterile saline stay of 1% carrageenan generate the beneath the sole of the foot of right hind paw of each mouse and the left hind paw served as control. The hind paw diameter was measured immediately the nat 60, 120, 180, 240 and 300min after carrageenan administration trough vernier caliper. The virtue of the drug was approved on its capability to inhibit paw volume. The percentage of reduction (% inhibition) was designed like this:

$$\% \text{ inhibition } = \frac{(St - So) \text{ control} - (St - So) \text{ treated}}{(St - So) \text{ control}} X100$$

Where: St= the mean paw diameter for every group next the carrageenan introducing and So= the mean paw diameter for various group prior to the carrageenan inoculation.

Xylene induced ear edema

Mice lughole swelling was generated by xylene solvent as previously described[15]. Thirty adults' mice of any sex were arbitrary allocated into 5 lots of six albinos each. At the end of the abstain from food moment, animals were received the BDME or standard medicament. Group 1 received physiological solutionat the dose of 10 mL/kg and served as negative group. Group 2 received diclofenac solution (10 mg/kg) and served as reference group. The grouping 3, 4 and 5 were pretreated with 100, 200, and 400 mg/kg of the BDME, respectively. At one hour following orally, edema was instantly persuaded on either surfaces of the right hearing of any mouse by employment of 0.05 mL of xylene utilizing a runner pipette. The left ear is preserved natural. Thirty minutes after xylene treatment by performing cervical dislocation, the mice were loss of consciousness under ether anesthesia then; 6 mm of both treated and natural ears were pierced and circular sections were taken utilizing a laboratory cork borer and massed. The difference in mass of either ears was used to analysis the formation of edema. The percentage of inhibition was determinate following the formula below:

$$\% \text{ inhibition } = \frac{(\text{Mass of swelling (control)} - \text{Mass of swelling (treated)})}{\text{Mass of swelling(control)}} x100$$

Serotonin-produced edema test

The paw swelling caused by the serotonin solution (0.05 ml) into the right hoof of albinos' mice was accorded on that described previously with slight modifications[14]. A total of thirty experimental animals were equally grouped into five (1-5) of 6 per group. Mice were impoverished of water only during the experiment to guarantee uniform hydration and to reduce variableness in edematous reaction. The mice were handled as follows: Group 1, the negative control, took physiological solution (10 mg/kg); Group 2, the reference group, administrated diclofenac sodium solution (10 mg/kg) and the remaining groups received the BDME of 100, 200 and 400 mg/kg, orally. The standard drug and plant material extract were carrying out 1 h prior to induce inflammation. The right hoof perimeter was determined through a Vernier caliper at 0, 60, 120, 240 and 360 min following the oral administrations of the conventional medicament and the plant extract. Edema was aimed as the variation in paw largeness between the negative group and the group tests.

Yeast-induced pyrexia in mice

The fever induced pyrexa tests in miceas previously described with minors' modifications[16]. Briefly, hyperthermia was inducted in albino's animals by intraperitoneal vaccination of 20 mL/kg of 20% aqueous stay of sterilized pyrexia stimulus compound. A well lubricated clinical thermometer (Panamedic, Cheonan Choongnam, Korea) was inserted about 2cm into the rectum of the animals. Eighteen hours' post-injection, animals showing an augment of rectal pyrexia of at smallest 0.5°C were chose for the study. The anal porehyperthermia was determinated on 30, 60, 120 and 240 minutes' time intervals through the thermal-probe. The experimental animals were completely randomized into 5 groupings containing 6 mice in anylot and were qualified to continue private in a bridle stockade. Physiological solution was administered to negative grouping (group 1); the second lot of animals received pharmaceutical drug, paracetamol (150 mg/kg), orally. While experimental group received doses of 100, 200 and 400 mg/kg of the BDME (groups 3, 4 and 5 respectively). The percentage decrease in fever (PD) was analyzedthrough the formula below:

$$PD\ (\%) = \frac{B-Cn}{B-A} x100$$

Where B is the weather later inducing fever; Cn is the weather later 60, 120, 180, 300 min and A is the usual basic weather.

Ethics approval

The experimental protocol was accepted by the Animal Ethical Committee, Cameroon (number 075/16/L/RA/ DREPIA) and in agreement with NIH-Care and Use of Laboratory Animals (8th Edition).

Statistical analysis

Results of this study were used three replicates values of antioxidant potentials of specimen for statistical inquiries. The data were evaluated with ANOVA (SPSS, version 20.0) and the Dunnett's post-hoc test to estimate variations between vehicle groups and treated

groups. p=0.05 or less were observed statistically significant.

RESULTS

Acute toxicity study

In this investigation during seventy-four hours of observation, test animals were found normal. Following the fifteen days, the mice were no significant change in characters such as decreased sensitivity to disconfort, noisy breathing, runs, muscular contractions, expectoration, fraily, movement, hypnosis, fight, discharge from eyes and ears, offence, refuse to take food or water, slim, fatigue, paralysis.

Phytochemical screening

The phytochemical profile from the BDME was detected the presence of cardiac glycosides, flavonoid, simple phenols, flavonoids, tannins, coumarins and alkaloids. The saponin and terpenes/sterols were not found.

Presence of Radical scavenging activity by DPPH

The capability of the methanol extract of *B. dalzielii* to reduce DPPH radicals was presented an decrease in the percentage inhibition with increasing concentrations (Figure 1). The DPPH unpaired electrons scavenging effects results of BDME and ascorbic acid (standard antioxidant) were presented in Figure 1. The maximum scavenging capacity of methanolic extract was 51.12 % at 0 mg/ml concentration as compared to conventional drug, vitamin C (60.12%) at the same concentration.

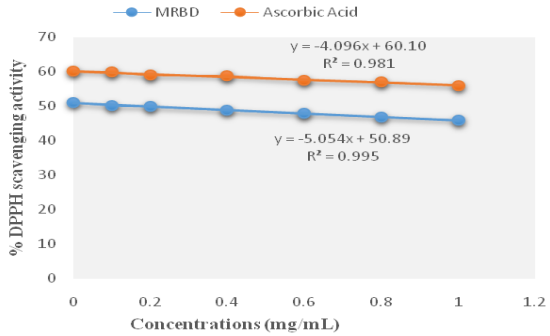

Figure 1: DPPH free radical scavenging assay (% inhibition).

The IC_{50} being inversely linked to the antioxidant capacity of the plant extract, it expressed the quantity of antioxidants needed to decline the concentration of the free radical to fifty per cent. The IC_{50} was determined from the logarithmic regression equations of plotted curves illustrated in Figures 1. The BDME was presented an average IC_{50} of the order of 0.17 mg/mL compared to an IC_{50}=2.47 mg/mL of that of vitamin C.

Ferric-reducing antioxidant power (FRAP) assay

The decreasing power effect results of BDME and ascorbic acid are shown in Figure 2. According to the results obtained, the methanolic extract has an important reducing power; their IC_{50} is 0.03 mg/ml, a value slightly lower than that of ascorbic acid whose IC_{50} value is around 0.14 mg/ml.

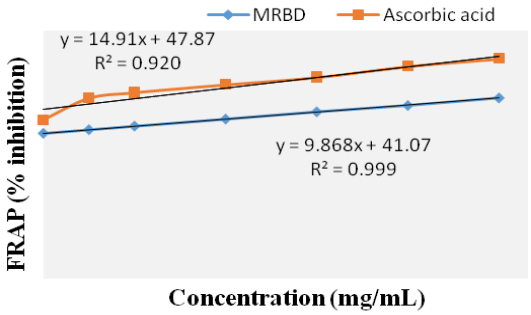

Figure 2: Ferric reducing power assay (% inhibition).

Carrageenan produced mice hoof edema

The results of the carrageenan-induced paw swelling and percentages of inhibition in mice were presented in Table 1. The results were showed that in the first hour, the extract strongly inhibited edema (p<0.001) at all the doses (100, 200 and 400 mg/kg comparable to negative groups. The great reduction 72.22% was watched with 400 mg/kg of methanol extract at 5 h, while the 200 mg/kg presented 59.52% at four hours next the treatment. Diclofenac sodium (10 mg/kg) was showed 55.56%, the maximum inhibition, at 5 h of oral administration. Data are reported as mean ± SEM, n = 5. Each value in parentheses designate the proportion of reduction. ** Highly significant (p<0.01), *** Very highly significant (p<0.001) compared with the normal saline at the same time.

Table 1: Effect of the *B. dalzielii* methanolic extract on carrageenan-induced paw edema in mice.

Groups	Doses (mg/kg)	Paw circumference (S_t - S_0) 1 h	2 h	3 h	4 h	5 h
NaCl 0.9%	0	0.41±0.00	0.39±0.00	0.4±0.00	0.42±0.00	0.36±0.00
Diclofenac	10	0.32±0.00 (21.95)**	0.26±0.00 (33.33) ***	0.30±0.00 (25.00) **	0.21±0.00 (50.00) ***	0.16±0.00 (55.56) ***
BDME	100	0.25±0.01 (39.02) ***	0.28±0.00 (28.21) ***	0.2±0.00 (50.00) ***	0.14±0.00 (66.67) ***	0.11±0.00 (69.44) ***
BDME	200	0.17±0.00 (58.54) ***	0.19±0.00 (51.28) ***	0.24±0.00 (40.00) ***	0.17±0.00 (59.52) ***	0.21±0.00 (41.67) ***
BDME	400	0.14±0.00 (65.85) ***	0.22±0.00 (43.59) ***	0.21±0.00 (47.50) ***	0.29±0.00 (30.95) **	0.1±0.00 (72.22) ***

Data are reported as mean ± SEM, n = 5. Each value in parentheses designates the proportion of reduction.
** Highly significant (p< 0.01), *** Very highly significant (p<0.001) compared with the normal saline at the same time.

Table 2: Effect of the *B. dalzielii* methanolic extract on xylene-induced mice ear edema.

Groups	Doses (mg/kg)	Edema (mg)	Inhibition (%)
NaCl 0.9%	-	2.45±0.03	-
Diclofenac	10	1.04±0.01***	56.73
BDME	100	1.33±0,02***	45.71
BDME	200	1.44±0.03***	41.22
BDME	400	1.07±0.46***	56.33

Data are reported as mean ± S.E.M. n=6. ** Highly significant (p<0.01), *** Very highly significant (p<0.001) compared with the normal saline at the same time.

Table 3: Effect of the *B. dalzielii* methanolic extract on serotonin-induced mice paw edema.

		Paw circumference (S_t - S_0)				
Groups	Doses (mg/kg)	1h	2h	3h	4h	5h
NaCl (0.9%)	0	0.41±0.00	0.39±0.00	0.4±0.00	0.42±0.00	0.36±0.00
Diclofenac	10	0.32±0.00 (21.95)**	0.26±0.00 (33.33)***	0.30±0.00 (25.00) **	0.21±0.00 (50.00)***	0.16±0.00 (55.56)***
BDME	100	0.25±0.01 (39.02)***	0.28±0.00 (28.21)***	0.2±0.00 (50.00) ***	0.14±0.00 (66.67)***	0.11±0.00 (69.44)***
	200	0.17±0.00 (58.54)***	0.19±0.00 (51.28)***	0.24±0.00 (40.00)***	0.17±0.00 (59.52)***	0.21±0.00 (41.67)***
	400	0.14±0.00 (65.85)***	0.22±0.00 (43.59)***	0.21±0.00 (47.50)***	0.29±0.00 (30.95) **	0.1±0.00 (72.22) ***

Data are reported as mean ± S.E.M. (n = 6). ** Highly significant (p< 0.01), *** Very highly significant (p<0.001) compared with the normal saline at the same time**.** Each data in parentheses denote the proportion of inhibition.

Xylene induced animal's ear edema

The results of the mice ear swelling induced by xylene were presented in Table 2. Compared to the normal saline, methanol extract of *B. dalzielii* at 100 and 200 mg/kg presented a highly significant of the ear inflammation. The doses tested of methanol extract (100 and 200 mg/kg) was presented highly significant (p<0.001) inhibition ear edema by 45.71% and 41.22% respectively. The vegetable extract at a dose of 400 mg /kg produced 56.33% sixty minutes following the induction of inflammation and used a highly significant anti-edematous property (p<0.001) in comparison with the vehicle grouping, considered to be 100% swelling. Diclofenac at the quantity of 10 mg/kg had had a very highly significant (p<0.001) decreasing effect on the ear edema in mice induced by application of 0.05 mL of xylene (56.73%).

Mice paw inflammation induced by serotonin

The BDME and diclofenac sodium effects on mice hoof swelling induced by serotonin was showed in Table 3. In untreated mice (vehicle grouping) paw edema was grown progressively and was reached its best point 4 hours following the serotonin solution injection. Oral administration of BDME at a dose 400 mg/kg was presented very highly significant (p<0.001) percentage inhibition compared to control grouping. The maximum reduction percentages caused at the three respective test doses(100, 200 and 400 mg/kg) were 72.97 %, 62.16% and 81.08% paw edema, next 1, 4 and 4 hours respectively of serotonin injection. The diclofenac showed the maximum inhibition percentages of paw swelling (51.35%) afterward 3 h of serotonin injection (Table 4).

Table 4: Effect of the methanolic extract of *B. dalzielii*on yeast induced pyrexia.

Group	Dose (mg/kg)	Rectal temperature (°C) after yeast injection After administration of drug					
		Basis	Next 18 h	60 min	120 min	180 min	300 min
Control		36.95±0.29	39.68±1.11	39.3±0.81 (2.46)	39.00±1.0 (17.78)	38.72±0.7 (34.73)	38.82±0.62 (17.69)
Paracetamol	150	36.91±0.25	38.4±0.49	37.68±0.93 (37.00)***	36.83±0.57 (73.23)***	37.00±0.56 (51.67)**	37.6±0.56 (57.37)***
BDME	100	37.18±0.18	40.22±1.14	38.18±0.39 (62.05)***	37.92±0.82 (69.32)***	36.98±0.41 (90.35)***	37.06±0.38 (94.72)***
	200	37.00±0.17	39.55±0.5	38.98±0.54 (17.49)	37.98±0.17 (56.1)***	36.76±0.11 (90.91)***	37.18±0.24 (85,07)***
	400	37.26±0.12	39.55±0.78	38.78±0.95 (29.15)***	37.88±0.53 (67.20)***	37.16±0.60* (83.43)***	37.25±0.19 (61.26)***

Each value is the mean ± S.E.M. Five groups of 6 animals each. The values in parentheses designate the proportion of reduction. A data less than 0.05 or 0.001 was analyzed statistically significant.

Antipyretic effect on yeast induced pyrexia

The results of yeast induced pyrexia test was shown in Table 4. All the mice in different groups were received DBME (100, 200 and 400 mg/kg, respectively) and diclofenac sodium solution (10 mg/kg). The results were showed highly significant percentage inhibition of fevers (***p<0.001). The highest antipyretic effect was remarked at 400 mg/kg (81.08%) at 5 hrs, an activity higher than that of the pharmaceutical medicament. The antipyretic properties of the

conventional medicament, paracetamol, were 51.35% at 5 hrs.

DISCUSSION

Qualitative chemical contents screening of BDME (Table 1) was revealed its richness of cardiac glycosides, flavonoid, simple phenols, tannins and coumarins. These chemical components were generally known for their effects against oxidative stress that had been implicated in inflammation pathologies and the mechanism of action of a methanol extract used in this work[17].

For the toxic effect study, the results indicated that albinos' mice do not presented signs of acute toxicity at the tested dose (3000 mg/kg) of BDME. During the fifteen days, the acute toxicity assessment observation period, there were presented no signs of toxicity. Accordingly, the finding indicates that this methanol extract was been presented non-toxic and was considered safe for mice testing. The LD_{50} was considered superior at 3000 mg/kg body weight.

The Vitamin C used as the standard antioxidant compound. DPPH radical scavenging capacity has been extensively utilized for studying antioxidant activities of different natural drugs. It is when the value of IC_{50} is very low that the antioxidant effect of the extract is strong, so the methanolic extract has a very powerful capacity to trap DPPH ROS. The DPPH (proton sensor) is an easy, acceptable and great extent used method to study antioxidant effects of pure molecules as well as plant extract[18]. It is fast, sufficiently and duplicable method. Noting that the powerful vertue of these substances in stopping or neutralizing unpaired electrons is basically due to their phenolic contents with the presence of hydroxyl groups acting as an electron donor, which makes them important antioxidant agents[19]. There is a power full relationship between phenolic compounds and antioxidant effects[20]. Reducing power ability of a substance is the indicator of the potential antioxidant properties of a compound. Under not pathological conditions, natural antioxidants kept for happening oxidative stress[21]. Indeed, the antioxidant properties of a compound depend not only on its chemical structure, the nature, the concentration, and the power of this molecule but also according to the type of the generated radical which it can neutralize. These substances, thanks to their redox capacities, act as reducing agents, donors of hydrogen and singular oxygen[22]. Therefore, the inhibiting power of a substance can serve as anessential indicator of its antioxidant capability. The presence of great oxidant molecules and unpaired electrons-reducing abilities of plants justifies the importance of plants for medical purposes[23].

Paw edema induced by carrageenan was usually studied in detecting orally active anti-inflammatory compounds and to predict the vertue of anti-inflammatory drugs acting by reducing the mediators of acute and local inflammation[24,25]. This work is an acute study using carrageenan as a phlogistic agent. The mice paw swelling induced by carrageenan is triphasic: the first phase (0-1 h) directly to release of 5-Hydroxytryptamine, histamine, bradykinin from mast cells, after which grown vascular permeability is maintained by the release of (2-4 h) maintained by kinins (second phase), third phase (4-5 h) produced by prostaglandins, protease and lysosomes[26]. These mediators augmented quantity of prostanoids generally such as prostaglandin E_2 (PGE_2) and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) also lipoxygenase secretein the region and reduce arteriolar resistance[27]. As a result, the evacuate break out from the bloodstream to the interstitial space. This exudate is responsible of localized swelling, which, in turn, contracts the nerve endings and thus determines a feeling of sorrow, the greatest dreadful sign of inflammation[28]. Thus, this suggests that the inhibitory action of BDME could have an antagonistic action on histamine, bradykinin, serotonin and the biosynthesis of prostaglandins[29,30].

The test of mice ear edema induced by xylene was associated to neurogenous edema released of inflammatory molecules such as histamine, kinins, prostaglandin, and bradykinins[31,32]. These mediators induce ear edema the formation of edema leading to an increase in vascular permeability and plasma leakage. Edema, characteristic of acute inflammation, gradually increases in volume and its thickness reaches its maximum half hour next employment of xylene. The results (Table 2) can be claimed that the BDME was presented pathological alterations occurred through reducing free radicals and attenuation of cytokines as well as causing edematous conditions. The phytoconstituents observed in this methanol extract is known to possess these properties[23].

Sserotonin is the first inflammation mediator, a powerful vasodilator which increases vascular permeability[33]. Since the methanol extract effectively suppressed the oedema caused by serotonin, it is evident that methanolic extract has an acute effect on inflammation. The same is true for pharmaceutical medicament (non-steroidal anti-inflammatory drugs, corticosteroids and glucocorticoids) that have been widely employed to effectively inhibit inflammation[34]. This indicates an activity of the BDME which is equivalent to that of aspirin (NSAID) which is a pure molecule. Pyrexia manifests itself clinically by an increase in body temperature above normal limits. Pyrexia is the rise of body temperature above normal range cause of PGE_2 synthesis in hypothalamus, which occurs owing to produce ILs, TNF-α and interferon[35]. Intradermal injection of the yeast solution provoked fever by increasing prostaglandin secretion. These chemical mediators synthetize this substrate called arachidonic acid by the action of cyclooxygenase enzyme. Their production increases in the inflamed zone and may function either in the production and reduction of swelling[36]. The hyperthermia induced by yeast solution is mentioned to as pyrexia, and its origin call for prostaglandin production. Blocking of prostaglandin synthesis is attaining by inhibiting cyclo-oxygenase (COX) enzyme activity[37].

The antipyretic effect of the methanol extract could be due to the reduction of cytokine release and prostaglandin biosynthesis. The fever induced by the injection of yeast is associate to the release of

cytokines (TNFα, IL-1β, IL-6) which, having reached the blood vessels, stimulate the biosynthesis of prostaglandins (PGE_2) around the center hypothalamic thermoregulatory[38].

CONCLUSIONS

This study constitutes a scientific basis which validates the folkloric medicine of the methanolic extract used in the northern part of Cameroon in the treatment of inflammatory pathologies. The healing power of plants comes from the effects of their secondary metabolites including cardiac glycosides, flavonoid, phenols (simple phenols, flavonoids, tannins and coumarins), and alkaloids. For the rest, it is urgent if not necessary to isolate and analysis the active compounds of the extract in order to have a better comprehension of the mechanism's action.

ACKNOWLEDGEMENTS

Authors are thankful for the University of Ebolowa, Ebolowa, and University of Ngaoundere, Ngaoundere, Cameroon to provide necessary facilities for this work.

AUTHORS' CONTRIBUTIONS

Vedekoi J: investigation, data analysis and wrote the draft paper. **Dadaya E:** editing and formal the idea**. Juliette K:** methodology, data analysis and reviewed the manuscript. **Hélène EC:** methodology, formal analysis. **Sélestin SD:** statistical work, calculations to manuscript proofing and carried out discussion. Final manuscript was checked and approved by all authors.

DATA AVAILABILITY

The data will be available to anyone upon request from the corresponding author.

CONFLICT OF INTEREST

None to declare.

REFERENCES

1. Sies H. Oxidative eustress: The physiological role of oxidants. Sci China Life Sci 2023; 66(8):1947–1948. *https://doi.org/10.1007/s11427-023-2336-1*
2. Sies H, Belousov VV, Chandel NS. Defning roles of specifc reactive oxygen species (ROS) in cell biology and physiology. Nat Rev Mol Cell Biol 2022; 23(7):499–515. *https://doi.org/10.1038/s41580-022-00456-z*
3. Singh N, Sherin GR, Mugesh F. Antioxidant and prooxidant nanozymes: From cellular redox regulation to next-generation therapeutics. Angew Chem Int Ed Engl 2023; 62(33): e202301232. *https://doi.org/10.1002/anie.20230123*
4. Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol 2007; 39(1): 44-84. *https://doi.org/10.1016/j.biocel.2006.07.001*
5. Trist BG, Hilton JB, Hare DJ. Superoxidedismutase 1 in health and disease: How a frontline antioxidant becomes neurotoxic. Angew Chem Int Ed Engl 2021; 60(17):9215–9246. *https://doi.org/10.1002/anie.202000451*
6. Jomova K, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M. Several lines of antioxidant defense against oxidative stress: antioxidant enzymes, nanomaterials with multiple enzyme- mimicking activities, and low-molecular- weight antioxidants. Archives of Toxicology. 2024; 98:1323–1367. *https://doi.org/10.1007/s00204-024-03696-4*
7. Danlami U, Daniel GJ, David BM, Galadanchi KM. Phytochemical, nutritional and antimicrobial screening of hexane, ethyl acetate and ethanolic extracts of b. dalzielii leaves and bark. American J Biosci Bioeng 2015; 3:76–9. *https://doi.org/10.33003/fjs-2023-0706-2111*
8. Uzama D, Gbubele JD, Bwai MD, Kabir MG. Phytochemical, nutritional and antimicrobial screening of hexane, ethylacetate and ethanolic extracts of *B. dalzielii* leaves and bar. Am J Biosci Bioeng 2015 ; 3 : 76-9 *https://doi.org/10.11648/j.bio20150305.19*
9. Nazif AB, Danjuma NM, Olurishe TO, Ya'u J. Anticonvulsant activity of methanol stem bark extract of *B. dalzielii* Hutch. (*Burseraceae*) in mice and chicks. African J Pharmacol Therap 2017; 6.
10. OECD Guidelines for the Testing of Chemicals. Testing no. 423 acute oral toxicity acute toxicity class method. 2010;1(4) :1-14.
11. Rakib A, Ahmed S, Islam MA, Haye A, Uddin SMN, Uddin MMN. Antipyretic and hepatoprotective potential of *Tinospora crispa* and investigation of possible lead compounds through *in silico* approaches. Food Sci Nutr 2020 ;8(1) :547-56. *https://doi.org/10.1002/fsn3.1339*
12. Oyaizu M. Studies on the product of browning reaction prepared from glucose amine. Japanese J Nutri 1986, 44: 307-315.
13. Winter C, Risley E, Nuss G. Carrageenan-induced Edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proceedings of the society for experimental biology and medicine 1962; 111: 544– 547.
14. Junping K, Liang L, Zhi-Hong H. Analgesic and anti-inflammatory activities of total extract and individual fractions of Chinese medicinal plants *Polyrhachis lamellidens*. Biol Pharm Bullet 2005; 28:176-180. *https://doi.org/10.1248/bpb.28.176*
15. Trouillas P, Calliste CA, Allais DP, *et al*. Antioxidant, anti-inflammatory and antiproliferative properties of sixteen plant extracts used in the Limousin countryside as herbel tea. Food Chem 2003; 3: 399-407. *https://doi.org/10.1016/s0308-8146(02)00282-0*
16. Kang JY, Khan MN, Park NH, Cho JY, Lee MC, Fujii H, *et al*. Antipyretic, analgesic, and anti-inflammatory activities of the seaweed *Sargassum fulvellum* and *Sargassum thunbergii* in mice. J Ethnopharmacol 2008;116(1) :187-90. *https://doi.org/10.1016/j.jep.2007.10.032*
17. Ani N, ObinnaOkolo K, OgbonnaOfah R. Evaluation of antibacterial, antioxidant, and anti-infammatory properties of GC/MS characterized methanol leaf extract of *Terminalia superba* (*Combretaceae*, Engl. & Diels). Future J Pharm Sci 2023; 9:3. *https://doi.org/10.1186/s43094-022-00455-z*
18. Rice-Evans CA, Miller NJ, Bolwell PG, Bramley PM, Pridham JB. The relative antioxidant activities of plant derived polyphenolic flavoids. Free Rad Res 1995; (4): 375-383.
19. Hisamuddin N, Shaik Mossadeq WM, Sulaiman MR, *et al*. Anti-edematogenic and anti-granuloma activity of a synthetic curcuminoid analog, 5-(3,4-Dihydroxyphenyl) - 3-hydroxy-1-(2-hydroxyphenyl) penta-2,4-dien-1-one, in mouse models of inflammation. Molecules 2019; 4(14): 2614. *https://doi.org/10.3390/molecules24142614*
20. Aryal S, Baniya MK, Danekhu K, Kunwar P, Gurung R, Koirala N. Total phenolic content, flavonoid content and antioxidant potential of wild vegetables from Western Nepal. Plants (Basel) 2019; 8(4) :96. *https://doi.org/10.3390/plants8040096*
21. Cheniti W, Amraoui N, Roumili I, Abdelouhab K, Charef N, Baghiani A, Arrar L. Anti-inflammatory effects of different

parts of Algerian caper (*Capparis spinosa*) on animal models. South Asian J Exp Biol 2022; 12(5):661-70. *https://doi.org/10.38150/sajeb.12(5).p661-670*
22. Dirosa M, Giroud JP, Willoughby DA. Studies of the acute inflammatory response induced in mice in different sites by carrageenan and turpentine. J Pathol 1971; 104: 15-29.
23. Mapunda EP, Mligo C. Nutritional content and antioxidant properties of edible indigenous wild fruits from miombo woodlands in Tanzania. Int J Biol Chem Sci 2019; 13(2):849- 60. *https://doi.org/10.4314/ijbcs.v13i2.22*
24. Ni L, Wang L and Fu X. *In vitro* and *in vivo* anti-inflammatory activities of a fucose-rich fucoidan isolated from *Saccharin ajaponica*. Int J Biol Macromol 2020; 156(156):717-729. *https://doi.org/10.1016/j.ijbiomac.2020.04.012*
25. Yimer T, Birru EM, Adugna M, Geta M, Emiru YK. Evaluation of analgesic and anti-inflammatory activities of 80% methanol root extract of *Echino pskebericho* M. (*Asteraceae*). J Inflammation Res 2020; 13: 647–658. *https://doi.org/10.2147/JIR.S267154*
26. Bouassid KZ, Makni S, Tounsi A, Jlaiel L, Trigui M, Tounsi S. Effects of *Juniperus phoenicea* hydroalcoholic extract on inflammatory mediators and oxidative stress markers in carrageenan-induced paw oedema in mice. Bio Med Res Int 2018; 3785487. *https://doi.org/10.1155/2018/3785487*
27. Sesaazi CD, Peter EL, Mtewa AG. The anti-nociceptive effects of ethanol extract of aerial parts of *Schkuhria pinnata* in mice. J Ethnopharmacol 2021; 271:113913. *https://doi.org/10.1016/j.jep.2021.113913*
28. Ravelo-Calzado Y, Molina-Cuevas V, Jiménez-Despaine S, *et al*. Effects of D-002 on xylene-induced edema in ear of mice Revista CENIC. Biol Sci 2011; 42(1): 13-16.
29. Zanini JC, Medeiros YS, Cruz AB, Yunes RR, Calixto JB. Action of compounds from *Mandevilla velutinaon* croton oil-induced ear edema in mice. A comparative study with steroidal and nonsteroidal anti-inflammatory drugs. Phytother Res 1992; 6(1): 1–5.
30. Myers MJ, Deaver CM, Lewandowski AJ. Molecular mechanism of action responsible for carrageenan-induced inflammatory response. Mol Immunol 2019; 109: 38–42. *https://doi.org/10.1016/j.molimm.2019.02.020*
31. Kudumela RG, McGaw LJ, Masoko P. Antibacterial interactions, anti-inflammatory and cytotoxic effects of four medicinal plant species. BMC Complement Altern Med 2018; 18(199): 199-211. *https://doi.org/10.1186/s12906-018-2264-z*
32. Singsai K, Charoongchit P, Chaikaew W, Boonma N, Fhanjaksai P, Chaisatan K. Antilipoxygenase and anti-infammatory activities of *Streblus asper* leaf extract on xylene-induced ear edema in mice. Adv Pharmacol Pharm Sci 2020; (3176391):1–5. *https://doi.org/10.1155/2020/3176391*
33. Wu X, Xie J, Qiu L, *et al*. The anti-inflammatory and analgesic activities of the ethylacetate extract of *Viburnum taitoense* Hayata. J Ethnopharmacol 2021; 269: 113742. *https://doi.org/10.3109/13880209.2010.520322*
34. Li LS, Chiroma SM, Has him T, Adam SK, Mohd Moklas MA, Yusuf Z, Rahman SA. Antioxidant and anti-inflammatory properties of *Erythroxylum cuneatum* alkaloid leaf extract. Heliyon 2020; 6(6): e04141. *https://doi.org/10.1016/j.heliyon.2020.e04141*
35. Ashour ML, Youssef FS, Gad HA, *et al*. Evidence for the anti-inflammatory activity of *Bupleurum marginatum* (*Apiaceae*) extracts using *in vitro* and *in vivo* experiments supported by virtual screening. J Pharm Pharmacol 2018; 70(7):952-963. *https://doi.org/10.1111/jphp.12904*
36. Ames NJ, Powers JH, Ranucci A, Gartrell K, Yang L, Van Raden M, *et al*. A systematic approach for studying the signs and symptoms of fever in adult patients: The fever assessment tool (FAST). Health Qual Life Outcomes 2017; 15(1):1-11. *https://doi.org/10.1186/s12955-017-0644-6*
37. Zammel N, Saeed M, Bouali N, *et al*. Antioxidant and anti-inflammatory effects of *Zingiber officinale* roscoe and *Allium subhirsutum*: *in silico*, biochemical and histological study. Foods 2021; 10(6):1383. *https://doi.org/10.3390/foods10061383*
38. Gonçalves C, Fernandes D, Silva I, Mateus V. Potential anti-inflammatory effect of *Rosmarinus ofcinalis* in preclinical *in vivo* models of inflammation. Molecules 2022; 27(3):609. *https://doi.org/10.1002/ptr.6648*