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ANTINOCICEPTIVE AND ANTIINFLAMMATORY ACTIVITIES OF AERIAL PART OF NEPHROLEPIS BISERRATA (SW) SCHOTT (DAVALLIACEAE)

Shorinwa Olusayo A.[1*] and Ogeleka Nwakaego O.[1]

Department of Experimental Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Port Harcourt, Rivers State, Nigeria.

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***Correspondence for Author**
Dr. Shorinwa Olusayo A.
Department of Experimental Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Port Harcourt, Rivers State, Nigeria.

ABSTRACT

Nephrolepis biserrata (Davalliaceae) commonly known as Giant sword fern is traditionally used in the treatment of wounds. Ethanolic extract of the aerial part of this species obtained from palm trees was investigated for the antinociceptive effect by using radiant tail flick method and anti-inflammatory activity by egg-albumin induced paw edema in albino rats. The extract was administered at doses of 250mg/kg, 500mg/kg and 1000mg/kg through the oral route. Preliminary phytochemical screening revealed the presence of steroids, tannins, saponins, carbohydrate and flavonoids. The plant extract at a dose of 500mg/kg exhibited a significant ($P<0.05$) analgesic activity at 30 and 180 minutes whereas 1000mg/kg of extract showed significant ($P<0.05$) analgesic activity at 30minutes. Oral administration of 250mg/kg of the extract significantly ($P<0.05$) inhibited acute inflammation caused by egg albumin induced paw edema at 1hour, 500mg/kg of the extract showed anti-inflammatory effect at 4 hour while 1000mg/kg of the extract showed significant ($P<0.01$) inhibition at 1hr respectively. The findings of this study has shown that the plant extract seems to possess antinociceptive and anti-inflammatory activities. Thus, the aerial part of N. biserrata may be a potential source for the development of drugs with antinociceptive and anti-inflammatory activities.

KEYWORDS: Antinociceptive, Anti-inflammatory activity, Nephrolepis biserrata, Tail flick

INTRODUCTION

Plants have being a source of shelter, oxygen, food and medicine needed by man and animals. Overtime and with the beginning of societies, human learned to recognize and categorize plant materials for various uses. For instance, herbs and herbal extracts have being used for their healing powers and can be traced to earliest of myths, traditions and writings used to distinguish those plants.[1] Most individuals of the developing world still depend on traditional herbal medicine as the basic source of treatment for illnesses.[2] Currently, the world is facing high increase in the incidence of many systemic diseases and hence cost effective complementary therapies are needed. Medicinal plants have been the subject of intense research due to their possibility as sources of commercial drugs or as lead compounds in drug development.[3] Several modern drugs are used for the management of pain and inflammatory conditions but, their prolonged use may cause severe adverse side effects , the most common being gastrointestinal bleeding and peptic ulcers.[4] Consequently there is a need to develop anti-inflammatory agents with minimum side effects. N. biserrata (Davalliaceae) is commonly known as giant sword fern which is widely distributed throughout the tropical regions. It has short, erect, rhizome with long stolons and the fronds appear tufted, sub erect to arching up to 4m long. N. biserrata grows usually in lowlands (sea level up to 750 m, rarely higher, to 1500 m), in open, disturbed situations, occasionally in forest; terrestrial or less commonly epiphytic in forested, relatively wet habitats, e.g., swamps, but occasionally thickets, roadsides, or clearings.[5] In India, the rhizome of N. biserrata is used in the treatment of respiratory conditions while in Sarawak, it is used for treating blister, boils, abscesses and sores of the skin.[6] Boils and abscesses are usually caused by bacterial infections and blisters are due to fungal infections. This implies that N. biserrata has the potential of fighting pathogenic microorganisms. It is also used to treat jaundice by local people in Brunei.[7] The paste of the leaves is also applied on cuts and wounds.[8] Decoction of the fronds is also used to treat abdominal pains in Cameroon.[9] Due to its use in the management of cuts and wounds, an attempt was made in the present study to determine the antinociceptive and anti-inflammatory properties of the aerial part of N. biserrata.

MATERIALS AND METHODS

Plant materials

The fresh aerial part of N. biserrata was collected from Isuochi in Umunneochi Local Government Area of Abia State, Nigeria. The plant material was authenticated by Mr.

Esimonokhai of Botany Department of the University of Ibadan with herbarium number UIH22447. The aerial part was sliced into smaller pieces and dried under shade for about 3 weeks. The air dried plant material was mechanically reduced to powder form and was stored in an air-tight container. Successive solvent extraction by maceration for 72hours using absolute ethanol was done by using 2346g of the powdered aerial parts of the plant. The extracts were concentrated using rotary evaporator and carefully evaporated to dryness over a water bath at a temperature of 40^{o}C after which the percentage yield was calculated.

Experimental animals

Albino rats weighing 130-180g of both sexes were obtained from the animal house of the Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt. The animals were kept in groups of five in separate cages. The animals were maintained under standard conditions, had free access to diet and water and were allowed to acclimatize for 7 days before the commencement of the study. All the standard ethical requirements for experimental animals were complied with.

Phytochemical screening

Acute oral toxicity studies

Acute oral toxicity studies were done using the.[10] The animals were randomly allocated into six groups of three animals each. Animals were fasted for 12h with free access to water only. The first three groups were treated with 10, 100 and 1000mg/kg of ethanolic extract of N. biserrata through the oral route. They were observed frequently on the day of treatment for 24 hours for unwanted or adverse effects and death. After 24 hours, no animal died nor showed any adverse effect. Then, doses of 1600, 2900 and 5000mg/kg ethanolic extract of the plant material was administered to the remaining three groups of three animals each and were observed as above.

ANTINOCICEPTIVE ACTIVITY

Radiant heat tail flick test

This test was done using the methods of.[11] Albino rats weighing 130-180g were randomly divided into five groups, five animals each (n=5). Control group (Group 1) received 0.2ml of distilled water orally. The reference group (Group 2) received diclofenac (10mg/kg dissolved in distilled water, p.o) and groups 3, 4 and 5 were orally pretreated respectively with 250, 500 and 1000mg/kg ethanolic extract aerial part of N. biserrata. An IR (intensity) of 50 and cut-off time of 15seconds was fixed to prevent tissue injury during the process.[11] Radiant heat

applied to the tail was maintained at 2cm measured from the tip of the tail. The tail flick latency or reaction time was taken immediately before administration of the test and standard drug as well as distilled water and then 30, 60, 90, 120, 150 and 180 minutes after administration. The time at which each animal withdrew its tail from the radiant heat source was taken as the reaction time or tail flick latency. Ugo-basile (N 7200) tail flick analgesiometer was used to assess the tail flick latency of the rats. Analgesia produced by the test and standard drugs was expressed by the difference in tail flick latency or mean increase in latency after drug administration.[12]

ANTIINFLAMMATORY ACTIVITY

Egg albumin-induced paw edema

The anti-inflammatory activity was evaluated by fresh egg albumin induced rat paw edema model [13]. Albino rats of either sex were weighed (130-180g) and normal paw size of all the rats were measured initially and then divided into five groups each comprising of five animals (n=5). Inflammation was induced in all rats by single sub plantar injection of 0.1mL fresh egg albumin into the left hind paw of the rat. Control group (Group 1) received 0.2ml of distilled water orally. Group 2 received diclofenac (10mg/kg dissolved in distilled water) and groups 3, 4 and 5 were orally pretreated respectively with 250, 500 and 1000mg/kg ethanolic extract aerial part of N. biserrata. Thirty minutes after treatment, acute inflammation was induced in all rats by single sub plantar injection of 0.1mL fresh egg albumin into the left hind paw of the rat.[14] Paw size or volume was measured using a vernier caliper (Fowler, USA) at time 0, 1, 2, 3 and 4 hours after the fresh egg albumin administration.[15] Change in paw thickness was considered as a measure of inflammation [16]. Percentage inhibition of paw thickness was calculated using the formula:

$$\textbf{Inhibition of edema (\%)} = \left(\frac{Vc - Vt}{Vc}\right) \times 100$$

Where V_c = inflammatory increase in average paw volume of control group of animals.

$\mathbf{V_t}$ = inflammatory increase in average paw volume of treated animals.

Statistical analysis

The values were presented as mean±SEM. Statistical analysis of data was done using one-way analysis of variance (ANOVA) followed by student's t-test using Graph pad prism 6.5. The statistical analysis was done to determine the significance of difference between the

control groups and the treated groups. P-values <0.05 were considered to be statistically significant.

RESULTS

PHYTOCHEMICAL SCREENING

Preliminary phytochemical screening showed that the extract contains steroids, tannins, saponins, carbohydrate and flavonoids.

ACUTE ORAL TOXICITY

The acute oral toxicity test showed that the lethal dose (LD_{50}) of the ethanolic extract of aerial part of Nephrolepis biserrata is greater than 5000mg/kg since no death was recorded. This implies that the aerial part of plant can be said to be relatively safe since the LD_{50} is greater than 5000mg/kg [15]. However, reduced appetite and restlessness were observed in the group of albino rats that received 1600, 2900 and 5000mg/kg body weight of the test extract.

ANTINOCICEPTIVE ACTIVITY

The result of the radiant heat tail flick test showed that 250mg/kg of the ethanolic extract of N. biserrata showed no significant analgesic activity,500mg/kg of extract possessed significant (P<0.05) at 30 and 180minutes and 1000mg/kg of extract possessed significant (P<0.05) analgesic activity at 30minutes when compared to the control.

Table 1: Effect of ethanolic aerial part extract of Nephrolepis biserrata on the radiant heat tail flick test in albino rats. (Mean±SEM)

GROUPS	DOSE mg/kg	TAIL FLICK LATENCY(secs)±SEM						
		0min	30mins	60mins	90mins	120mins	150mins	180mins
Distilled Water	0.2ml	3.98±0.27	2.6±0.40	2.8±0.23	2.98±0.30	2.48±0.26	2.72±0.12	2.34±0.07
Diclofenac	10	4.38±0.91	5.64±1.03*	4.12±0.42*	3.74±0.37	3.64±0.48	2.54±0.28	3.74±0.33 **
Extract	250	3.78±0.14	3.04±0.35	3.18±0.29	2.54±0.29	2.5±0.23	2.98±0.27	2.76±0.22
Extract	500	4.04±0.47	3.8±0.27*	3.22±0.35	3.3±0.36	2.64±0.21	3.84±0.49	3.28±0.34*
Extract	1000	3.06±0.28	5.64±1.11*	2.66±0.45	3.48±0.63	2.5±0.17	2.42±0.17	2.8±0.31

Values are expressed as mean±SEM, n=6 in each group. *P<0.05, **P< 0.01 ANOVA followed by t-test compared with control.

ANTIINFLAMMATORY ACTIVITY

The result from the egg albumin-induced paw edema showed that the plant extract at 250 and 500mg/kg body weight significantly (P<0.05) inhibited acute inflammation caused by egg albumin induced paw edema at 1 and 4 hours when compared with the control respectively, while at 1000mg/kg.

Table 2: Effect of ethanolic aerial part extract of Nephrolepis biserrata on egg albumin-induced paw edema in albino rats. (Mean±SEM).

GROUPS	DOSE mg/kg	PAW EDEMA SIZE MEAN (mm) ± SEM				
		0hr	1hr	2hr	3hr	4hr
Distilled water	0.2ml	1.6±0.24	6.8±0.37	7.0±0.32	5.4±0.24	5.0±0.00
Diclofenac	10	2.2±0.20	6.0±0.00	8.2±0.37*	7.0±0.32**	5.4±0.24
Extract	250	2.0±0.00	5.8±0.20*	6.6±0.24	5.4±0.24	4.6±0.24
Extract	500	2.2±0.20	5.6±0.40	6.2±0.66	5.4±0.40	4.0±0.32*
Extract	1000	2.6±0.24	5.0±0.32**	6.0±0.55	5.0±0.32	4.8±0.37

Values are expressed as mean±SEM, n=6 in each group. *P<0.05, **P< 0.01 of ANOVA followed by t-test compared with control.

Table 3: Percentage inhibition of egg albumin-induced paw edema

GROUPS	DOSE mg/kg	PERCENTAGE INHIBITION (%)			
		1hr	2hr	3hr	4hr
Diclofenac	10	26.92	-11.1	-31.58	5.88
Extract	250	26.92	14.81	10.53	23.53
Extract	500	34.62	25.93	15.79	47.06
Extract	1000	53.85	37.04	31.58	35.29

Indicates that the absolute edema paw volume change for the control was less than that of the treated groups.

DISCUSSION

From the results obtained, it was observed that the ethanolic extract of N. biserrata at a dose of 250mg/kg did not show any significant increase in tail flick latency. It was observed that oral administration of 500mg/kg of extract produced (P<0.05) analgesic activity at 30 and 180 minutes while 1000mg/kg of extract produced analgesic activity at 30 minutes when compared with the control.

Based on the anti-inflammatory studies, the plant extract at 250mg/kg and 500mg/kg significantly (P<0.05) inhibited acute inflammation caused by egg albumin induced paw edema at 1 and 4 hours respectively whereas, at 1000mg/kg the extract showed significant (P<0.01) inhibition at 1hr. Also, 1000mg/kg of the ethanolic extract produced the highest percentage (53.85%) of paw edema inhibition which was observed at 1hr.

The presence of some phytochemical constituents as stated earlier reveals the possibility of some biological activity of the ethanolic aerial part extract of Nephrolepis biserrata. A range of pharmacological activities has been associated with flavonoid compounds present in medicinal plants. Some flavonoids have been reported to have analgesic and anti-

inflammatory activities.[17] Some of them can significantly inhibit majority of inflammatory mediators.[18] Also, terpenoids produce significant analgesic and anti-inflammatory activities.[19] Such activities have been ascribed to its ability to inhibit phospholipase A2 and thus eventually blocking the metabolism of arachidonic acid.[20] Saponins has been reported to possess anti-inflammatory and analgesic activities and its molecular mechanism might be associated with the inhibition of the elevated expression of cyclooxygenase-2 (COX-2) protein and the overproduction of the pro-inflammatory cytokines, as well as augmentation of the anti-inflammatory cytokines of paw edema.[20] The findings of this study is similar to that of[21] which stated that the ethanolic roots of Mimosa pigra possess anti-inflammatory and analgesic activities. Therefore, the antinociceptive and anti-inflammatory activities of this plant extract may be attributed to its phytochemical constituents.

CONCLUSION

The ethanolic extract of aerial part of N. biserrata possesses promising analgesic and anti-inflammatory activities. The presence of steroids, carbohydrates, saponins, flavonoids and tannins in the ethanolic extract of the plant under study may be responsible for these activities. Hence, N. biserrata may be considered as a potent source of drugs for the management of inflammatory conditions.

CONFLICT OF INTEREST

The authors hereby declare that there is no conflict of interest.

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