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ANTIINFLAMMATORY AND ANTIPYRETIC ACTIVITIES OF LEAF EXTRACT OF *SACCHARUM OFFICINARUM* IN RODENTS

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ABSTRACT

Background and Objective: *Saccharum officinarum* (Family-Poaceae) is used by the Ibibios of South South Nigeria in treating diseases such as malaria and fever among others. **Material and Methods:** Investigation for anti-inflammatory and antipyretic activities in rodents using known experimental models was carried out on the leaf extract of *S. officinarum.* 170-510 mg/kg of *S. officinarum* leaf extract was investigated for anti-inflammatory activity against carrageenin, egg albumin and xylene - induced edema models and antipyretic activity against D-amphetamine, 2,4-dinitrophenol and yeast-induced pyrexia models. **Results:** There was a significant ($p<0.05$ - 0.001) dose-dependent reduction of inflammation by the extract of *S. officinarum*. These reductions in inflammation were comparable to the effect of one of the standard drugs, (ASA, 100 mg/kg) used. The extract also caused significant ($p<0.05–0.001$) dose-dependent inhibition of pyrexia on amphetamine, dinitrophenol and yeast-induced pyrexia from 3 to 5 hrs of its post-administration. The anti-inflammatory and antipyretic activities of the extract of *S. officinarum* may in part be mediated through the chemical constituents present in the plant. **Conclusion:** The findings of this work confirm the ethnomedical uses of *S. officinarum* in the treatment of ailments of inflammatory and febrile origin.

KEYWORDS: Ethnomedicine**,** *Saccharum officinarum,* anti-inflammatory, antipyretic, fever, swelling.

1. INTRODUCTION

Saccharum officinarum (Family-Poaceae) also called sugarcane, is present in the tropical and subtropical regions of the world. Its traditional uses include the treatment of diarrhoea, dysentery, eye infirmities, fever, arthritis, bedsores, boils, cancer, colds, cough, skin sores, sore throat, hiccups, inflammation, laryngitis, splenic challenges, tumors, and wounds.[1] The leaf has been reported to have such biological effects as antibacterial and anthelmintic,[2] anti-hyperglycaemic, anti-hyperlipidaemic,[3] antioxidant,[3][4] diuretic and antiurolithiatic,[5] antidepressant and anticonvulsant,[6] analgesic[7] and antimalarial.[8] SAABMAL®: an ethnomedicinal polyherbal formulation containing *S. officinarum* has been approved for the treatment of uncomplicated malaria infection in Nigeria,[9] and *Saccharum officinarum* is also used to treat malaria in the Dangme West District of Ghana.[10] Phytochemical screening of leaf extract of *Saccharum officinarum* has reported the presence of glycosides, phytosterols, saponins, tannins, flavonoids.[2][11] Coutinho *et al.* (2016)[12] had also discovered the presence of flavones, phenolics and their derivatives from *S. officinarum* leaves. This work therefore reports the antiinflammatory and antipyretic activities of *S. officinarum* leaves.

2. MATERIALS AND METHODS

2.1 Plant materials

Fresh leaves of *Saccharum officinarum* were collected in June, 2020 from residential quarters in Uyo village in Uyo LGA, Akwa Ibom State, Nigeria. Identification and authentication of *Saccharum officinarum* was done in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria with a voucher specimen (UUPH 215b) prepared and deposited at the herbarium of the Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo.

2.2 Extraction

Fresh leaves of *S. officinarum* were washed, cut into smaller pieces and dried under shade for two weeks. The leaves were then pulverized to powder with the use of an electric grinder. The powdered leaf material (2 kg) was soaked in 7.5L of 50% ethanol at room temperature (28 ± 2 °C) for a period of 72 hours. Afterwards, it was filtered and the liquid filtrate was concentrated and evaporated to dryness in *vacuo* at 40°C using a rotary evaporator (BuchiLab Switzerland). The dried extract was stored at a temperature of -4 °C in a refrigerator until ready to be used for the experiments.

2.3 Anti-inflammatory studies

2.3.1 Evaluation of anti-inflammatory activity of *S. officinarum* extract using Carrageenin-induced mice hind paw oedema

Adult albino male mice were used after a 24-hour fast, and deprived of water only during the experiment. Induction of inflammation was by injecting 0.1 mL of freshly prepared carrageenin suspension in normal saline into the sub plantar surface of the mice hind paw. The linear circumference of the injected paw was measured before and 0.5, 1, 2, 3, 4 and 5 hrs after administering the phlogistic agent. The increase in paw circumference after administration of phlogistic agent was used as the parameter for measuring inflammation.[13][14] The difference in paw circumference between the control and 0.5, 1, 2, 3, 4 and 5 hrs after administering the phlogistic agent was used as a measure to assess the level of inflammation.[15] The leaf extract (170, 340 and 510 mg/kg i.p) was administered to various groups of 6 mice each, 1 hr before induction of inflammation. Control mice received carrageenin while reference group received ASA (100 mg/kg). The average (mean) edema was assessed by measuring with vernier calipers.

2.3.2 Egg albumin-induced inflammation

Inflammation was induced in mice by the injection of egg albumin (0.1mL, 1% in normal saline) into the sub plantar tissue of the right hind paw.[16][17] The linear circumference of the injected paw was measured before and 0.5, 1, 2, 3, 4 and 5 hrs after the administration of the phlogistic agent. The leaf extract (170, 340 and 510 mg/kg i.p) and ASA (100 mg/kg orally) were administered to groups (n=6) of 24 hrs fasted mice 1 hr before the induction of inflammation. The control group was given 10 mL/kg of distilled water orally. Edema (inflammation) was assessed as the difference in paw circumference between the control and 0.5, 1, 2, 3, 4 and 5 hrs post administration of the phlogistic agent.[15] The average (mean) edema was assessed by measuring with vernier calipers.

2.3.3 Xylene-induced ear oedema

Inflammation was induced in mice by topical administration of 2 drops of xylene at the inner surface of the right ear. The xylene was left to act for 15 mins. *S. officinarum* extract (170, 340 and 510 mg/kg i.p), dexamethasone (4 mg/kg) and distilled water (0.2 mL/kg) were orally administered to various groups (n=6) of mice 1 hr before the induction of inflammation. The animals were sacrificed under light anaesthesia and the left ears were cut off. The difference between the ear weights were taken as the oedema induced by the xylene.[18][17]

2.4 Evaluation of Antipyretic activity

2.4.1 Effect of *S. officinarum* leaf extract on D-amphetamine-induced pyrexia

Adult female and male albino rats were fasted for 24 hrs, but allowed water *ad libitum* before the experiment. They were randomly placed into groups of 6 rats each. Amphetamine (5 mg/kg, i.p) was administered to the animals after obtaining basal temperatures. Hyperthermia developed about 0.5 hrs of administering amphetamine. *S. officinarum* leaf extract (170, 340 and 510 mg/kg i.p), aspirin (100 mg/kg) and distilled water (10 mL/kg, orally) were respectively administered to the treatment and control groups of animals. Rectal temperatures of the animals were obtained at hourly intervals for 5 hrs.[19][20]

2.4.2 Effect of *S. officinarum* leaf extract on 2,4-Dinitrophenol (DNP)-induced pyrexia

Adult male and female albino rats that were fasted for 24 hrs but allowed water *ad libitum* were used for this experiment. They were placed randomly into groups of 6 rats each. DNP (10 mg/kg, i.p.) was administered to the rats after obtaining the basal rectal temperatures. Hyperthermia developed within 30 mins of DNP administration. *S. officinarum* leaf extract (170, 340, and 510 mg/kg i.p.), aspirin (100 mg/kg), and distilled water (10 mL/kg, orally) were administered to the treatment and control groups of animals. Rectal temperatures of the animals were obtained at 1hr intervals for 5hrs.[20]

2.4.3 Effect of *S. officinarum* leaf extract on yeast-induced pyrexia

Adult albino rats of both sexes fasted for 24 hrs but allowed water *ad libitum* were randomly placed into groups containing 6 rats each. At zero hour, the basal temperature of the rats was taken using digital clinical thermometer. Then, each animal received 10 mL/kg of 20% W/V aqueous suspension of yeast subcutaneously.[21][22] At suitable intervals beginning one hour after yeast injection, rectal temperature of animals was taken, and animals with increased temperature of 1˚C were selected and grouped for the study. *S. officinarum* **(**170, 340 and 510 mg/kg I.p) was then administered. after the pyrogen to respective groups of rats. The control group received distilled water (10 mL/kg) and the reference group was given ASA (100 mg/kg) both orally. The rectal temperatures of the groups were taken at 1hr interval for 5 hrs.

2.5 Statistical analysis

Data collected were analyzed using one way analysis of variance (ANOVA) followed by Tukey's multiple comparison post-test (Graph pad prism software Inc. La Jolla, CA, USA). Values were expressed as mean ± SEM and significance relative to control were considered at $p<0.001$ and $p<0.05$.

3. RESULTS

3.1 Evaluation of anti-inflammatory activity of the leaf extract

3.1.1 Carragenin-induced oedema in mice

The effect of ethanol leaf extract of *S. officinarum* on carragenin-induced oedema is as shown in Table 1. The extract (170-510 mg/kg) exerted a significant ($p<0.05$-0.001) anti-inflammatory effect in a non dose–dependent manner. The effect was pronounced in the different treatment group 30 min post-induction with carragenin.

The effect was sustained throughout the duration of the study (5 hrs) but was not comparable to the standard drug, ASA, 100 mg/kg (Table 1a and 1b).

Table 1a: Effect of *S. officinarum* leaf extract on carrageenan-induced oedema in rats.

TREATMENT/ DOSE (mg/kg)		TIME INTERVALS (hr)						
		0	0.5	1	2	3	4	5
CONTROL		2.36±0.02	3.62±0.05	4.23±0.04	3.93±0.03	3.75±0.01	3.51±0.02	3.11±0.02
Extract	170	2.32±0.05	3.14±0.11[a]	2.88±0.11[c]	2.64±0.12[c]	2.46±0.04[c]	2.40±0.10[c]	2.36±0.01[c]
	340	2.27±0.03	3.23±0.10	2.96±0.04[c]	2.71±0.01[c]	2.55±0.05[c]	2.41±0.01[c]	2.35±0.02[c]
	510	2.33±0.02	3.24±0.02	3.05±0.01[c]	2.80±0.03[c]	2.61±0.01[c]	2.52±0.02[c]	2.40±0.03[c]
ASA 100		2.29±0.11	3.11±0.03[a]	2.92±0.10[c]	2.78±0.10[c]	2.46±0.02[c]	2.39±0.02[c]	2.30±0.01[c]

Data are expressed as mean ±SEM. Significant at [a]p<0.05; [b]p<0.01;[c]p<0.001 when compared to control. n=6.

Table 1b: Effect of *S. officinarum* leaf extract on carrageenin-induced oedema in rats.

TREATMENT/ DOSE (mg/kg)		AVERAGE INFLAMMATION/OEDEMA (mm) ± SEM					
		0.5hr	1hr	2hr	3hr	4hr	5hr
CONTROL		1.26±0.03	1.87 ± 0.01	1.57 ± 0.02	1.39 ± 0.03	1.15 ± 0.04	0.75 ± 0.01
Extract	170	0.82±0.02[b]	0.56±0.01[c]	0.32±0.06[c]	0.14± 0.06[c]	0.08±0.03[c]	0.04±0.01[c]
	340	0.96±0.09	0.69± 0.02[c]	0.44±0.03[c]	0.28 ± 0.05[c]	0.14±0.03[c]	0.08±0.01[c]
	510	0.91±0.15[a]	0.72±0.03[c]	0.47±0.04[c]	0.28 ± 0.06[c]	0.19±0.01[c]	0.07±0.01[c]
ASA 100		0.82±0.02[b]	0.63±0.01[c]	0.49±0.05[c]	0.17 ± 0.02[c]	0.10±0.01[c]	0.01±0.01[c]

Data are expressed as mean ±SEM. Significant at [a]p< 0.05; [b]p<0.01; [c]p<0.001 when compared to control. n=6

3.1.2 Egg albumin-induced edema

Administration of leaf extract of *S. officinarum* (170-510 mg/kg) on egg albumin-induced edema in mice caused a significant (p<0.05-0.001) non dose-dependent anti-inflammatory effect against edema caused by egg albumin. The effect was intensed at 3-5hrs but not comparable to that of the standard drug, ASA (100 mg/kg)(Table 2a and 2b).

Table 2a: Effect of *S. officinarum* leaf extract on egg albumin-induced oedema in mice.

TREATMENT/ DOSE (mg/kg)		TIME INTERVALS (hr)						
		0	0.5	1	2	3	4	5
CONTROL		2.30 ± 0.02	3.60± 0.03	3.63 ± 0.09	3.56 ± 0.03	3.47 ± 0.08	3.08 ± 0.16	2.90 ± 0.18
Extract	170	2.33 ± 0.10	3.40 ± 0.03	3.44 ± 0.11	3.40 ± 0.02	3.38 ± 0.04	2.85 ± 0.15	2.47 ± 0.12
	340	2.27 ± 0.11	3.43 ± 0.10	3.45 ± 0.12	3.36 ± 0.09	2.73± 0.04c	2.50± 0.07a	2.32 ± 0.02
	510	2.31 ± 0.06	3.41 ± 0.08	3.40 ± 0.02	3.28 ± 0.04	2.84 ± 0.0c	2.66 ± 0.03	2.35 ± 0.02
ASA 100		2.30 ± 0.05	3.38 ± 0.02	3.43 ± 0.02	3.41 ± 0.03	2.71± 0.03c	2.58± 0.13a	2.31± 0.23a

Data are expressed as mean ±SEM. Significant at [a]p<0.05; [b]p< 0.01 when compared to control. n = 6.

Table 2b: Effect of *S. officinarum* leaf extract on egg albumin-induced oedema in rats.

TREATMENT/ DOSE (mg/kg)		AVERAGE INFLAMMATION/OEDEMA (mm) ± SEM					
		0.5hr	1hr	2hr	3hr	4hr	5hr
CONTROL		1.30 ± 0.02	1.33 ± 0.01	1.26 ± 0.01	1.17 ± 0.01	0.78 ± 0.02	0.60 ± 0.02
Extract	170	1.07 ±0.01	1.11 ± 0.02	1.07 ± 0.05	1.05 ± 0.01	0.52± 0.02c	0.14 ± 0.01c
	340	1.16 ±0.03	1.18 ± 0.02	1.09± 0.03	0.46 ± 0.03c	0.23± 0.01c	0.05 ± 0.02c
	510	1.10 ±0.02	1.09± 0.02	0.97 ± 0.05	0.53± 0.06c	0.35 ± 0.02c	0.04 ± 0.01c
ASA 100		1.08 ±0.01	1.13 ± 0.12	1.11 ± 0.13	0.41± 0.13c	0.28± 0.01c	0.01 ± 0.01c

Data are expressed as mean ±SEM. Significant at [a]p<0.05; [b]p<0.01, [c]p< 0.001 when compared to control. n = 6.

3.1.3 Xylene- induced ear edema

The anti-inflammatory effect of leaf extract of *S. officinarum* (170-510 mg/kg) against xylene-induced ear edema in mice is shown in Table 3. The extract exerted a dose-dependent anti-inflammatory effect which was significant (p<0.0-0.01). The effect of the highest dose (510 mg/kg) was more than that of the standard drug, dexamethasone (4.0 mg/kg).

Table 3: Effect of *S. officinarum* leaf extract on xylene-induced ear oedema in mice.

Treatment/Dose (mg/kg)		Weight of right ear (g)	Weight of left ear (g)	Increase in ear weight (g)	% inhibition
Control (normal saline) 0.2 mL		0.034 ± 0.002	0.125 ± 0.003	(267.64) 0.091 ± 0.002	
Extract	170	0.036 ± 0.001	0.07 ± 0.004	(94.44) 0.034 ± 0.005[a]	62.63
	340	0.040 ± 0.002	0.053 ± 0.005	(32.5) 0.013 ± 0.001[b]	85.71
	510	0.036± 0.002	0.046± 0.003	(27.77) 0.010 ± 0.01[c]	89.01
Dexamethasone 4.0		0.040 ± 0.003	0.056 ± 0.003	(50.00) 0.016 ± 0.003[c]	82.41

Values are expressed as mean ± SEM. Significance relative to control. [a]p<0.05; [b]p<0.01; [c]p<0.001. n = 6.

3.2 Evaluation of antipyretic activity of the extract

3.2.1 Effect of ethanol leaf extract of *S. officinarum* on D-amphetamine induced pyrexia

The antipyretic effect of the extract on amphetamine-induced pyrexia is shown in Table 4. The leaf extract (170-510 mg/kg), in the presence of the pyrogen, caused significant (p<0.05-0.001) reductions in the temperatures of the extract- treated rats when compared with the control. These effects were pronounced and sustained at 2-5 hrs post treatment with the extract. The antipyretic effects of the extract were comparable with that of the standard drug, ASA, 100 mg/kg (Table 4).

Table 4: Antipyretic effect of *S. officinarum* leaf extract on D-amphetamine-induced pyrexia.

Treatment/ Dose(mg/kg)		TIME INTERVALS (hrs)							
		Basal Temp	0	0.5	1.0	2.0	3.0	4.0	5.0
Control		34.45±0.12	36.10±0.13	36.26±0.22	36.44±0.65	36.91±0.66	37.09±0.22	37.28±0.33	37.10±0.18
Extract	170	34.57±0.10	35.76±0.38	35.78±0.15	35.70±0.27	35.62±0.05[a]	35.41±0.31[b]	34.22±0.39[a]	34.08±0.25[b]
	340	35.10±0.24	36.54±0.15	36.50±0.56	36.22±0.20	35.70±0.26[a]	34.88±0.16[a]	34.20±0.15[b]	33.88±0.52[c]
	510	34.85±0.08	35.66±0.24	35.64±0.18	35.55±0.18	34.90±0.12[a]	34.64±0.24[b]	34.17±0.18[b]	33.75±0.31[c]
ASA 100		34.95±0.36	35.30±0.29	35.20±0.20	35.01±0.25	34.87±0.14[a]	34.25±0.10[c]	33.97±0.14[c]	33.51±0.11[c]

Figures in parenthesis indicate % increase in ear weight, significant at [a]p<0.05, [b]p < 0.01, [c]p < 0.001 when compared with control. n = 6.

3.2.2 Effect of ethanol leaf extract of *S. officinarum* on 2,4-dinitronitrophenol (DNP)-induced pyrexia in rats

The leaf extract (170-510 mg/kg) exerted significant (p<0.05-0.001) dose-dependent lowering of temperature in DNP-induced pyretic rats. The antipyretic effect was however, pronounced (p<0.05-0.001) and sustained at 4 - 5 hrs in all the extract-treated groups. The effect of the highest dose (510 mg/kg) was comparable to that of the standard drug, ASA, 100 mg/kg (Table 5).

Table 5: Antipyretic effect of *S. officinarum* leaf extract on Dinitrophenol-induced pyrexia.

Treatment/ Dose(mg/kg)		TIME INTERVALS (hrs)							
		Basal Temp	0	0.5	1.0	2.0	3.0	4.0	5.0
Control		34.80±0.25	37.30±0.26	37.56±0.12	37.62±0.21	37.70±0.30	37.73±0.24	37.60±0.16	37.54±0.21
Extract	170	34.68±0.28	37.18±0.33	36.91±0.24	36.88±0.66	36.52±0.54	36.38±0.14[a]	36.24±0.17[a]	36.32±0.53
	340	35.05±0.21	37.27±0.36	36.55±0.56	36.31±0.20	36.23±0.21	36.24±0.12[a]	36.16±0.33[a]	35.91±0.37[a]
	510	35.15±0.24	37.41±0.22	36.34±0.64	36.23±0.32	36.01±0.24	36.00±0.14[b]	35.95±0.66[b]	35.32±0.26[b]
ASA 100		34.64±0.32	37.16±0.18	36.51±0.15	36.13±0.12	36.00±0.25	35.77±0.22[b]	35.34±0.12[c]	35.27±0.36[c]

Values are expressed as mean ± SEM. Significance relative to control. [a]p<0.05; [b]p<0.01; [c]p<0.001. n = 6.

3.2.3 Effect of leaf extract of *S. officinarum* on yeast-induced pyrexia in rats

Administration of leaf extract of *S. officinarum* (170-510 mg/kg) caused significant (p>0.05-0.001) reduction of body temperature of rats elevated by the administration of yeast. The effect of the extract was pronounced and sustained at 3 - 5 hrs. The antipyretic effects of the extract was not comparable to that of the standard, ASA, 100 mg/kg (Table 6).

Table 6: Antipyretic effect of *S. officinarum* leaf extract on yeast-induced pyrexia.

Treatment/ Dose(mg/kg)		TIME INTERVALS (hrs)							
		Basal Temp	0	0.5	1.0	2.0	3.0	4.0	5.0
Control		34.28±0.14	36.50±0.56	36.62±0.31	36.68±0.37	36.73±0.65	36.41±0.28	36.28±0.25	36.05±0.12
Extract	170	34.05±0.16	36.64±0.43	36.85±0.52	36.76±0.26	36.22±0.28	35.68±0.22	33.85±0.16[c]	33.64±0.26[b]
	340	34.50±0.15	36.58±0.45	36.60±0.38	36.56±0.33	35.83±0.45	34.23±0.24[b]	33.86±0.11[c]	33.21±0.24[b]
	510	35.10±0.38	36.80±0.18	36.91±0.24	36.76±0.21	35.41±0.33	34.32±0.16	34.02±0.14[c]	33.25±0.60[c]
ASA 100		34.36±0.22	36.46±0.16	35.96±0.44	35.35±0.36	34.78±0.10	34.15±0.18	33.14±0.20[c]	33.02±0.33[c]

Values are expressed as mean ± SEM. Significance relative to control. [a]p<0.05; [b]p<0.01; [c]p<0.001. n=6.

4. DISCUSSION

In this study, the ethanol leaf extract was evaluated for anti-inflammatory and antipyretic activities using various experimental models. In the carragenin-induced oedema, the extract (170 - 510 mg/kg) was observed to have exerted a strong effect at the early stage of inflammation (1-2 hrs) indicating strong effect probably on histamine, serotonin and kinnins that are involved in the early stage of carragenin-induced oedema.[23] The extract further caused prominent reduction of the later stage of the oedema suggesting its ability to inhibit prostaglandin which is known to mediate the second phase of carragenin induced inflammation.[23] However, ASA (100 mg/kg) a prototype NSAID, a cyclooxygenase inhibitor whose mechanism of action involves inhibition of prostaglandin, produced a considerable inhibition of the paw swelling induced by carragenin injection.

The extract also inhibited egg albumin-induced oedema demonstrating that it can inhibit inflammation by blocking the release of histamine and 5-HT, two mediators that are released by egg albumin.[24] However, ASA, a cyclooxygenase inhibitor significantly reduced oedema produced by egg albumin.

The extract exerted a significant ($p<0.01$) inhibition of xylene-induced ear oedema when given at higher doses, suggesting the inhibition of phospholipase A_2 (PLA_2) that is involved in the pathophysiology of inflammation due to xylene.[25] However, dexamethasone, a steroid anti-inflammatory agent produced significant reduction in the mean right ear weight of positive control rats indicating an inhibition of PLA_2.

According to Okokon *et al*, 2022,[8] phytochemical screening of the leaf extract revealed the presence of alkaloids, cardiac glycosides, tannins, saponins, terpenes and flavonoids, and GC-MS analysis of the different fractions showed the presence of pharmacologically active compounds such as 2,3 dihydro benzofuran, and polyunsaturated fatty acids such as 9-Octadecenoic acid (Z)-, 2- hydroxyethyl ester, p-Hydroxycinnamic acid, Hexadecanoic acid, ethyl ester and methyl ester which have been implicated in the anti-inflammatory activity of plants.[26][27][28] Furthermore, LCMS-TOF identified the presence of p-cumaric acid in the DCM fraction,[8] and LC-TOF-MS/MS analysis of the butanol fraction indicated the presence of a phenolic acid, 4-hydroxycinnamic acid, a flavonoid, 3,4',5,6,7-pentamethoxyflavone, and a flavonoid glycoside, tricin-7-O-neohesperidoside.[8] The presence of these phytochemicals could have contributed to the observed activity.

Moreso, anti-inflammatory activities of plants have been linked to antioxidant potentials.[29] The plant extract has been revealed by GCMS to contain phenolic compounds with antioxidant potentials such as p-Hydroxycinnamic acid, ethyl ester and, Phenol, 2,6-dimethoxy-4-(2-propenyl)-.[30] Also Triterpene-fatty acid esters and free fatty acids including long chain C16-C20 unsaturated fatty acids have been suggested to be responsible for the anti-inflammatory activity of plants.[31]

Flavonoids are known anti-inflammatory compounds acting through inhibition of the cyclo-oxygenase pathway.[32] Some flavonoids are reported to block both the cyclooxygenase and lipoxygenase pathways of the arachidonate cascade at relatively high concentrations, while at lower concentrations they only block lipoxygenase pathway.[33] Some flavonoids exert their antinociception via opioid receptor activation activity.[34][35][36] Flavonoids also exhibit inhibitory effects against PLA_2 and phospholipase C,[37] and cyclooxygenase and/or lipoxygenase pathways.[38]

Triterpenes have been implicated in anti-inflammatory activity of plants.[39][40] Ursolic acid is a selective inhibitor of cyclooxygenase-2.[41] The anti-inflammatory activity demonstrated by the leaf extract in this study may in part be due to its phytochemical constituents which maybe acting through antioxidant action and other mechanisms.

On antipyretic activity, the extract significantly inhibited amphetamine, dinitrophenol and yeast-induced pyrexia. Amphetamine acts on the brain causing the release of biogenic amines from their storage sites in nerve terminals resulting in increased level of cAMP, and subsequent synthesis of prostaglandins from arachidonic acids produced in neurons by receptor-mediated hydrolysis of phospholipids.[42] This leads to hyperthermia. Dinitrophenol induces hyperthermia by uncoupling oxidative phosphorylation causing release of calcium from mitochondrial stores and also prevents calcium reuptake. This results in increased level of intracellular calcium, muscle contraction and hyperthermia.[43] Yeast induces pyrexia by increasing the synthesis of prostaglandins.[44] The extract may have reduced pyrexia by reducing brain concentration of prostaglandin E_2 especially in the hypothalamus through its action on COX-2, or by enhancing the production of the body's own antipyretic substances such as vasopressin and arginine.[45] The hypothermic activity of the extract could also have been mediated by vasodilatation of superficial blood vessels leading to increased dissipation of heat following resetting of hypothalamic temperature control center.[46] This action may be due to the phytochemical compounds in this plant. Therefore, the temperature lowering activity of the extract may not be unconnected with the inhibition of one or combination of the above-mentioned mechanisms. The GC-MS analysis of the dichloromethane fraction has revealed the presence of terpinen-4-ol[8], which has been reported to suppress production of prostaglandin and in vitro of TNF-α, IL-1β, as well as IL-8, IL-10 and PGE_2 by LPS-activated human blood monocytes.[47][48] These compounds may in part be responsible for the observed antipyretic activities of the leaf extract.

CONCLUSION

The results of the study indicates that the leaf extract of *Saccharum officinarum* possesses antiinflammatory and antipyretic potentials which are due to the activities of its phytochemical constituents.

Significance Statement: This study shows that the plant leaf has positive effects on inflammation and pyrexia. The study will help researchers to dig deeper in these areas that has not been previously explored. New discoveries can then be arrived at.

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Ethical Approval: The research was ethically approved by the Experimental Ethics Committee on Animal Use of the Faculty of Pharmacy, University of Uyo, Nigeria and was conducted in accordance with the National Institute of Health Guide for the Use of Laboratory Animals (NIH, 1996).

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