

## Anti-inflammatory and analgesic activities of *Jateorhizamacrantha* (Menispermaceae)

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### Abstract

*Jateorhizamacrantha* (Hook.f.)Exell and Mendonça (Menispermaceae) is a common medicinal plant found in tropical Africa. *Jateorhizamacrantha* is used as an anti-hemorrhagic, to combat syphilis and headache. This study was performed to evaluate the analgesic and anti-inflammatory activities of its extract.

The analgesic activity of the methanolic extract of *Jateorhizamacrantha* was investigated using the acetic acid (chemical) and tail-clip (mechanical) models of nociception in mice and the anti-inflammatory activity was investigated using the carrageenan-induced paw oedema in rats. In acetic acid-induced writhing test, the extract at doses 100, 200 and 400 mg/kg significantly ( $P < 0.05, 0.01$ ) reduced the writhing reflex in a dose dependent manner. In the application of the metal artery clip unto the tail of animals, the extract caused a significant ( $P < 0.05$ ) dose dependent increase in reaction latency with peak effect (7.0%) inhibition produced at the highest dose of 400 mg/kg. In the carrageenan induced paw oedema test, the extract produced a dose dependent significant ( $P < 0.05, 0.01, 0.001$ ) inhibition of oedema.

The results obtained in this study lend credence to the ethnomedicinal use of the plant in the management of pain and inflammatory conditions.

**Keywords:** *Jateorhizamacrantha*, methanolic extract, analgesic and, anti-inflammatory activities.

### Introduction

*Jateorhizamacrantha* is a climbing woody herb that widely grows in the South-western parts of Nigeria and Cameroon [1]. It is commonly known as “calumba” and locally as “atutu” in Yoruba, Nigeria (Odugbemi, 2008). The leaves have been used in traditional medicine for the management of abscesses, boils, antidote to snake bites, ulcers, cuts, tonic and aphrodisiac[2, 3]. *J. macrantha* has also been reported to be used in the management of dysmenorrhoea [4] and hypertension [5].

### Materials and methods

#### Plant Collection and Identification

The fresh leaves of *Jateorhizamacrantha* (Menispermaceae) were collected from Abataolu village in Osun State, Nigeria. It was authenticated at the Department of Botany, Faculty of Science, University of Lagos, Akoka, Nigeria by Mr T.K. Odewo. The herbarium specimen number is LUH 2749.

#### Preparation of Extract

The fresh leaves of *J. macrantha* were air dried at room temperature; the leaves were reduced to smaller pieces after which they were powdered using a blender. A portion (750g) of the

powdered leaves was macerated using 5 litres of 70% methanol for 48 hours. Then the extract was filtered through muslin cloth and the filtrate was evaporated to dryness using the rotary evaporator. The yield of the extract was 8.28% of the powdered leaf sample. The extract was then stored in the refrigerator for further use.

#### Experimental Animals

Male albino rats weighing 100 – 200g were used for anti-inflammatory activity studies, while male and female albino mice weighing between 20 – 40g were used for analgesic activity studies. The animals were maintained under standard environmental conditions of room temperature and fed with standard pelleted feed formulated by Raaf Animal farm Ltd. Water was also given *ad libitum*. All animals were acclimatized to the laboratory environment for one week before the experiment.

#### Anti-inflammatory model

#### Carrageenan Induced Rat-Paw Oedema

Adult albino rats (100-200 g) fasted overnight were divided into five groups of five animals each and were treated as follows: Group 1 (10 ml/kg saline), Group 2 (100 mg/kg extract), Group 3 (200 mg/kg extract), Group 4 (400 mg/kg extract), and Group 5 (10 mg/kg indomethacin). All treatments were given through oral route.



One hour post-treatment, oedema was induced by injection of carrageenan (0.1 ml, 1% w/v in saline) into the subplantar tissue of the right hind paw [6, 7]. The linear circumference was measured using cotton thread method. Measurements were made immediately before injection of carrageenan and at 30 minutes interval for 3 hours. The mean increase in paw swelling was measured and the percentage inhibition was calculated [7, 8]

### Anti-nociceptive assay (Analgesic)

#### Mouse Writhing Test

Albino mice (20-30g) fasted overnight were divided into five groups of five animals each. The animals were treated as follows: Group 1 (10 ml/kg saline), Group 2 (100 mg/kg extract), Group 3 (200 mg/kg extract), Group 4 (400 mg/kg extract), and Group 5 (100 mg/kg ASA). All treatments were given through oral route. Sixty minutes after treatment, the mice were administered acetic acid (0.6% v/v in saline, 10 ml/kg, *i.p.*). The number of writhes (characterized by contraction of the abdominal musculature and extension of the hind limbs) was then counted for 30 min [9, 10].

$$\% \text{ Inhibition} = \frac{\text{Number of writhes (control)} - \text{Number of writhes (Treatment)}}{\text{Number of writhes (control)}} \times 100 \%$$

#### Tail Clip Test

Albino mice were initially screened by applying a metal artery clip to the root of the tail to induce pain and animals which failed to attempt to dislodge it in 10 seconds were discarded. Eligible mice were divided into five groups of five mice each. Pre-treatment reaction time of all mice to the clip was determined after which treatment was done as follows: Group 1 (10 ml/kg saline), Group 2 (100 mg/kg extract *p.o.*), Group 3 (200 mg/kg extract *p.o.*), Group 4 (400 mg/kg extract *p.o.*), and Group 5 (1 mg/kg Morphine *s.c.*). The reaction time of each mouse was then determined 60 minutes post-treatment for oral administration and 30 minutes post-treatment for subcutaneous administration [11]. A post-treatment cut-off time of 30 seconds was used.

$$\% \text{ Inhibition} = \frac{(\text{Post-treatment Latency}) - (\text{Pre-Treatment Latency})}{(\text{Cut-off time} - \text{Pre-treatment Latency})} \times 100 \%$$

### Statistical Analysis

All data obtained were presented as the mean  $\pm$  standard error of the mean (SEM) calculated from Microsoft Excel Program, 2006. Statistical analyses were carried out using ANOVA.  $P < 0.05$ ,  $P < 0.01$ ,  $P < 0.001$  were considered to be statistically significant.

## Results

### Anti-inflammatory assay

#### Carrageenan Induced Rat Paw Oedema Model

Extract of *J. macrantha* produced a significant ( $P < 0.05$ ,  $P < 0.01$ ,  $P < 0.001$ ) inhibition of oedema when compared with control group given saline (Table I). The effect was dose dependent. The highest inhibition was obtained with the highest dose 400 mg/kg (61.5%, 66.67%, 72.73%, 50%, 44.44%, and 40%) respectively for 30, 60, 90, 120, 150, and 180 minutes of observation compared to (37.5%, 37.5%, 50%, 100%, 60% and 30%) inhibition produced by indomethacin 10mg/kg at the above stated hours of observation. For doses of 100, 200, and 400 mg/kg of *J. macrantha* extract, the highest effect was observed at 90 minutes which suggest a faster onset of action compare to indomethacin, which peaked at 120 minutes.

### Anti-nociceptive assay (Analgesic)

#### Acetic Acid Induced Writhes

*J. macrantha* extract produced a significant dose-dependent ( $P < 0.05$ ,  $P < 0.01$ ) reduction in the number of writhes with peak effect (75.65%) inhibition produced at the highest dose of 400 mg/kg. This effect was comparable and not significantly different ( $P < 0.05$ ) from that produced by 100 mg/kg Aspirin (91.75%) Table 2.

#### Tail Clip Test

*J. macrantha* extract caused a significant ( $P < 0.05$ ) dose dependent increase in reaction latency with peak effect (7.0%) inhibition produced at the highest dose of 400 mg/kg. This effect was less than that elicited by 1mg/kg morphine (19.6%) Table 3.



**Table 1: Effect of aqueous extract of *Jateorhizamacrantha* on carrageenan induced rat paw oedema.**

Rat paw oedema (cm) measured at various times								
Groups	Dose (mg/kg)/ % inhibition	0 min	30 mins	60 mins	90 mins	120 mins	150 mins	180mins
Control (10ml/kg) Saline		1.72±0.07	2.34±0.04	2.42±0.04	2.42±0.02	2.48±0.02	2.48±0.02	2.48±0.02
<i>J. macrantha</i>	100	1.84±0.05	2.14±0.04 <sup>*,*</sup>	2.04±0.02 <sup>***</sup>	2.02±0.05 <sup>**</sup>	2.12±0.04 <sup>*</sup>	2.14±0.02 <sup>*,a</sup>	2.16±0.02 <sup>**,a</sup>
	% inhibition		25.0	3.3	35.71	26.32	25.0	23.8
<i>J. macrantha</i>	200	1.80±0.05	2.0±0.03 <sup>***</sup>	1.96±0.05 <sup>***</sup>	1.92±0.04 <sup>*</sup>	1.90±0.03 <sup>**</sup>	2.0±0.03 <sup>***</sup>	2.0±0.03 <sup>**</sup>
	% inhibition		23.1	27.27	33.33	37.50	23.0	23.0
<i>J. macrantha</i>	400	1.90±0.05	2.0±0.05 <sup>***</sup>	1.98±0.02 <sup>***</sup>	1.96±0.02 <sup>**</sup>	2.06±0.02 <sup>*</sup>	2.10±0.03 <sup>**,a</sup>	2.14±0.02 <sup>*,a</sup>
	% inhibition		61.5	66.67	72.73	50.0	44.44	40.0
Indomethacin	10	1.80±0.08	1.90±0.08 <sup>***</sup>	1.90±0.04 <sup>***</sup>	1.86±0.06 <sup>**</sup>	1.80±0.08 <sup>**</sup>	1.84±0.07 <sup>***</sup>	1.94±0.07 <sup>**</sup>
	% inhibition		37.5	37.5	50	100	60	30

±S.E.M: Standard Error of mean. \*P < 0.05 (statistically significant compared to control) (n=5)

\*\*P < 0.01 (statistically significant compared to control)

\*\*\*P < 0.001 (statistically significant compared to control) <sup>a</sup>P < 0.01 (statistically significant compared to indomethacin)

**Table 2: Effect of *Jateorhizamacrantha* acetic acid-induced writhing in mice**

TREATMENT	DOSE (mg/kg)	TOTAL NUMBER OF WRITHES	% INHIBITION
Control Saline	(10 ml/kg)	99.0 ± 11.29	-
<i>J. macrantha</i>	100	62.0 ± 8.32 <sup>a,*</sup>	37.63
<i>J. macrantha</i>	200	48.6 ± 10.69 <sup>*</sup>	51.11
<i>J. macrantha</i>	400	24.2 ± 4.85 <sup>a,*</sup>	75.65
ASA	100	8.2 ± 2.62 <sup>*</sup>	91.75

±S.E.M: Standard Error of mean. (n=5)

\*P < 0.05 (statistically significant compare to control)

<sup>a</sup>P < 0.01 (statistically significant compare to control)

ASA: Acetyl Salicylic Acid (Aspirin)

**Table 3: Effect of *Jateorhizamacrantha* tail clip induced pain in mice**

TREATMENT	DOSE (mg/kg)	Pre-treatment reaction latency (s)	Post-treatment reaction latency (s)	% INHIBITION
Control Saline	(10ml/kg)	0.89 ± 0.13	0.88 ± 0.04	-
<i>J. macrantha</i>	100	1.57 ± 0.17	2.74 ± 0.03 <sup>*</sup>	2.0
<i>J. macrantha</i>	200	2.30 ± 0.23	6.32 ± 1.04 <sup>*</sup>	6.95
<i>J. macrantha</i>	400	1.62 ± 0.02	5.52 ± 0.84 <sup>*</sup>	7.0
Morphine	1	0.8 ± 0.11	6.53 ± 0.05 <sup>**</sup>	19.6

±S.E.M: Standard Error of mean. (n=5)

\*P < 0.05 (statistically significant compare to control)



## Discussion

The anti-inflammatory activity of *J. macrantha* extract was evaluated in this study using the carrageenan induced oedema test. Carrageenan induced inflammation consist of three distinct phases including an initial release of histamine and serotonin; a second phase mediated by kinins; and a third phase involving prostaglandin [7, 12]. In this study, *J. macrantha* extract showed significant inhibitory effect on the rat paw oedema development in the early and middle phase and reduced effect in the late phase. This suggests that *J. macrantha* extract possibly acts by inhibiting the release and/or interfering with the actions of histamine, serotonin and kinins.

The writhing test is simple, reliable and affords rapid evaluation of analgesic activity [9]. The induction of writhings by chemical substances injected *i.p.* results from the sensitization of nociceptors by prostaglandins [13] and the test is useful for evaluation of mild analgesic non-steroidal anti-inflammatory drugs [14]. The dose dependent inhibition of writhing induced by acetic acid in this study by *J. macrantha* extract suggested a peripherally mediated analgesic activity based on the association of the model with stimulation of peripheral receptors especially the local peritoneal receptors at the surface of cells lining the peritoneal cavity [15, 16].

To investigate the involvement central mechanism in the analgesic activity of *J. macrantha*, extract tail clip test was used based on the fact that centrally acting analgesic drugs elevate the pain threshold of rodent towards pressure [9]. Based on the ineffectiveness of *J. macrantha* extract in the tail clip test, *J. macrantha* is devoid of a centrally acting mechanism of action for its anti-nociceptive effect.

From the results, the methanolic extract of *J. macrantha* has been shown to possess anti-inflammatory and anti-nociceptive properties which are comparable with the standard drugs used in models employed in this study.

## Conclusion

The experimental findings suggest that the methanolic leaf extract of *J. macrantha* contains bioactive constituents with analgesic and anti-inflammatory activities. This study justifies the traditional use of the plant in the treatment of some inflammatory conditions.

## Authors' contribution

Conception and design of the study: G. O. Ajayi, Salako, O. A.  
 Performing of the experiments: G. O. Ajayi, Mosebolatan M. I., Salako, O. A.  
 Data Analysis: Salako O. A., Mosebolatan, M. I.  
 Contribution of reagents and materials: G. O. Ajayi, Mosebolatan, M. I.  
 Writing of manuscript: G. O. Ajayi, Salako, O. A.  
 All authors have approved the final manuscript:

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## Conflict of interest

The authors declare no potential conflict of interest exists.

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