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Anti-inflammatory potential of ethanol leaf extract of *Sphenocentrum jollyanum* in experimental mice

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Abstract

Anti-inflammatory potential of the ethanol leaf extract of *Sphenocentrum jollyanum* (ELESJ) was assessed in-vivo in mice by using carrageenan-induced paw oedema, egg albumin-induced paw oedema, and xylene-induced ear oedema model at doses of 474.34, 948.68, and 1423.03 mg/kgbw respectively. A total of seventy-five matured mice of both sexes weighing between 20 g and 24 g (divided into three groups of 25 mice each for the 3 different studies) were used for this study. Treatment was done intraperitoneally. Distilled water (10 mL/kgbw), acetylsalicylic acid (ASA) (100 mg/kgbw) or dexamethasone (4 mg/kgbw) served as the normal and standard drugs respectively. The results showed that ELESJ produced significant ($p < 0.05$), dose-dependent and time-dependent reductions in mean paw thickness in groups III-V compared with control group. Similarly, the extract caused a dose-dependent increase in percentage inhibition of carrageenan-induced paw oedema and egg-albumin induced paw oedema (34.49%, 36.71%) at the highest dose (1423.03 mg/kg), comparable with the anti-inflammatory effects of the standard drug ASA (34.69%, 31.54%). The ELESJ also caused significant ($p < 0.05$), dose-dependent decreases in xylene-induced ear oedema weight in all the test groups relative to control group and standard drug group. In addition, ELESJ showed a dose-dependent percentage inhibitory effect (44%) at the highest dose (1423.03 mg/kg) comparable with that of the standard drug, dexamethasone (48%). The results obtained from this study support the use of the leaf in folk medicine as it has significant anti-inflammatory properties and this may be attributed to the phytochemical constituents of the leaf.

Keywords: Anti-inflammatory; Sphenocentrum jollyanum; Carrageenan; Egg albumin; Xylene-induced oedema

1. Introduction

Inflammation is the body's defense mechanism to eliminate or limit the spread of a variety of etiologic injurious agents such as immune reactions, physical, chemical, foreign bodies, and infectious agents, followed by removal of the necrosed cells and tissues [1]. It is characterized by swelling, redness, pain, increased heat, and loss of function, which result from the invasion of infectious agents or physical injury [2, 3]. [4] reported that inflammation involves a sequence of events that occurs in three distinct phases: acute or transient phase, delayed sub-acute phase and chronic proliferate phase. The acute phase inflammation is a short-term physiological response against pathogens and tissue injury. It is associated with enhanced blood flow to the injured tissue, followed by vasodilatation and increased vascular permeability with leakage of plasma from microcirculation, and migration of phagocytic leukocyte from blood to the surrounding tissue [5, 6, 7]. In contrast, chronic inflammation is a prolonged pathological condition characterized by the infiltration of mononuclear immune cells (monocytes, macrophages, lymphocytes), tissue destruction, angiogenesis, and fibrosis [8]. The body synthesizes and secretes different pro- and anti-inflammatory mediators such as cytokines, chemokines, eicosanoids, and nuclear factor kappa-beta (NF-kβ) to the site of injury for immune surveillance, optimal repair, and regenerate injured tissues as a result of inflammation caused by numerous agents [9].

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[10] had reported the use of several nonsteroidal anti-inflammatory drugs (NSAIDs) and steroidal drugs such as acetylsalicylic acid, diclofenac, ibuprofen, indomethacin, naproxen, nimesulide, celecoxib, and betamethasone, prednisolone, and dexamethasone in controlling and suppressing inflammatory diseases. However, their prolonged use has been associated with serious adverse effects such as rheumatoid arthritis, osteoarthritis, asthma, inflammatory bowel disease, colitis, and hepatitis as well as other chronic diseases, including cardiovascular and neurodegenerative diseases [11]. These diseases can cause disability, impair social function, reduced quality of life, and sometimes death of people [12].

The African continent is richly endowed with diverse medicinal plants used to treat practically all types of illness, ranging from bacterial or fungal infections to metabolic and neurological disorders. These natural plant products have also been used to develop drugs in orthodox medicine [13]. Thus, there is a need to develop natural anti-inflammatory drugs that are safe, efficacious, biocompatible, and cost-effective to treat inflammatory diseases [14].

Sphenocentrum jollyanum, a perennial plant native to the tropical forest zone of West Africa, belongs to the family *Menispermaceae*. It *is* a small, erect, sparsely branched undergrowth shrub that grows up to 1.5 m in height *with very few branches*. The leaves are wedge-shaped, about 5-12 cm wide, smooth on both sides, and can grow up to about 20 cm long with a small arrowed apex and with a bright yellow root [15,16]. Locally the plant is known in Ibibio as Ibong Isong and it's widely distributed in Sierra Leone, Nigeria, Ghana, Ivory Coast, and Cameroun [17]. The plant can also be identified as "Aduro kokoo" (red medicine), "Okramankote" (dog's penis), Oban abe, and Ouse-abe among the people of Ghana, Republic of Benin, and Côte d'Ivoire respectively [18].

Sphenocentrum jollyanum is one of the medicinal plants which are famous for a plethora of important biological functions and widely used for the treatment of various disease conditions. The root has been used for its effectiveness in stimulating the central nervous system, the management of mental and inflammatory disorders, pain, and depression [19] while the dried powdered root has been used in combination with some anti-malarial plants as a cure for fever and muscular pains [20]. [21] have also reported the anti-inflammatory, anti-angiogenic, and analgesic properties of the methanol extracts of the leaves, roots, and fruits. Therefore, there is a need to investigate the anti-inflammatory potential of ethanol extract of *Sphenocentrum jollyanum* leaves in experimental mice to ascertain the folkloric claim of its medicinal properties in the management of various ailments such as inflammatory diseases.

2. Material and methods

2.1. Sample collection, Identification, and Preparation of extract

Fresh leaves of *Sphenocentrum jollyanum* were collected from Aka in Ibiono Ibom Local Government Area of Akwa Ibom State, Nigeria, and authenticated by a taxonomist in the Department of Pharmacognosy and Natural Medicine, University of Uyo, Nigeria, with a voucher specimen NUUH: 040/15 deposited at the herbarium. The leaves were properly washed with clean water to remove any contaminants, air-dried under shade for two (2) weeks. The dried leaves were pulverized into a coarse powder using VTCL Solitaire mixer grinder (VTCL, India). Four hundred grams (400 g) of the powdered sample was macerated in 60 % ethanol (Sigma Aldrich, St Louis, USA) for 72 hours with intermittent stirring/ shaking [22] and filtered using Whatman filter paper No.1 (Whatman Ltd., England) to remove all unextractable matters, including cellular materials and other constituents that were insoluble in the extraction solvent. The filtrate obtained was concentrated in a water bath at 40 ^{o}C to obtain the crude extract and stored in the refrigerator at 4 ºC until when needed for the study. A total yield of 188.5 g of crude extract was obtained [23].

2.2. Experimental Animals and Treatments

Seventy-five (75) matured and healthy Swiss Albino mice of both sexes weighing between 20 and 24 g were used. They were housed in the animal house, Department of Pharmacognosy and Toxicology, University of Uyo, and they were fed with rodent feed (Ladokun Livestock Feeds Limited, Ibadan, Nigeria) and had access to distilled water *ad libitum.* They were allowed to acclimatize for one week before the commencement of the experiment [24]. Three sets of twenty-five (25) experimental mice (for each experiment), were divided into five groups of five animals each based on the treatments received.

- Group I mice (control) received 10 mL/kg of distilled water
- Group II (standard) received 100 mg/kg of acetylsalicylic acid (ASA) or 4mg/kg dexamethasone (DEX) for comparison
- Group III received 474.34 mg/kgbw of the extract
- Group IV received 948.68 mg/kgbw of the extract

- Group V received 1423.03 mg/kgbw of the extract

Acetylsalicylic acid (ASA) was used as the standard drug for animals used in the investigation of carrageenan and egg albumin-induced paw oedema and dexamethasone was used as the standard drug for animals used in the investigation of xylene-induced ear oedema. The animals were fasted for 24 hours before the experiment and deprived of water only during the experiment. All administrations were done intraperitoneally [25].

2.3. Drugs, Chemicals, and Instruments

The drugs and chemicals used in the present study include: carrageenan, acetylsalicylic acid and dexamethasone (Sigma Aldrich, USA), fresh egg-albumin (Merck, Germany), xylene (Nihon Shiyaku Industries, Japan), ethanol (JHD, China), and VTCL Solitaire mixer grinder (VTCL, India). Digital Vernier caliper (V. Tech digital caliper, India) and electronic weighing scale (Ohaus Scout pro-SPU 202). All other chemicals and reagents used were of analytical grade and acquired from local firms.

2.4. Evaluation of Anti-inflammatory Effect

The anti-inflammatory effect of the ethanol leaf extract of *Sphenocentrum jollyanum* was investigated using carrageenan and egg albumin-induced paw oedema as well as xylene-induced ear oedema in mice.

2.5. Carrageenan-Induced Paw Oedema

Carrageenan-induced paw oedema was done according to the procedure described by [26]. After one hour of treatment with the extract and drug (acetylsalicylic acid), oedema was induced by injecting 0.1 mL freshly prepared (1%) carrageenan aqueous suspension into the sub-plantar surface of the right hind paw of the mice under moderate anaesthesia using chloroform [27] while the control received 10 mL/kg of distilled water into the left hind paw and served as a reference non-inflamed paw for comparison. The right and left paws were cut and weighed [28]. The linear circumference of the injected paw was measured by digital Vernier caliper at intervals of 0, 0.5, 1, 2, 3, 4 and 5 hours after the injection of carrageenan [29]. The percent increase in the weight of the right paw in comparison with that of the left paw of each mouse was calculated as an indication of inflammation using the following equation [28].

$$\% \text{ Increase in paw weight} = [(R-L) / L] \times 100$$

Where R = weight of the right hind and L = weight of the left hind

The percent inhibition of oedema was expressed as mean values of control group compared with a treated group using the following formula [30]:

$$\text{Inhibition (\%)} = \frac{\text{Control paw circumference} - \text{Treated paw circumference}}{\text{Control paw circumference}} \times 100$$

2.6. Egg albumin-induced paw oedema

Egg albumin-induced oedema was done following the method described by [31]. One hour after administration of the extract and ASA, inflammation was induced by injecting 0.1 mL of fresh egg albumin into the sub-plantar of the right hind paw of the mice under moderate anaesthesia using chloroform [27]. The linear circumference of the injected paw was measured at 0, 0.5, 1, 2, 3, 4, and 5 hours of administration of the phlogistic agent using a digital Vernier caliper. Oedema formation was assessed as the difference in paw circumference between the control and 0, 0.5, I 2, 3, 4, 5 h after the administration of the phlogistic agent [29]. The percentage of inhibition was calculated according to the following formula:

$$\text{Inhibition (\%)} = \frac{\text{Control paw circumference - Treated paw circumference}}{\text{Control paw circumference}} \times 100$$

2.7. Xylene-induced ear oedema

Xylene-induced ear oedema in mice was performed as described by [32]. One hour after treatment with the extract and drug intraperitoneally, ear oedema was induced in each mouse by topical application of 2 drops of xylene on the inner surface of the right ear using a dropper pipette [33,34]. The left ear served as a control. After 15 minutes, the mice were sacrificed under mild anaesthesia using chloroform and both ears were removed and weighed [35]. The ear oedema was measured by the weight difference between the right (treated) and the left (control) ear of the same animal caused

by the irritant. The percentage inhibition of oedema in the treated groups compared to that of the control group was calculated using the formula described by [36].

$$\text{Inhibition \%} = \frac{\text{Weight of oedema (control) - Weight of oedema (test)}}{\text{Weight of oedema (control)}} \times 100$$

2.8. Statistical Analysis

All results are presented as mean ± standard error of the mean (SEM). The experimental data collected were analyzed using one-way analysis of variance (ANOVA). Post hoc analysis (comparison across groups) was carried out using least significant difference (LSD) incorporated into the IBM SPSS software version 20. The values of $p < 0.05$ were considered to be statistically significant.

3. Results

3.1. Carrageenan-induced paw oedema

The effect of the ethanol leaf extract of *Sphenocentrum jollyanum* and ASA on carrageenan-induced paw oedema in mice was sustained over 5 hours as shown in Table 1. The sub-plantar injection of carrageenan showed a significant ($p < 0.05$), time-dependent, progressive reduction in hind paw size when compared with the control group. The administration of the extract caused a dose and time-dependent significant ($p < 0.05$) reduction in the mean paw thickness in groups III - V from 5.01 ± 0.04 to 3.72 ± 0.03, 5.03 ± 0.04 to 3.38 ± 0.04, and 4.97 ± 0.03 to 3.38 ± 0.02 mg/kgbw (from the first hour to the fifth hour respectively) after treatment, compared with the control group. However, the paw circumferences of the test groups (IV- V) were found to be comparable with ASA standard drug group at the fifth hour of treatment. The highest percentage of inhibition (34.49%) of the extract obtained at doses of 948.68 and 1423.03 mg/kg was comparable with the anti-inflammatory effects of the standard drug, ASA (34.69%) at a single dose of 100 mg/kgbw at the fifth hour.

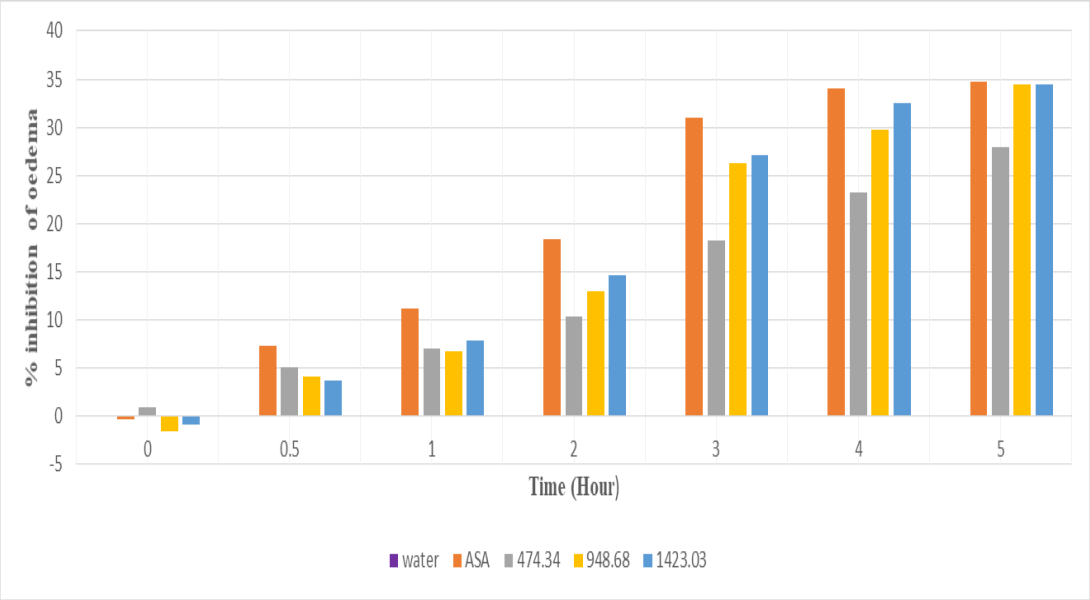

Figure 1 Percentage inhibition of ethanol leaf extract of *Sphenocentrum jollyanum* on carrageenan-induced paw oedema.

Table 1 Effect of ethanol leaf extract of *Sphenocentrum jollyanum* on carrageenan-induced paw oedema in mice.

Group	Treatment	Dosage	Mean Paw circumference (mm) at the indicated time						
			0 Hour	0.5 Hour	1 Hour	2 Hour	3 Hour	4 Hour	5 Hour
I	Distilled Water (mL/kg)	10	3.32±0.03	5.36±0.02	5.39±0.02	5.38±0.02	5.36±0.02	5.24±0.01	5.16±0.02
II	ASA (mg/kgbw)	100	3.33±0.03	4.97±0.02[a]	4.79±0.02[a]	4.39±0.02[a]	3.70±0.02[a]	3.46±0.05[a]	3.37±0.03[a]
III	*S. jollyanum* (mg/kgbw)	474.*34*	3.29±0.03	5.09±0.03[a,b]	5.01±0.04[a,b]	4.82±0.04[a,b]	4.38±0.03[a,b]	4.02±0.03[a,b]	3.72±0.03[a,b]
IV	*S. jollyanum* (mg/kgbw)	948.68	3.37±0.04	5.14±0.04[a,b]	5.03±0.04[a,b]	4.68±0.05[a,b,c]	3.95±0.04[a,b,c]	3.68±0.04[a,b,c]	3.38±0.04[a,c]
V	*S. jollyanum* (mg/kgbw)	1423.03	3.35±0.02	5.16±0.02[a,b]	4.97±0.03[a,b]	4.59±0.03[a,b,c]	3.91±0.03[a,b,c]	3.54±0.03[a,c,d]	3.38±0.02[a,c]

Results presented as mean ± S.E.M; n =5; p< 0.05 is considered significant. a = significant when all test groups are compared with control group 1, b = significant when group 2 is compared with control. c = significant when groups 4&5 are compared with 3. d = significant when groups 4vs5 are compared. ASA: acetylsalicylic acid. bw = body weight.

Table 2 Effect of ethanol leaf extract of *Sphenocentrum jollyanum* on egg-albumin induced paw oede**ma in mice.**

Group	Treatment	Dosage	Mean Paw circumference (mm) at the indicated time						
			0 Hour	0.5 Hour	1 Hour	2 Hour	3 Hour	4 Hour	5 Hour
I	Distilled Water (mL/kg)	10	3.17±0.01	5.39±0.04	5.41±0.04	5.39±0.04	5.06±0.17	5.04±0.17	4.67±0.20
II	ASA (mg/kgbw)	100	3.30±0.06[a]	4.83±0.02[a]	3.84±0.02[a]	3.69±0.04[a]	3.52±0.02[a]	3.46±0.04[a]	3.37±0.04[a]
III	*S. jollyanum (*mg/kgbw)	474.34	3.37±0.04	5.25±0.04[a,b]	4.73±0.03[a,b]	4.35±0.02[a,b]	4.14±0.03[a,b]	3.97±0.03[a,b]	3.65±0.04[a,b]
IV	*S. jollyanum* (mg/kgbw)	948.68	3.26±0.00	5.09±0.02[a,b,c]	4.21±0.01[a,b,c]	3.79±0.06[a,c]	3.70±0.02[a,c]	3.49±0.02[a,c]	3.29±0.01[a,c]
V	*S. jollyanum* (mg/kgbw)	1423.03	3.15±0.03[b,c,d]	5.04±0.03[a,b,c]	3.92±0.03[a,c,d]	3.46±0.09[a,b,c,d]	3.23±0.01[a,b,c,d]	3.19±0.03[a,b,c,d]	3.17±0.01[a,b,c,d]

Results presented as mean ± S.E.M; n =5; p< 0.05 is considered significant. a = significant when all test groups are compared with control group 1, b = significant when group 2 is compared with control. c = significant when groups 4&5 are compared with 3. d = significant when groups 4vs5 are compared. ASA: acetylsalicylic acid. bw = body weight.

3.2. Egg albumin-induced paw oedema

The effect of the ethanol leaf extract of *Sphenocentrum jollyanum* and standard drug, ASA in egg albumin-induced inflammation in mice was sustained over 5 hours as presented in Table 2. The administration of the extract caused significant reductions in egg albumin-induced mean paw thickness in groups III-V in a dose-dependent manner compared with the control group from the first to the fifth hour. The reduction in mean paw circumference for the extract- treated groups (III-V) were from 4.73 ± 0.03 to 3.65 ± 0.04, 4.21 ± 0.01 to 3.29 ± 0.01, and 3.92 ± 0.03 to 3.17 ± 0.01 respectively at doses of 474.34 ,948.68 and 1423.03 mg/kgbw respectively, comparable with ASA standard drug group which reduced from 3.84 ± 0.02 to 3.37 ± 0.04 from the first to the fifth hour. The paw circumference of the test group V was found to be lower comparable with ASA standard drug group at the 5th hour of treatment. Oedema induced by egg albumin was significantly ($p < 0.05$) inhibited by the ethanol extract of *Sphenocentrum jollyanum* from 0.5th to the 5th hour. The highest percentage inhibition of 36.71% was observed in the group administered the highest dose of the extract (1423.03 mg/kg) at the 4th hour which was higher than that of the standard drug ASA (31.54%) at the same hour.

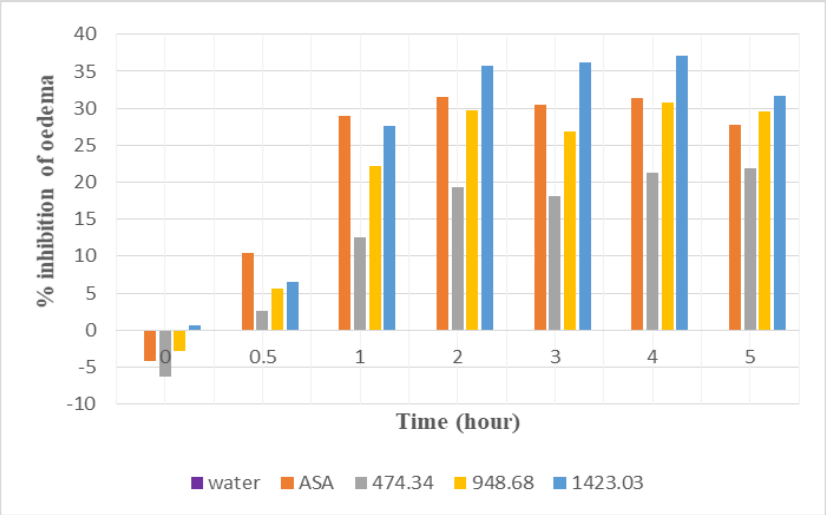

Figure 2 Percentage inhibition of ethanol leaf extract of *Sphenocentrum jollyanum* on egg albumin-induced paw oedema.

3.3. Xylene-induced ear oedema

The effect of the ethanol leaf extract of *Sphenocentrum jollyanum* and Dexamethasone on xylene-induced ear oedema in mice is presented in Table 3. Administration of the extract caused dose-dependent, significant ($p < 0.05$) decreases in xylene-induced oedema weight in all the test groups relative to the control group and Dexamethasone standard drug group II. Similarly, the extract showed significant ($p < 0.05$) dose-dependent percentage inhibitions of ear oedema at 8, 24, and 44% respectively. The inhibitory effect at the highest dose of 1423.03 mg/kg (44%) was comparable with that of Dexamethasone, with inhibition of (48%).

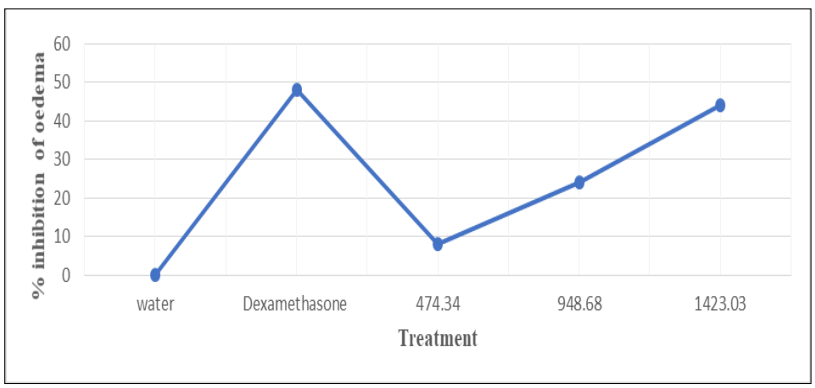

Figure 3 Percentage inhibition of ethanol leaf extract of *Sphenocentrum jollyanum* on xylene-induced ear oedema.

Table 3 Effect of ethanol leaf extract of *Sphenocentrum jollyanum* on xylene-induced ear oedema in mice.

Group	Treatment	Dosage	Weight of right ear (g)	Weight of left ear (g)	Increase in ear weight (g)	% Inhibition
I	Distilled Water (mL/kg)	10	0.14±0.01	0.09±0.01	0.05±0.00	
II	ASA (mg/kgbw)	100	0.12±0.00[a]	0.09±0.00	0.03±0.00[a]	48
III	*S. jollyanum (*mg/kgbw)	474.34	0.14±0.00[b]	0.09±0.00	0.05±0.00[b]	8
IV	*S. jollyanum* (mg/kgbw)	948.68	0.13±0.00[a,b]	0.09±0.00	0.04±0.00[a,b,c]	24
V	*S. jollyanum* (mg/kgbw)	1423.03	0.12±0.00[a,c,d]	0.09±0.00	0.03±0.00[a,c,d]	44

Results presented as mean ± S.E.M; n =5; p< 0.05 is considered significant. a = significant when all test groups are compared with control group 1, b = significant when group 2 is compared with control. c = significant when groups 4&5 are compared with 3.
d = significant when groups 4vs5. bw =body weight.

4. Discussion

Several medicinal plants and their derived phytochemicals have been evaluated for their analgesic and anti-inflammatory effects [37]. The anti-inflammatory drugs derived from these natural sources have been the rationale and productive strategy towards the cure of inflammatory ailments. These natural products have been reported to be safe, efficacious, biocompatible, and cost-effective alternatives to treat inflammatory diseases in folk medicine [38,14]. [39] has reported that several substances of plant origin such as flavonoids, saponins and tannins, are potential therapeutic agents in inhibiting or even decreasing inflammatory activity. An earlier study had shown that the presence of these phytochemicals, may be responsible for the anti-inflammatory activities demonstrated by the ethanol leaf extract of *Sphenocentrum jollyanum* [40].

In the present study, the ethanol leaf extract of *Sphenocentrum jollyanum* was evaluated for its anti-inflammatory effects against inflammation in mice using animal standard models like carrageenan-induced paw oedema, egg albumin-induced paw oedema, and xylene-induced ear oedema [41].

Carrageenan-induced paw oedema is a distinct in-vivo model widely used for assessing the anti-inflammatory properties of several natural, synthetic and novel products, due to its high reproducibility [42,43,44]. [45,46] reported carrageenan to be sensitive to cyclooxygenase inhibitors and suitable for the assessment of non-steroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase involved in prostaglandin synthesis. Carrageenan-induced paw oedema response involves three distinct phases through the sequential release of several inflammatory mediators. The first phase (0 - 1.30 hours after carrageenan injection), involves the release of histamine, 5-HT (5-hydroxytryptamine or serotonin), and neuropeptides from mast cells. The second phase (1.30- 2.30 hours) is mediated with the release of kinins while the third phase (after 3 hours) is mediated by prostaglandins, thromboxane A2, prostacyclin, resolvins, and lipoxygenase products [47,1]. The result obtained from this study suggests that the dose-dependent, significant anti-inflammatory effect of the extract at the 5th hour post-carrageenan induction, may be by inhibiting the cyclooxygenase enzyme mechanism involved in converting arachidonic acid to mediators such as prostaglandins, thromboxane A2, prostacyclin, and resolvins [1]. This result is comparable to ASA, a suitable non-steroidal anti-inflammatory drug that inhibited the triphasic response of carrageenan-induced inflammation. Therefore, the result of the present study revealed that the extract can effectively inhibit carrageenan-induced paw oedema.

The development of oedema in the paw of mice after the administration of egg albumin, has been a well-established model for testing anti-inflammatory agents [48]. It is described as a triphasic event. The first phase (0 – 1.30 hours after egg albumin injection) of the oedema, is attributed to the release of histamine, 5-hydroxytryptamine, or serotonin in the damaged tissue surroundings while the second (1.30 – 2.30 hours) and third phases (after 3 hours) are mediated by the release of bradykinin and prostaglandin-like substances respectively [47]. In the present study, the extract showed significant percentage inhibition of the egg albumin-induced inflammation in a dose-dependent manner comparable with ASA from 0th to 5th hour post egg-album induction. The result indicated that the extract exerted more inhibition on the egg albumin-induced oedema at the late phase by blocking the release of kinin, histamine,5-hydroxytryptamine (5-HT) and prostanoids known to mediate acute inflammation induced by phlogistic agents such as egg albumin, which significantly reduced at the fifth hour after treatment with varying doses of the extract [49]. The result of the present study revealed that the extract showed a more potent inhibition of egg albumin -induced oedema compared to the standard ASA.

Xylene-induced ear oedema is a simple animal model used to evaluate potential anti-inflammatory agents [50, 51]. Topical administration of xylene induces neurogenic oedema in mice ear mediated through the release of inflammatory mediators such as histamine, 5-hydroxytryptamine (5-HT) or serotonin, and neuropeptides such as substance P, neurokinin A, vasoactive intestinal polypeptide (VIP), and somatostatin that are produced in the central and peripheral nervous systems, and functions in transmission of pain stimuli [1]. Some studies have reported that the release of these inflammatory mediators, especially substance P, is associated with vasodilation of the arterioles and venules, neuronal hypersensitivity from sensory neurons, and plasma extravasation after tissue injury [52,53,54,55]. However, these effects orchestrate the formation of oedema on mice ear [56]. [57,38] reported that xylene ear oedema model permits the evaluation of anti-inflammatory steroids from non-steroidal anti-inflammatory drugs (NSAIDs). From the results obtained in this study, the control group showed an increase in ear weight, whereas group II showed the highest percent inhibition of ear oedema. The extract exhibited a more potent mitigation of the ear oedema at the highest dose (1423.03 mg/kg). However, the extract significantly inhibited xylene-induced neurogenic oedema in a dose-related manner which may be by inhibiting neurogenic inflammation through suppression of the release of an inflammatory mediator such as substance P. These reductions suggest that the extract may interfere with the actions of inflammatory mediators and produce anti-inflammatory efficacy. The results have shown that both the anti-inflammatory steroid (dexamethasone) and the NSAID (ASA) produced anti-inflammatory effects

5. Conclusion

The present study revealed that ethanol leaf extract of *Sphenocentrum jollyanum* is effective against carrageenan-induced paw oedema, egg albumin-induced paw oedema, and xylene-induced mice ear oedema. This may be due to the presence potent anti-inflammatory phytochemicals such as alkaloids, tannins, saponins, flavonoids and cardiac glycoside present in the extract. Thus, this study has justified the traditional use of *Sphenocentrum jollyanum* in several West African sub-regions in managing inflammatory diseases and could be a potential source for new anti-inflammatory drugs.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors report no declarations of interest.

Statement of ethical approval

All authors hereby declare that the "Guiding principles for the care and use of the animals in compliance with standard protocols of the National Institute of Health guidelines for the care and use of Laboratory Animals [58] were followed as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

References

[1] Harsh Mohan. Textbook of Pathology 6th ed. New Delhi, India: Jaypee Brothers Medical Publishers (P) Ltd. 2010.

[2] Kunnumakkara AB, Sailo BL, Banik K, Harsha C, Prasad S, Gupta SC.: Chronic diseases, inflammation, and spices: How are they linked? Journal of Translational Medicine. 2018; 16(1): 1-14.

[3] González-Costa M, Padrón González AA.: Inflammation from an immunologic perspective: A challenge to medicine in the 21st century. Rev. Haban. Cienc. Méd. 2018; (18): 30–44.

[4] Eddouks M, Chattopadhyay D, Zeggwagh NA. Animal Models as Tools to Investigate Antidiabetic and Anti-Inflammatory Plants. Evid. -Based Complement. Altern. Med. 2012; 142-087.

[5] Schmid-Schonbein, GW. "Analysis of inflammation," ¨ Annual Review of Biomedical Engineering. 2006; (8): 93–151.

[6] Markiewski MM, Lambris JD. "The role of complement in inflammatory diseases from behind the scenes into the spotlight," American Journal of Pathology. 2007; (171): 715– 727.

[7] Kobayashi H, Higashiura Y, Shigetomi H, Kajihara H. "Pathogenesis of endometriosis: the role of initial infection and subsequent sterile inflammation (Review)," Molecular Medicine Reports. 2014; (9): 9–15.

[8] Bengmark S. Acute and "chronic" phase reaction-a mother of disease. Clin Nutr. 2014; (23): 1256–66.

[9] Vignali DA, Kuchroo VK. IL-12 family cytokines: Immunological playmakers. Nat. Immun. 2012; (13): 722–728.

[10] Lima AS, Alvim HGO. Review on non-steroid anti-inflammatory: Acetylsalicylic acid. Rev. Inic. Ciente. Ext. 2018; (1): 169–174.

[11] Allison D, Ditor D. Immune dysfunction and chronic inflammation following spinal cord injury. Spinal Cord. 2015; (53)1: 14-18.

[12] Fürst R, Zündorf I. Plant-derived anti-inflammatory compounds: Hopes and disappointments regarding the translation of preclinical knowledge into clinical progress. Mediators of Inflammation. 2014; 1-9.

[13] Stankovic N, Mihajilov-Krstev T, Zlatkovic B, Stankov-Jovanovic V, Mitic V, Jovic J, Comic L, Kocic B, Bernstein N. Antibacterial and antioxidant activity of traditional medicinal plants from the Balkan Peninsula. NJAS—Wageningen J. Life Sci. 2016; (78): 21–28.

[14] Uddin G, Rauf A, Siddiqui BS, Muhammad N, Khan A, Shah SUA, Rauf DA. Anti-nociceptive, anti-inflammatory and sedative activities of the extracts and chemical constituents of Diospyros lotus L. Phytomedicine. 2014; (21): 954–959

[15] Dalziel JM. The Useful Plants of West Tropical Africa. London, UK: Crown Agents. 1985.

[16] Iwu MM. Handbook of African Medicinal Plants. Boca Raton, FL, USA: CRC Press. 1993.

[17] Nia R, Paper DH, Essien EE. Evaluation of the anti-oxidant and anti-angiogenic effects of *Sphenocentrum jollyanum* Pierre. Afr. J. Biomed. Res. 2004; (7):129–132.

[18] Amidu N. An Evaluation of the Central and Sexual Behavioral Effects and Toxicity of the Root Extract of *Sphenocentrum jollyanum* Pierre (Menispermaceae) [Ph.D. Thesis]. Department of Molecular Medicine, Kwame Nkrumah University of Science & Technology, Kumasi, Ghana. 2008.

[19] Oke J, Hamburger M. Screening of some Nigerian Medicinal Plants for Antioxidant Activity Using 2,2-diphenyl-picryl-hydrazyl radical. African Journal of Biomedical Research. 2002; (5): 77-79.

[20] Abbiw DK. Useful Plants of Ghana. Kew, UK: Intermediate Technology Publications and Royal Botanic Gardens. 1990.

[21] Moody JO, Robert VA, Connolly J D, Houghton P J. Anti-inflammatory activities of the methanol extract and isolated furanoditerpenes constituent of *Sphenocentrum jollyanum* Pierre (Menispermaceae). Journal of biomedical research. 2006; (7): 129-132.

[22] Olugbami JO, Gbadegesin MA, Odunola OA. In vitro evaluation of the antioxidant potential, phenolic and flavonoid contents of the stem bark ethanol extract of Anogeissus leiocarpus. Afr J Med Sci. 2014; 43(1): 101–9.

[23] Uka Emmanuel, Jessie IN, Patrick AI, Esther OA. In-vivo analgesic activity of ethanol leaf extract of *Sphenocentrum jollyanum* in albino mice. International Journal of Research Publication. 2020(a); 64: 1.

[24] Whiteley PE, Dalrymple SA. Models of Inflammation: Carrageenan-Induced Paw Edema in the Rat. Curr. Protoc. Pharmacol. 2001; 5–6.

[25] Bukhari IA, Khan RA, Gilani AH, Shah AJ, Hussain J, Ahmad VU. The Analgesic, Anti-inflammatory and Calcium Antagonist Potential of Tanacetum artemisioides. Arch. Pharm. Res. 2007; 30(3): 303-312.

[26] Winter EA, Risley EA, Nuss GV. Carrageenin-induced oedema in hind paw of rats as an assay for anti-inflammatory drug. Proceedings of the Society of Experimental Biology and Medicine. 1962; 111: 544-547.

[27] Buodonpri W, Wichitnithad W, Rojsitthisak P, Towiwat P. Synthetic curcumin inhibits carrageenan-induced paw edema in rats. J Health Res. 2009; 23:11-6.

[28] Aly, AM, Alousi LA, Salem HA. Licorice: A Possible Anti-inflammatory and Anti-ulcer Drug. AAPS Pharm.Sci.Tech. 2005; 6(1)13.

[29] Hess SM, Milonig RC. Inflammation In: Lepow LH, Ward PS (Eds). Inflammation, Mechanism and control. New York, USA: Academic Press. 1972.

[30] Balamurugan K, Sakthidevi G, Mohan VR. "Anti-inflammatory activity of leaf of Melastoma malabathricum L. (Melastomataceae)," International Journal of Research in Ayurveda and Pharmacy. 2012; 3(6): 801-802.

[31] Akah PA, Nwambie AI. Evaluation of Nigerian traditional medicines, Plants used for rheumatic (inflammatory) disorders. J Ethnopharmacol. 1994; 42(3):179-182.

[32] Dai YL, Liu H, Kou JP. Anti-inflammatory effect of aqueous extract of Wu-HU-Tang," China Pharmaceutical University. 1995; 6: 362–364.

[33] Kou J, Ni Y, Li N, Wang J, Liu L, Jiang Z. Analgesic and anti-inflammatory activities of total extract and individual fractions of Chinese medicinal ants Polyrhachis lamelliden. Biol Pharm Bull. 2005; 28(1): 176-180.

[34] Xu Q, Wang Y, Guo S, Shen Z, Wang Y, Yang L. Anti-inflammatory and analgesic activity of aqueous extract of Flos populi. J. Ethnopharmacol. 2014; 152: 540–545.

[35] Igbe I, Ching FP, Eromon A. Anti-inflammatory activities of aqueous fruit pulp extract of Hunteria umbellate K. Schum in acute and chronic inflammation: Acta pol. pharm. drug res. 2010; 7(1): 81-85.

[36] Zhu Y, Shi H, Cheng X, Wang C, Cheng J. In-vivo evaluation of the anti-inflammatory and analgesic activities of compound Muniziqi granule in experimental animal models. BMC Complement Altern Med. 2016; 16: 20.

[37] Raza M, Shaheen F, Choudhary MI, Suria A, Rahman UA, Sompong S, Delorenzo RJ. Anticonvulsant activities of the FS-1 subfraction isolated from roots of Delphinium denudatum. Phytotherapy Research. 2001; 15: 426–430..

[38] Sofidiya MO, Imeh E, Ezeani C, Aigbe FR, Akindele AJ. Antinociceptive and anti-inflammatory activities of ethanolic extract of Alafia barteri. Rev. Bras. De Farm. 2014; 24: 348–354.

[39] Fialho L, Cunha-E-Silva JA, Santa-Maria AF, Madureira FA, Iglesias AC. Comparative study of systemic early postoperative inflammatory response among elderly and non-elderly patients undergoing laparoscopic cholecystectomy. Rev. Col. Bras. Cir. 2018; 45(1): e1586.

[40] Uka E, Oboso EE, Akaninyene OE, Imoh EJ. Phytochemicals, acute toxicity and in-vitro antioxidant activity of ethanol extract of *Sphenocentrum jollyanum* leaves. Journal of Drugs and Pharmaceutical Science. 2020(b); 4(2): 10-20.

[41] Ismail TS, Gopalakrishnan S, Begum VH, Elango V. Anti-inflammatory activity of Salacia oblonga Wall. and Azima tetracantha Lam. J Ethnopharmacol. 1997; 56: 145-152.

[42] Boominathan R, Parimaladevi B, Mandal S, Ghoshal S. Anti-inflammatory evaluation of Ionidium suffruticosam Ging. in rats. J. Ethnopharmacol. 2004; 91: 367–370.

[43] Panthong A, Norkaew P, Kanjanapothi D, Taesotikul T, Anantachoke N, Reutrakul V. Anti-inflammatory, analgesic and antipyretic activities of the extract of gamboge from Garcinia hanburyi Hook f. J. Ethnopharmacol. 2007; 111: 335–340.

[44] Wilches I, Tobar V, Peñaherrera E, Cuzco N, Jerves L, Heyden YV, León-Tamariz F, Vila E. Evaluation of anti-inflammatory activity of the methanolic extract from Jungia rugosa leaves in rodents. J. Ethnopharmacol. 2015; 173:166–171.

[45] Sarkhel S. Evaluation of the anti-inflammatory activities of Quillaja saponaria Mol. saponin extract in mice. Toxicol. Rep. 2016; 3: 1–3.

[46] Winyard PG, Willoughby DA, Morris CJ. Carrageenan-Induced Paw Edema in the Rat and Mouse. In Inflammation Protocols. Berlin/Heidelberg, Germany: Springer Science and Business Media LLC. 2003; 225: 115–122.

[47] Okpo S, Fatokun F, Adeyemi O. Analgesic and anti-inflammatory activity of Crinum glaucum aqueous extract. J. Ethnopharmacol. 2001; 78: 207–211.

[48] Xu S, Bian R, Chen X. Experimental Methodology of Pharmacology 3rd ver. Beijing: Peoples' Medical Publishing House. 2002.

[49] Gupta M, Mazumder UK, Gomathi P, Selvan VT. Anti-inflammatory evaluation of leaves of Plumeria acuminata. BMC Complement Altern Med 2006; 6: 36.

[50] Zhang Z, Luo P, Li J, Yi T, Wang J, An J, Zhang H. Comparison of the anti-inflammatory activities of three medicinal plants known as 'meiduoluomi' in Tibetan folk medicine. Yakugaku Zasshi. 2008; 128: 805-810.

[51] Wang D, Wang S, Chen X, Xu X, Zhu J, Nie L, Long X. Antitussive, expectorant and anti-inflammatory activities of four alkaloids isolated from Bulbus of Fritillaria wabuensis. J Ethnopharmacol. 2012; 139: 189-193.

[52] Black PH. Stress and the inflammatory response: a review of neurogenic inflammation. Brain Behav Immun. 2002; 16: 622–653.

[53] Pernow B. Substance P. Pharmacol Rev. 1983; 35(2): 85-141.

[54] Devillier P, Regoli D, Asseraf A, Descours B, Marsac J, Renoux M. Histamine release and local responses of rat and human skin to substance P and other mammalian tachykinins. Pharmacology. 1986; 32: 340-347.

[55] Lundberg JM, Saria A, Brodin E, Rosell S, Folkers K. A substance P antagonist inhibits vagally induced increase in vascular permeability and bronchial smooth muscle contraction in the guinea pig. Proc Natl Acad Sci U S A. 1983; 80(4): 1120-1124.

[56] Agbaje EO, Fageyinbo M S. Evaluating Anti-Inflammatory activity of aqueous root extract of Strophanthus hispidus (DC) (Apocynaceae). International Journal of Applied Research in Natural Products. 2012; 4(4): 7-14.

[57] Zanini J, Medeiros Y, Cruz A, Yunes R, Calixto J. Action of compounds from Mandevilla velutina on croton oil-induced ear oedema in Mice. A comparative study with steroidal and nonsteroidal anti-inflammatory drugs. Phytother Res. 1992; 6: 1-5.

[58] National Institute of Health. Public health service policy on human care and use of laboratory animals. OLAW.nih.gov. 2015.