Research Article
Anti-Inflammatory, Antipyretic and Anti-Nociceptive Activities of the Ethanol Stem Bark Extract of *Salacia lehmbachii*

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Abstract: The aim of this study is to scientifically elucidate the effects of Ethanol Stem Bark Extract (ESBE) on inflammation, pyrexia and pains induced in rats and mice, following the claim that decoction from stem-bark of *Salacia Lehmbachii* (*SL*) is used in treating feverish and painful conditions in south-eastern parts of Nigeria. The anti-inflammatory activities of the ESBE of this plant were studied, using carrageenan and egg albumin-induced paw edemain albino Wistar rats; and antipyretic activities were examined, using Dinitrophenol and Brewer's yeast-induced pyrexia in Wistar rats, while acetic acid- induced writhing and tail immersion models were used for analgesic study. LD_{50} and ED_{50} of the ESBE were carried out to determine its safety and dosing regimen, respectively. Thirty animals were randomly selected and grouped into five with six animals per group for each experiment. Group 1 and 5 (controls) received 20 mL/kg of distilled water and150 mg/kg of aspirin and 10 mg/kg of morphine (tail immersion study) respectively; while groups 2 to 4 received 75, 150 and 300 mg/kg of the extract respectively. The ED_{50} was 150 mg/kg. The ESBE of *SL* exhibited significant ($p<0.05$) dose related effects in all the experimental models. Doses of 150 and 300 mg/kg abolished the induced edema, induced pyrexia and pains, highly comparable to respective positive controls. Therefore, ESBE of *Salacia lehmbachii* possesses potent anti-inflammatory, antipyretic and analgesic activities, likely resulting from its phytochemical constituents. Hence, its folkloric use in herbal medicines for pains and fever is justified.

Keywords: Dinitrophenol, inflammation, nociception, pyrexia, *Salacia lehmbachii*-stem bark, tail-immersion

INTRODUCTION

The reaction to any inflammatory phenomenon could include fever and pain which is characteristic responses by all living tissues. These responses represent the usual symptoms implicated in many various clinical presentations irrespective of the causative factors (Dhara *et al.*, 2000). This inflammatory reaction is complex and is brought about by cascade of various mediators like histamine, prostaglandins E_2 and I_2 etc. that are synthesized per novo when there is an interaction of the noxious substances or micro-organisms with the tissue (Barnes and Karin, 1997; Ganesh *et al.*, 2008). Subsequent release of cascade of other inflammatory mediators that usually follows makes inflammatory reaction to involve both vascular and cellular components (Luster, 1998; Akuodor *et al.*,2015).

Some phytochemical constituents of plants, usually synthesized by them, that are meant to defend these plants from variety of predators are now seen to be useful in maintaining human health (Lai and Roy,

2004). Before synthetic drugs were produced, man was completely dependent on medicinal plants for curing diseases (Tapsell *et al.*, 2006; Singh *et al.*, 2008). Extracted substances obtained from variety of plants are commonly and widely used by traditional healers in Nigeria (Akuodor *et al.*, 2011). The World Health Organization (WHO, 2006) estimated 80% of the world's population depending on herbal medicines and hence advocates their inclusion in primary health care due to their great potentials. Constituents in many plants' products have proven to exhibit biological and pharmacological activities, which include anti-inflammatory, antipyretic, antiviral and other effects (Hakiman and Maziah, 2009). Therefore, searching for novel pain relievers with antipyretic and anti-inflammatory activities is a welcome idea (Ravelo *et al.*, 2011; Elisabetsky *et al.*, 1995).

Salacia Lehmbachii (SL) is one of such plants. It is a shrub-like to small tree of about three meters high and belongs to the family *Celastraceae* (Willcox and Bodeker, 2004). It is widely distributed in the tropical rain forest of West, Central and East Africa. In South

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East of Nigeria its decoctions from roots and leaves are commonly used by traditional healers for treatment of different diseases such as renal dysfunction, fever, pain and gastrointestinal disorders (Essien *et al*., 2015, 2016). So far, no scientific reports had been made on stem bark and inflammation. Thus, the aim of this study on the stem bark of *SL* is to prove scientifically, the claim by the traditional users that the ethanol extract of it possesses potent anti-inflammatory, antipyretic and analgesic activities, by using experimental animal models.

MATERIALS AND METHODS

Plant collection: The plant *Salacia lehmbachii* was collected from OrukOtong village in Ukanafun Local Government Area of AkwaIbom state, Nigeria, in the month November 2014. It was identified and authenticated by a taxonomist, Mr. Frank Apojoye, of the Department of Botany, university of Calabar, Nigeria, where a voucher specimen (No. 688) is kept for reference. The stem bark was devoid of the leaves and thereafter, was cut into smaller pieces and dried at room temperature for 10 days. *S. lehmbachii* stem bark was later ground to dry powder using a mortar and pestle.

Extraction: The dry stem bark powder (600 g) was defatted by distilling with petroleum ether (May and Baker Ltd, Dagenham, England) and thereafter, extracted in ethanol 99% (BDH Chemicals Ltd, Brole, England) using Soxhlet extractor (Friedrich Polzime, England). The distillate was thereafter concentrated to dryness in a vacuum at 40°C. The yield was (13.8% w/w). The extract was stored in an air-tight container and kept in a refrigerator at 4°C until when it would be reconstituted during the experiment.

Phytochemical screening: The qualitative phytochemical screening of the ethanol stem bark extract of *Salacia lehmbachii* was carried out according to standard methods (Sofowora, 1993; Evans, 2005) in the Department of Biochemistry, University of Calabar.

Pharmacological tests:
Animals: Approval for this study was obtained from the Faculty of Basic Medical Science Animal Research Ethics Committee, University of Calabar (ETHIC REF No.: 025PA30517). Healthy adult Wistar rats (150-200 g) and mice (18-22 g) of both male and female were obtained from the animal house, Department of Pharmacology, College of Medical Sciences, University of Calabar. Nigeria. The animals were kept in cages in an environment that was conducive, having 12:12 h light/dark cycle. They were allowed free access to standard pellets and water. NIH guideline for the caring and usage of the Laboratory Animals was applied throughout this study (National Academy of Sciences, 2011).

Acute toxicity test: The acute toxicity test of the ethanol extract of *Salacia lehmbachii* was determined in the randomized albino mice following OECD guidelines (OECD,2010) and Ghosh (2005). The procedure as reported by Essien *et al*. (2016) was adopted.

Effective dose: The ED_{50} was determined using Traditional Dose Response procedure (with slight modification) described by Ahmad *et al*. (2011).

Carrageenan-induced inflammatory edema: Adult Wistar rats of both sexes were selected and grouped into 5 groups of 6 rats in each cage. Group 1 received 20 mL/kg of distilled water. Groups 2, 3 and 4 received 75, 150 and 300 mg/kg of ESBE of *S. lehmbachii*, respectively, while group 5 received 150 mg/kg of aspirin. All doses were administered orally. After 30 min of above drug administration, the initial size of the right hind paw of each rat was measured using caliper (Letica 7500, Spain). Thereafter, paw edema was induced by injecting (phlogesic) 0.5 mL of 1% carrageenan (Sigma Aldrich, France) into the sub-plantar of the right hind paw of each rat. Thereafter, the circumference (size) of the edematous right hind paw was measured and recorded after 30 min and then hourly for 5 has reported by Akah and Nwambie (1994) and Ravelo *et al*. (2011).

Egg-albumin-induced inflammation: Method described by Al-Ghamdi (2001) and Xu *et al*.(2014)with little modification was adopted for this study. Thirty adult Wistar rats of both sexes were randomly selected and grouped into 5 with 6 rats per cage. Group 1 received orally, 20 mL/kg of distilled water, while group 5 received150 mg/kg of aspirin orally. Groups 2, 3 and 4 received orally, 75, 150 and 300 mg/kg of ESBE of *S. lehmbachii*, respectively. After 30 min of above treatment, the initial volume (size) of each rat's right hind paw was measured and recorded. Thereafter, inflammation was induced in rats by injecting subcutaneously, 0.2 mL of fresh egg-albumin into the sub-plantar of the right hind paw. The paw volumes were again measured at 30 min intervals and for 120 min, using Calliper (Letica 7500, Spain).

Yeast-induced pyrexia: The modified method by Mukherjee *et al*. (2002), Akuodor *et al*. (2011) and Essien *et al*. (2015) was used for this study. Thirty Wistar rats were randomly selected and divided into 5 groups of 6 rats per cage. Clinical thermometer (Boots Birmingham England) was used in measuring their initial basal rectal temperature. Thereafter, pyrexia was induced in rats by injecting subcutaneously 20 mL/kg

of 15% brewer's yeast (Danbaoli, China) suspended in 0.5% methylcellulose (Searle, England) solution. After 24 h, rectal temperature was again measured and any rat(s) without elevated temperature above by 0.5°C was disregarded for the study.

Thereafter, 75, 150 and 300 mg/kg of ESBE of *S. lehmbachii* were administered orally to groups 2, 3 and 4 respectively; while control groups 1and 5 received distilled water (20 mL/kg) and aspirin (150 mg/kg) respectively. Their rectal temperature was again recorded at 1h interval and for 6 h after drug administration.

4-Dinitrophenol (DNP)-induced pyrexia: The modified method by Okokon and Nwafor (2010) and Essien *et al.* (2015) was adopted. After 24 hour-fast with free access to water, 30 rats were divided into 5 groups of 6 rats per cage. Their basal rectal temperature was recorded before inducing pyrexia intraperitoneally, with 10 mg/kg of DNP. Thirty minutes post DNP administration, rectal temperature was measured to confirm the state of pyrexia and to disregard rats without temperature elevation above 0.5°C.

Thereafter, 75, 150 and 300 mg/kg of ESBE of *S. lehmbachii* were administered orally to groups 2, 3 and 4 respectively; while control groups 1and 5 received distilled water (20 mL/kg) and aspirin (150 mg/kg) respectively. Thereafter, the rectal temperature was measured and recorded at 1 h interval and for 6 h.

Acetic acid-induced writhing test: Thirty randomly selected adult albino mice of both sexes were used for this analgesic study. They were subjected to 24 h fast but had free access to water and later, were divided into 5 groups of 6 mice per cage. According to procedure described by Singh and Majumbar (1995) and Akuodor *et al.* (2011), control groups 1 and 5 received orally, 20 mL/kg of distilled water and 150 mg/kg of aspirin respectively; while group 2, 3 and 4 received orally 75, 150 and 300 mg/kg of the ESBE of *S. lehmbachii* respectively. Thirty minutes following above treatment, each mouse in all groups received intraperitoneally, 20 mL/kg of 0.7% acetic acid to induce pain sensation. Each mouse was then placed in a transparent observation chamber. Five minutes post acetic acid administration, the number of abdominal constrictions or writhing behavior for each mouse was noted, counted and recorded for a period of 30 min.

Tail immersion test: The method described by Ramabadran *et al.* (1989) and Akuodor *et al.* (2015) was used for this study. Thirty randomly selected adult albino mice of both sexes were divided into 5 groups of 6 mice in each cage and were subjected to 24 h fast, but free access to water. Control groups 1 and 5 were treated orally with 20 mL/kg of distilled water and subcutaneously, with 10 mg/kg of morphine, respectively; While groups 2, 3 and 4 received orally, 75, 150 and 300 mg/kg of ESBE of *S. lehmbachii* respectively. Thirty minutes after above treatment, each mouse was placed in the restrainer cage (Grieve Cooperation, Illinois, U.S.A.), leaving the tail hung out and freely exposed to be dipped in a hot water bath that was maintained thermo-statistically at 51±1°C. The duration of stay (latency) of the tail in the hot-water bath before the animal withdrew its tail out of the water was recorded. The latency was evaluated at 30, 60, 90 and 120 min (Akuodor *et al.*, 2015).

Statistical analysis: Results were expressed as mean±S.E.M. These data were analyzed using one-way ANOVA followed by Neuman-Keuls post hoc test and their differences between means of treated and control groups were considered significant at p<0.05.

RESULTS

Phytochemical screening of the ethanol stembark extract revealed the presence of some active phytochemical constituents such as carbohydrates, saponins, flavonoids, steroids, terpenoids, alkaloids, anthraquinones and tannins. These phytochemical are reported to exhibit potent biological activities (Hadacek, 2002; Ghoghari and Rajani, 2006).

Acute toxicity test: Oral administration of graded concentration of the ethanol stem bark extract of *SL* did not exhibit any lethality nor any sign of toxicity in the experimental mice.

Effective dose: The result showed that ED_{50} of the ethanol stem bark extract of *SL* was 150 mg/kg; hence doses of 75, 150 and 300 mg/kg were conveniently used.

Carrageenan/egg albumin-induced edemata: The ethanol stem bark extract of *SL* significantly (p<0.05) showed dose-related inhibition of the paw edema induced by both carrageenan and egg-albumin when compared to control (Table 1 and 2 respectively). In carrageenan model, the effect exhibited prolonged beyond the five-hour observation. The effect exhibited with doses of 150 and 300 mg/kg of the stem-bark extract started after 30 min of treatment and was highly comparable to the effect produced with150 mg/kg of aspirin in both parameters.

Yeast-induced pyrexia: The ethanol stem bark extract of *SL* significantly (p<0.05) showed dose-related suppression of the pyrexia induced by brewer's yeast and the reduction of temperature was observed after 1 h with doses of 150 and 300 mg/kg; while 75 mg/kg produced effect after 2 h. This antipyretic effect was maintained up to 6 h and was highly comparable to that of aspirin (Table 3).

Table 1: Effect of ethanol stem bark extract of SL on Carrageen an-induced paw edema in rats

	Treatment		
Distilled water	Dose (mg/kg)	0h	0.5h
S. lehmbachii	20 mL/kg	1.26±0.03	2.68±0.17
	75	1.24±0.02	2.68±0.07
	150	1.29±0.02	1.59±0.08*
	300	1.29±0.01	1.31±0.06*
Aspirin	150	1.26±0.01	1.31±0.08*

	Paw edema diameter (mm) within 5 h observation period				
Distilled water	1h	2h	3h	4h	5h
S. lehmbachii	2.83±0.01	2.83±0.03	2.72±0.02	2.74±0.02	2.72±0.02
	2.68±0.01	2.31±0.05	1.98±0.06*	1.68±0.06*	1.66±0.06*
	1.40±0.01*	1.33±0.04*	1.31±0.06*	1.26±0.06*	1.25±0.06*
	1.31±0.02*	1.20±0.05*	1.20±0.03*	1.19±0.03*	1.19±0.03*
Aspirin	1.26±0.02*	1.20±0.03*	1.18±0.03*	1.18±0.03*	1.16±0.03*

Data are express as mean ± SEM (n=6)* significantly different from control at $p < 0.05$

Table 2: Effect of ethanol stem bark extract of *SL* on egg albumin-induced paw edema in rats

	Treatment		Paw edema diameter (mm) at 30 min interval			
Distilled water	Dose (mg/kg)	0 min	30 min	60 min	90 min	120 min
S. lehmbachii	20 mL/kg	1.34±0.01	2.60±0.21	2.92±0.23	2.97±0.03	2.99±0.19
	75	1.30±0.03	2.32±0.02	2.32±0.06	2.28±0.05	2.04±0.04*
	150	1.30±0.03	2.16±0.05	1.31±0.04*	1.21±0.04*	1.20±0.03*
	300	1.24±0.02	1.29±0.03*	1.21±0.02*	1.19±0.03*	1.19±0.01*
Aspirin	150	1.34±0.02	1.28±0.03*	1.23±0.02*	1.20±0.01*	1.19±0.01*

Data are express as mean ± SEM (n=6) *significantly different from control at $p < 0.05$

Table 3: Effect of ethanol stem bark extract of *SL* on brewer's yeast-induced pyrexia in rats

Treatment	Dose(mg/kg)	0h	1h	2h	3h	4h	5h	6h
Distilled water	20 mL/kg	35.53±0.01	37.80±0.01	37.82±0.06	37.85±0.01	37.93±0.06	37.82±0.06	37.81±0.05
S. lehmbachii	75	35.55±0.05	37.79±0.01	36.89±0.04	36.85±0.13*	36.61±0.13*	35.98±0.11*	35.52±0.13*
	150	35.60±0.14	36.75±0.04*	36.48±0.03*	36.45±0.06*	36.38±0.11*	35.58±0.06*	35.51±0.08*
	300	35.58±0.11	36.67±0.10*	36.48±0.03*	36.31±0.12*	35.47±0.13*	35.35±0.12*	35.27±0.04*
Aspirin	150	35.51±0.04	36.69±0.11*	36.36±0.11*	36.29±0.09*	35.51±0.10*	35.35±0.11*	35.25±0.04*

Data are expressed as mean ± SEM (n=6) *significantly different from control at $p < 0.05$

Table 4: Effect of ethanol stem bark extract of *SL* on Dinitrophenol-induced pyrexia in rats

Treatment	Dose(mg/kg)	0 h	1 h	2 h	3 h	4 h	5 h	6 h
Distilled water	20 mL/kg	35.48±0.04	37.98±0.05	37.88±0.04	37.69±0.03	37.57±0.04	37.36±0.02	36.68±0.03
S. lehmbachii	75	35.46±0.02	37.57±0.06	36.43±0.04*	36.19±0.02*	35.63±0.06*	35.36±0.06*	35.21±0.04*
	150	35.45±0.02	36.65±0.06*	36.36±0.05*	36.17±0.03*	35.57±0.03*	35.31±0.04*	35.13±0.03*
	300	35.34±0.03	36.65±0.03*	36.59±0.02*	36.29±0.02*	35.56±0.02*	35.32±0.05*	35.10±0.00*
Aspirin	150	35.36±0.02	36.62±0.03*	36.57±0.04*	36.35±0.03*	36.07±0.03*	35.42±0.04*	35.24±0.04*

Data are expressed as mean ±SEM (n=6)*significant different from control at $p < 0.05$

4 Dinitrophenol-induced pyrexia: The ethanol stem bark extract *SL* exhibited significantly ($p < 0.05$) dose-dependent reduction of DNP-induced pyrexia. Significant reduction of pyrexia from 1 h was highly expressed at doses of 150 and 300 mg/kg as shown in Table 4. This result was highly comparable to the effect produced by aspirin.

The observed antipyretic effect was maintained beyond the experimental period in both yeast-induced DNP-induced models.

Acetic acid-induced writhing/abdominal constriction: The ethanol stem bark extract *SL* significantly ($p < 0.05$), exhibited dose-dependent reduction of abdominal contractions in mice. The dose of 300 mg/kg of the ethanol stem bark extract produced

an effect (88.4%) similar to that of aspirin (89.0%) as shown in Table 5.

Tail immersion: The ethanol stem bark extract of *SL* significantly ($p < 0.05$) produced dose-dependent protection of the animals from the heat stimuli of the hot-bath. The dose of 300 mg/kg of the extract produced effect similar to that produced by 10 mg/kg of morphine; while mice receiving distilled water had no protection at all (Table 6).

DISCUSSION

This study shows that the administration of ethanol stem bark extract of *Salacia lehmbachii* produces potent anti-inflammatory, fever reducing and pain

Table 5: Effect of ethanol stem bark extract of *SL* on acetic acid-induced writhing in mice

Treatment	Dose (mg/kg)	Abdominal constrictions	% Inhibition
Distilled water	20 mL/kg	29.2±0.58	0.00
S. lehmbachii	75	21.8±0.37*	25.3*
	150	7.2±0.49*	75.3*
	300	3.4±0.24*	88.4*
Aspirin	150	3.2±0.37*	89.0*

Data are expressed as mean ±SEM (n = 6) *significantly different from control at $p<0.05$

Table 6: Effect of ethanol Stem bark extract of *SL* on mouse-tail immersion in 51±1°C hot bath

Treatment	Dose (mg/kg) pretreatment after treatment	Duration of stay (tail) in hot water bathe (second)	
		0 min	30 min
Distilled water	20 mL/kg	5.50±0.60	5.53±0.45
S. lehmbachii	75	5.60±0.56	7.17±0.54
	150	5.83±0.48	12.08±0.77*
	300	6.00.0±73	14.08±0.83*
Morphine	10	5.80±0.64	13.87±1.23*

Treatment	Duration of stay (tail) in hot water bathe (second)		
	60 min	90 min	120 min
Distilled water	6.08±0.61	5.67±0.80	5.63±0.24
S. lehmbachii	9.03±0.13*	9.21±0.82*	10.65±0.80*
	13.17±0.83*	14.50±1.28*	16.63±0.95*
	18.88±0.92*	21.17±1.60*	21.60±0.83*
Morphine	19.78±1.71*	21.28±0.85*	21.56±1.09*

Data are expressed as mean ±SEM (n=6) *significantly different from control at $p<0.05$

relieving effects. Some plants possess therapeutic potential because they contain phytochemicals as their principal active ingredients that serve as important machinery for pharmaceutical research towards drug development (DaSilva *et al*., 2002). *Salacia lehmbachii* is one of such investigated plants' extracts that contain flavonoids, saponins, tannins, steroids, terpenoids and alkaloids, that exhibit potent pharmacological activities (Duke, 1992; Mutalik *et al*., 2003). Several plant products are used to relieve these symptoms in most traditional set-ups, including stem bark extract of *S. lehmbachii* that has exhibited significant anti-inflammatory, anti-pyretic and anti-nociceptive activities as shown in this study.

Inflammation, fever and pains are usually symptoms implicated in many various clinical manifestations irrespective of the causative factors (Dhara *et al*., 2000). Response by living tissues to an inflammatory reaction is complex and is brought about by various mediators like histamine, prostaglandins E$_2$ and I$_2$ etc. That are produced as a result of the interaction of the noxious substances or micro-organisms with the tissue (Barnes and Karin, 1997; Ganesh *et al*., 2008). The release of cascade of other inflammatory mediators usually follows, making the inflammatory reaction to involve both vascular and cellular components (Luster, 1998; Akuodor *et al*., 2015).

The ethanol stem bark extract of *S. lehmbachii* produced significant inhibition of Carrageenan and egg-albumin induced hind paw edema (inflammation) in rats. The induction of inflammatory reaction by these substances is usually in two phases, starting with the early phase mediated via the release of histamine, kinins, etc. to the release of prostaglandins mediated by bradykinin, leukotrienes and polymorphonuclear from tissue macrophages. Induced arachidonate COX-2, prostaglandins and thromboxane's are usually involved in inflammatory process (Rang *et al*., 1999) that is inhibited by NSAIDs. Aspirin is a potent NSAID and the anti-inflammatory effect exhibited by this stem bark is similar to that of aspirin. Hence, the mechanism could be same or via the inhibition of any of the released inflammatory mediators.

The ethanol stem bark extract of *S. lehmbachii* also exhibited significant antipyretic activity against induced pyrexia in the two models-Brewer's yeast and 4-Dinitrophenol. Fever (pyrexia) begins whenever exogenous or/and endogenous stimuli which may include pyrogens are exposed to host cells-monocytes and macrophages (Arai *et al*., 1990). Formation of cascade of other pyrogenic cytokines like interleukin-1, TNF-α, interleukin-6 etc. follows. As a result of an interaction of cytokines and their receptors in the preoptic region of the anterior hypothalamus, phospholipase A is activated to catalyze arachidonate (substrate for COX), leading to synthesis of prostaglandins, that could further trigger the temperature to be elevated (Dinarello, 1997; Vane and O'Grady, 1993).

Hence, drugs or agents that would inhibit activity on prostaglandin biosynthesis possess antipyretic effect. The NSAIDs, such as aspirin and others exhibit their suppression of fever mainly by inhibiting Prostaglandin E (PGE) synthesis in the hypothalamus (Rang *et al*., 1999). Therefore, ethanol stem bark extract of *S. lehmbachii* showed high efficacy similar to aspirin in inhibiting the elevated temperature in the yeast and

dinitrophenol-induced fever models; hence, suggesting the likely possible mechanism of action.

Nociception can occur by applying any stimulus or by injecting noxious substance into the tissue or peritoneal cavity. Increased muscle spasm or colicky pain could be associated with increased activity of the released prostaglandins into peritoneal fluids (Deraedt *et al.*, 1980; Akuodor *et al.*, 2015), or other inflammatory mediators like bradykinin that is a potent spasm genic to smooth muscles, including GIT muscles. Such phenomenon is observed following injection of acetic acid into peritoneal cavity.

Acetic acid-induced abdominal constriction/writhing is acceptable method that is simple and reliable to elucidate peripheral analgesic effect of compounds (Singh and Majumbar, 1995; Akuodor *et al.*, 2011). The study showed that acetic acid-induced abdominal constrictions in mice were significantly inhibited by the ethanol stem bark extract of *S. lehmbachii*. This action could be as a result of inhibitory effect on the cyclo-oxygenase pathway which plays important role in the biosynthesis of prostaglandins that are the endogenous mediators of pain. The anti-nociceptive action of this stem bark extract could be attributable to the inhibition of release of, or blockade of action of these the prostaglandins. The analgesic activity exhibited by this stem bark extract is similar to that of aspirin which possesses both peripheral and central analgesia (Rang *et al.*, 1999). It is therefore possible that the stem bark extract of *S. lehmbachii* could have similar action.

Furthermore, Singh and Majumbar (1995) reported that analgesic drugs acting centrally could elevate pain threshold towards heat and pressure. Tail immersion test further proved that the stem bark extract of *S. lehmbachii* possesses potent analgesic action by significantly protecting mice from heat stimuli from the hot-bath. Morphine acts by inhibiting central nociceptive neurons (Laurence and Bennett, 1994) and nociceptive spinal reflexes, thereby, blocking the transmission of nociceptive impulses through the dorsal horn (Fields and Basbaum, 1994; Oluwatoyin *et al.*, 2008). This effect is similar to that produced by Morphine, thereby, suggesting that the extract could possess similar central mechanism of action.

The pharmacological effects observed in stem bark of *S. lehmbachii* may be attributable to flavonoids, saponins, etc present in this plant. These findings from this study have revealed its potential for the possible development of novel herbal analgesic remedies. Further works are on the way to isolate, identify and characterize the specific substance of the stem bark responsible for these potent pharmacological activities.

CONCLUSION

The *Salacia lehmbachii* stem bark extract has potent anti-inflammatory, antipyretic and anti-nociceptive properties This study has clearly shown that the ethanol stem bark extract of *Salacia lehmbachii* markedly reduces/abolishes induced-inflammation, pyrexia and nociception in rodents used in all the experimental models; thereby justifying their widely use in folkloric herbal practice in Nigeria.

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