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In Vivo Antiplasmodial and Antipyretic Activities of Ethanol Leaf Extract of *Ananas comosus* (L.) Merr

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ABSTRACT

Ananas comosus (L.) Merr. (Bromeliaceae), an important herb used traditionally in the treatment of malaria, fever and other diseases was evaluated for antiplasmodial and antipyretic activities to ascertain the folkloric claim of its antimalarial and antipyretic activities. The leaf extract (150-450 mg/kg) was investigated for suppressive and curative antiplasmodial activities against chloroquine-sensitive *Plasmodium berghei* infection in Swiss albino mice and for antipyretic activity against D-amphetamine, 2,4-dinitrophenol and yeast-induced pyrexia. Artesunate (5 mg/kg) was used as a positive control for antiplasmodial models and acetyl salicylic acid (ASA),(100 mg/kg) was used as a standard for antipyretic models. Thin films made from tail blood of each mouse were used to assess the level of parasitaemia of the mice. The leaf extract progressively reduced parasitaemia induced by chloroquine-sensitive *P. berghei* infection in suppressive (3.00-36.09%), and curative (14.87–98.22%) models in mice. These reductions were statistically significant ($p<0.01$–0.001).They also improved significantly ($p<0.01$–0.001)the mean survival time (MST)from 13.75 to 26.10 d in curative model relative to control (13.75 d). The extract exerted considerable inhibition of pyrexia on amphetamine, dinitrophenol and yeast-induced pyrexia (5 h).Inhibitions were significant ($p<0.05$–0.001)from 3 to 5 h post-administration of extract and in a dose-dependent fashion. The plant may possess antiplasmodial and antipyretic effects which may in part be mediated through the chemical constituents of the plant.

Keywords: *Ananas comosus*, antimalarial, antipyretic, antiplasmodial

Introduction

Ananas comosus(L.) Merr. (Bromeliaceae) which is also known as pineapple is cultivated solely for its edible fruits worldwide. Different part of the plant is use medicinally for the treatment of various diseases. In Nigeria, the whole plant is used to treat typhoid fever,[1] while the fruits are used to treat convulsions.[2]The leaf is also use by the Ibibios of Niger Delta region of Nigeria to treat malaria, arthritis, pains and fever.[3] The Garo tribal community of Bangladesh use the fruit juice for fever and the leaf juice for helminthiasis and jaundice.[4] The leaf extract of *A. Comosus* have been reported to contain cyclotrisiloxane, furfural, D-glucose, 2,3-dihydro-4-H-pyran-4-one, 2-furancarboxaldehyde and 2,3-dihydrofuran.[5]Yeragamreddy *et al*.,[6] and Kalpana*et al*.,[7]also had reported that the leaf extract contain alkaloids, saponins, tannins, anthraquinones, terpenes, flavonoids, phenols, sterol and cardiac glycosides among others. Seven compounds, ananasate, 1-O caffeoylglycerol, 1-O-p-coumaroyl glycerol, caffeic acid, p-coumaric acid, beta-sitosterol and daucosterol have also been reported from theleaves of the plant.[8]Kargutkar and Brijesh,[9] also reported the presence of 4-hydroxy pelargonic acid, 3,4,5-trimethoxycinnamic, 4-methoxycinnamic acid, campesterol and ethyl isoallocholate in the leaf extract.

Biological activities on the leaf include; antidiabetic activity against streptozotocin (STZ)-induced diabetic rats,[7] increased sensitivity to insulin in STZ-treated diabetic rats and HepG2 cells,[10] hypoglycaemic activity in alloxan diabetic rats but not in normal rats in oral glucose tolerance tests (OGTT),[11] anti-inflammatory,[9,12] analgesic[13]and a weak *in vitro* antiplasmodial activities.[3] We report in this work the antimalarial and antipyretic activities of the leaf extract of *Ananas comosus* for the first time.

Materials and Methods

Collection of plant materials

The fresh leaves of *Ananas comosus* were collected in August, 2018 at a Farmland in Uyo in Uyo LGA, Akwa Ibom State, Nigeria. The leaves were identified and authenticated as *Ananas comosus* by Dr. Margaret Bassey, a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium Specimen was deposited at the Faculty of Pharmacy Herbarium, University of Uyo, Uyo with voucher no. UUH 114b.

Extraction

The plant parts (leaves) were washed and air- dried for 2 weeks. The dried leaves were pulverized using a pestle and mortar. The powdered leaf was macerated in 95% ethanol for 72 h. The ethanol extract obtained by filtration was evaporated to dryness over a water bath at

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60˚C. The extract was stored in a refrigerator at -4˚C until it was used for the experiment.

Animals
The animals (65 Swiss albino mice and 75 Wistar rats) of either sex were used for the experiments. The animals were housed in standard cages and were maintained on a standard pelleted feed (Guinea Feed) and water *ad libitum*.

Ethical Approval
Permission and approval for animal studies with reference number (CHS/AE/018/83) were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo, Uyo.

Microorganism (Parasite)
A chloroquine sensitive strain of *Plasmodium berghei* (ANKA) was obtained from the National Institute of Medical Research (NIMR), Yaba Lagos, Nigeria and was maintained by sub-passage in mice.

Determination of median lethal dose (LD_{50})
The median lethal dose (LD_{50}) of the extract was estimated using albino mice by intraperitoneal (i.p) route using a modified method of Lorke.[14]This involved intraperitoneal administration of different doses of the extract (1000 – 5000mg/kg) in aqueous suspension to groups of five mice each. The animals were observed for manifestation of physical signs of toxicity such as writhing, decreased motor activity, decreased body/limb tone, decreased breathing and death. The number of deaths in each group within 24 hours was recorded. The LD_{50} was calculated as geometrical means of the maximum dose producing 0% (a) and the minimum dose producing 100% mortality (b).

$$LD_{50} = \sqrt{ab}$$

Parasite inoculation
Each mouse used in the experiment was inoculated intraperitoneally with 0.2 mL of infected blood containing about 1 x 10^7 *P. berghei berghei* parasitized erythrocytes. The inoculum consisted of 5 x 10^7*P. berghei berghei* erythrocytes per mL. This was prepared by determining both the percentage parasitaemia and the erythrocytes count of the donor mouse and diluting the blood with isotonic saline in proportions indicated by both determinations.[15]

Drug administration
The drug(artesunate), and the extract used in the antiplasmodial study were orally administered with the aid of a stainless metallic feeding cannula.

Evaluation of anti-plasmodial activity of ethanol leaf extract of Ananas comosus
Evaluation ofsuppressive activity of the extract (4-day test).
This test was used to evaluate the schizontocidal activity of the extractand artesunate against early *P. berghei berghei*infection in mice. This was done as described by Knight and Peters.[16]Thirty mice (19-25 g) were randomly divided into five groups of six mice each. On the first day (D_O), the thirty mice were infected with the parasite and randomly divided into various groups. These were administered with the extract and artesunate 10-15 min post-infection. The mice in group 1 were administered with the 150 mg/kg, the group 2, 300 mg/kg and group 3, 450 mg/kg of crude extract, while group 4 was administered with 5mg/kg of artesunate (positive control), and 10 mL/kg of distilled water to group 5 (negative control) for four consecutive days ($D_0 – D_3$) between 8am and 9am. On day 4 (D_4), thin blood film was made from tail blood. The film was then stained with Giemsa stain to reveal parasitized erythrocytes out of 500 in a random field of the microscope. The percentage chemosuppression of parasitaemia was calculated in comparison with the controls as follows:

$$\frac{Avearge\ \%\ parasitaemia\ in\ negative\ control - Average\ \%\ parasitaemia\ in\ test\ group}{Average\ \%parasitaemia\ in\ negative\ control}$$

Evaluation of curative activity of extract (Rane's test)
This was used to evaluate the schizontocidal activity of the extract and artesunate in established infection. This was done as described by Ryley and Peters.[17]*P. berghei berghei* was injected intraperitoneally into another 30 mice (20 -25 g) on the first day (D_O). Seventy–two hours later (D_3), the mice was divided randomly into five groups of six mice each. Different doses of the extract, 150 mg/kg, 300 mg/kg and 450 mg/kg were orally administered respectively to mice in groups 1-3. Artesunate (5 mg/kg/day) was administered to the group 4 (positive control) and group 5 was given 10 mL/kg of distilled water (negative control). The extract and drugs were administered once daily for 5 days. Giemsa stained thin smears were prepared from tail blood samples collected on each day of treatment to monitor parasitaemia level. The mean survival time (MST) of the mice in each treatment group was determined over a period of 29 days post infection.

$$MST = \left(\frac{No.\ of\ days\ survived}{Total\ no.\ of\ days}\right) \text{ x } 100$$

Evaluation of antipyretic activity
Evaluation of antipyretic activity of the leaf extract of A. comosus on D-amphetamine-induced pyrexia
Thirty adult wistar rats (130 – 150 g) of both sexes fasted for 24 hours but allowed water *ad libitum* were used for the experiment. They were randomized into groups of 6 rats each. Amphetamine (5 mg/kg, i.p) was administered to the animals after obtaining basal temperatures. Hyperthermia developed 0.5 h following amphetamine administration. Different doses of extract (150, 300 and 450 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 an hour interval for 5 h.[18,19]

Effect of leaf extract of Ananas comosus on 2,4-dinitrophenol (DNP)-induced pyrexia
Thirty adult Wistar rats of both sexes fasted for 24 h but allowed water *ad libitum* were used for the experiment. They were randomized into groups of six rats each. DNP (10 mg/kg, i.p.) was administered to the rats after obtaining the basal rectal temperatures. Hyperthermia developed within 30 min of DNP administration. Different doses of extract (150, 300, and 450 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 1 h intervals for 5 h.[19]

Effect of leaf extract of Ananas comosus on yeast-induced pyrexia
Thirty adult wistar rats (125 – 130 g) of both sexes fasted for 24 hours but allowed water ad libitum were used for the experiment. They were randomized into groups of 6 rats each. At zero hour, the basal temperature of the rats was taken using digital clinical thermometer. Thereafter, each animal was administered subcutaneously with 20% W/V aqueous suspension of yeast at a volume of 10 mL/kg.[19,20] At suitable intervals beginning one hour after yeast injection, rectal temperature of animals were taken, animals with increase of 1˚C were selected and grouped forthestudy.The extract under study was administered i.p. after the pyrogen at doses of 150, 300 and 450 mg/kg to respective groups of rats. The control group received distilled water (10 mL/kg) and the reference group administered with ASA (100 mg/kg) both orally. The rectal temperature of the groups was taken at 1h interval for 5 h.

Statistical analysis
Data obtained were analyzed using Students' t-test and one way analysis of variance (ANOVA) followed by Turkey-Kramer multiple comparison test. Differences between means were considered significant at 1% and 5% level of significance, that is $p \leq 0.01$and 0.05.

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Results and Discussion

Determination of median lethal dose (LD_{50})
The median lethal dose (LD_{50}) was calculated to be 1520.33 mg/kg. The physical signs of toxicity included excitation, paw licking, increased respiratory rate, decreased motor activity, gasping and coma which was followed by death.

Effect on suppressive activity of leaf extract of Ananas comosus
The extract showed a dose-dependent chemosuppressive effect on the parasitaemia. These effects were statistically significant relative to the control ($p<0.05$ - 0.001).The chemo-inhibitory percentages ranged from 3.00 to 36.09% (Table 2). However, the effect of the extract was not comparable to that of the standard drug, artesunate, with a chemo-suppression of 98.82% (Table 1).

Antiplasmodial effect of ethanol leaf extract of Ananas comosus on established infection
The extract showed a dose-dependent schizonticidal effect on the parasitaemia. There were reductions in the percentage parasitaemia of the extract/artesunate-treated groups compared to that of the control in which prominent increases were recorded. These reductions were statistically significant relative to the control ($p<0.05$ - 0.001)(Figure 1). The effect of the extract (150 - 450 mg/kg) was not comparable to that of the standard drug, artesunate (Figure 1). The extract also protected the treated mice against malaria and thereby caused a prolongation of their survival time from 13.75 to 26.10 days (Table 2).

Effect of ethanol leaf extract of A. comosus on D-amphetamine induced pyrexia
The antipyretic effect of the extract on amphetamine-induced pyrexia is shown in Table 3. *A. comosus* leaf extract (150-450 mg/kg), in the presence of D-amphetamine, caused significant ($p<0.05$ – 0.001) reductions in the temperatures of the extract-treated rats when compared with the negative control. These effects were pronounced at the 4 h and 5 h post treatment with the extract. The antipyretic effects of the extract were comparable with that of the standard drug, ASA (100 mg/kg) (Table 3).

Effect of ethanol leaf extract of A. comosus on 2,4-dinitronitrophenol (DNP)-induced pyrexia in rats
The leaf extract (150-450 mg/kg) demonstrated 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)at the 5 h in all the extract-treated groups. The effect of the highest dose (450 mg/kg) was comparable to that of the standard drug, ASA (100 mg/kg) (Table4).

Effect of leafextract of on yeast-induced pyrexia in rats
Ethanol leaf extract of *A. comosus*(150-450 mg/kg) caused significant ($p<0.05$-0.001)reduction of rat body temperature of rats elevated by the administration of yeast. The effects of different doses of the extract were pronounced and dose-dependent at 3-5 h. The antipyretic effect of the extract was not comparable to that of the standard, ASA 100 mg/kg (Table 5).
The leaf of *A. comosus* is used traditionally by the Ibibios of Southern Nigeria and other parts of the world as a malarial remedy and febrifuge.[3] This work was designed to evaluate the antimalarial and antipyretic activities of the leaf extract of *A. comosus*. The median lethal dose (LD_{50}) value was calculated to be 1520.33 mg/kg which shows that the leaf extract is slightly toxic.[21]The antimalarial activity of the leaf extract was evaluated against rodent malaria parasite, *Plasmodium bergheiberghei* infection in mice using standard *in vivo* models. The extract was found to reduce parasitemia in suppressive and curative models in a dose-dependent fashion. However, the leaf was found to exert a weak suppressive activity in this study. The extract also prolonged the MST of the mice considerably suggesting that they were potentially able to offer significant degree of protection to the mice. This activity could have resulted from plasmodicidal or plasmodistatic activity of the extract and fractions. These results corroborate the report of Okokon *et al*.[3] who had earlier reported a weak *in vitro* antiplasmodial activity of the leaf extract against chloroquine-sensitive and resistant strains of *P. falciparum* and the involvement of immune system in the antimalarial activity of the leaf extract.
The observation that the extract showed considerable *in vivo* activity suggest also the involvement of antioxidant activity which may be due to the activities of phytochemical compounds present in the leaf extract such as flavonoids,[22]1-O caffeoylglycerol, 1-O-p-coumaroylglycerol, caffeic acid, p-coumaric acid, beta-sitosterol and daucosterol,[8]4-hydroxy pelargonic acid, 3,4,5-trimethoxycinnamic, 4-methoxycinnamic acid, campesterol,[9]cyclotrisiloxane, furfural, D-Glucose, 2,3-dihydro-4-*H*-pyran-4-one, 2-furancarboxaldehyde and 2,3-dihydrofuran,[5] alkaloids, saponins, tannins, anthraquinones, terpenes, flavonoids, phenols, sterol and cardiac glycosides.[6]
Antioxidant potentials of some plant and natural products especially flavonoids and other phenolic compounds have been found to promote schizonticidal activity by modulating the cellular signalling pathway[23]and this has been suggested to be responsible for antiplasmodial activity of compounds such as quercetin,[24,25] as elevated free radicals levels which are common features of malaria disease are implicated in severe malaria complications. This also could be one of the modes of action of this extract as it contains phenolics and flavonoids with antioxidant activity.

Table 1: Suppressive Activities of leaf extract of *Ananas comosus* (4-day test).

Drug/extract	Dose (mg/kg)	Parasitaemia	% chemo-suppression
Distilled water	10 mL/kg	44.33 ± 2.18	_
Extract	150	43.0 ± 2.15	3.00
	300	34.33 ± 6.96[a]	22.55
	450	28.33 ± 5.92[b]	36.09
Artesunate	5	0.52 ± 0.01[b]	98.82

Values are expressed as mean ± S.E.M. Significant relative to control:[a]$p< 0.05$;[b]$p < 0.001$. n = 6.

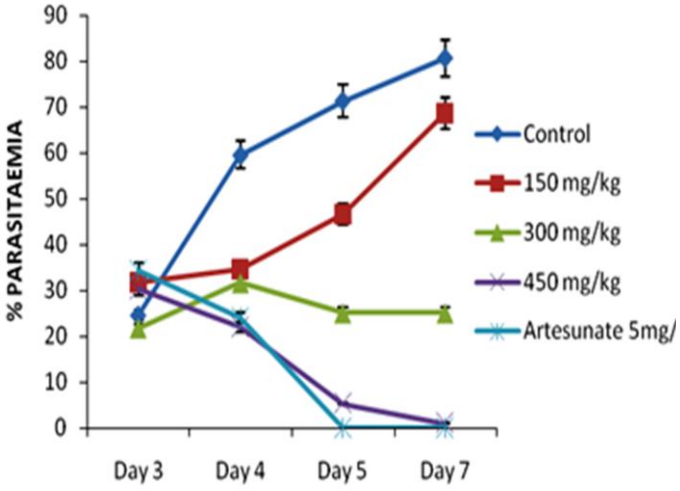

Figure 1: Antiplasmodial activity of leaf extract of *Ananas comosus* (Curative test).

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Table 2: Mean survival time of mice treated with leaf extract of *Ananas comosus* during established *Plasmodium berghei berghei* infection .

DRUG/Extract	DOSE mg/kg	Mean Survival Time (Days)
Distilled water	10 mL/kg	13.75 ±1.43
Extract	150	20.76±1.24[a]
	300	22.68±1.03[a]
	450	26.10±0.50[b]
Artesunate	5	30.00 ±0.00[a]

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

There are other mechanisms of antiplasmodial activity of flavonoids besides antioxidant activity such as chelation of nucleic acid base pairing of the parasite[26], modulation of host immunity to tackle disease and inhibition of plasmodialenoyl-ACP reductase (FAB I enzyme) - a key regulator of type II fatty synthases (FAS-II) in *P. falciparum*,[27,28] binding of the parasite's serinethreonine kinase with high affinity thus affecting development.[29] These compounds (flavonoids) present in this plant extract may in part have contributed to the plasmodicidal activity of this extract and therefore explained the mechanism of antiplasmodial effect of the extract.

Table 3: Antipyretic effect of leaf extract of *Ananas comosus* 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	34.47±0.18	36.23±0.64	36.67±0.61	36.83±0.46	36.93±0.15	37.15±0.71	37.22±0.66	36.80±0.70
Extract 150	34.67±0.16	36.16±0.33	36.77±0.32	36.74±0.02	36.28±0.66	36.04±0.06[b]	35.42±0.15[a]	34.24±0.12[b]
Extract 300	35.10±0.27	36.24±0.54	36.92±0.49	36.56±0.15	35.80±0.12[a]	35.15±0.10[a]	34.80±0.16[b]	34.30±0.33[c]
Extract 450	34.55±0.12	36.38±0.75	36.80±0.45	36.68±0.12	35.52±0.14[a]	35.16±0.14[b]	34.92±0.18[b]	34.12±0.02[c]
ASA 100	34.14±0.18	36.52±0.98	36.87±0.18	36.12±0.16	35.47±0.16[a]	34.80±0.11[c]	34.25±0.12[c]	33.85±0.16[c]

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

Table 4: Antipyretic effect of leaf extract of *Ananas comosus* 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	34.92±0.34	36.15±0.14	36.58±0.22	36.95±0.18	36.77±0.51	36.57±0.23	36.07±0.41	36.17±0.41
Extract 150	34.40±0.14	36.32±0.25	36.60±0.81	36.65±0.42	36.35±0.56	35.77±0.42	35.45±0.25[c]	34.32±0.42[b]
Extract 300	34.95±0.13	36.22±0.16	36.68±0.56	36.50±0.24	35.53±0.12	35.15±0.16[b]	34.71±0.22[c]	34.23±0.26[b]
Extract 450	35.00±0.20	36.27±0.10	36.51±0.49	36.70±0.13	35.45±0.36	34.80±0.22[c]	34.21±0.11[c]	34.11±0.43[c]
ASA 100	34.52±0.13	36.07±0.32	36.84±0.48	35.50±0.12	34.97±0.16[c]	34.57±0.11[c]	34.30±0.17[c]	34.03±0.18[c]

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

Table 5: Antipyretic effect of leaf extract of *Ananas comosus* 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	34.25±0.21	37.15±0.11	37.87±0.74	37.82±0.10	37.75±0.68	37.70±0.37	37.77±0.29	37.50±0.23
Extract 150	34.30±0.16	37.23±0.46	36.88±0.24	36.65±0.33	36.26±0.55	36.16±0.39[a]	36.27±0.39[a]	36.30±0.54
Extract 300	34.27±0.22	37.18±0.32	36.65±0.56	36.42±0.26	36.19±0.21	36.11±0.10[a]	36.03±0.45[a]	36.00±0.61[a]
Extract 450	34.34±0.32	37.34±0.40	36.24±0.16	36.35±0.15	36.08±0.16	36.00±0.22[b]	35.90±0.16[b]	35.15±0.18[b]
ASA 100	34.18±0.44	37.14±0.51	36.67±0.28	36.22±0.21	36.40±0.60	35.84±0.31[b]	35.35±0.49[c]	34.50±0.27[c]

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

On antipyretic activity, the extract inhibited significantly amphetamine, dinitrophenol and yeast-induced pyrexia. The leaf extract (150-500 mg/kg) showed considerable dose-dependent reduction in the elevated temperatures of the extract-treated rats in the three models (amphetamine, DNP and yeast-induced pyrexia) evaluated. The antipyretic effect was sustained throughout the duration of the work with the effect being quite comparable to ASA (100 mg/kg). Pyrexia (fever) is the body's response to tissue damage, inflammation, malignancy or graft rejection that results in the formation of large amount of cytokines, interleukin, interferon and TNF-α, and increasing PGE_2 to trigger the hypothalamus and then cause fever.

In the brain, amphetamine causes the release of biogenic amines that are stored in nerve terminals leading to increases in the cAMP level, resulting in prostaglandins synthesis from arachidonic acids in neurons through hydrolysis of phospholipids. This results in hyperthermia.[30]DNP causes hyperthermia by uncoupling oxidative phosphorylation resulting in calcium release from mitochondrial stores and preventing calcium reuptake. This leads to increased intracellular calcium level, muscle contraction and hyperthermia.[31]The extract through its components may have caused stimulation of the sarcoplasmic reticulum Ca^{2+}-ATPase thus promoting calcium reuptake into the sarcoplasmic reticulum, muscle contraction and hypothermia.[32]Yeast-induced pyrexia which is pathogenic and caused by PGE_2 production, which then resets the thermoregulatory center in the hypothalamus to a higher level.[33,34]

Antipyretics lower elevated body temperature by suppressing cyclooxygenase actions and decreasing PGE_2 levels in the hypothalamus.[35]Temperature regulation involves a delicate balance between heat production and loss, and the hypothalamic thermostat.[35] Cyclooxygenase-2(COX-2)activity leads to the synthesis of PGE_2 which is an imperative mediator of fever within the hypothalamus and most NSAIDs antipyretic activity results from suppression of prostaglandin synthetase in the hypothalamus. The resultant antipyretic effects could be due to reduced PGE_2 levels in the hypothalamus acting on COX-2, or through increased production of substances such as vasopressin and arginine that reduce temperature.[36,37]Another possible antipyretic mechanism of the extract is the mediation of the vasodilation of superficial blood vessels which causes improved heat loss from resetting of hypothalamic thermostat.[37,38]The extract may have caused hypothermia by acting through any of these mechanisms.

Flavonoids such as baicalin exhibit antipyretic activity by inhibiting tumour necrosis factor,[34] and related compounds also suppress arachidonic acid peroxidation, resulting in decreased prostaglandin levels and fever reduction.[39]The phytochemical constituents of this extract which include flavonoids and other phenolic compounds[40] may be responsible for its antipyretic effect through any or all mechanisms described here.

Conclusion

The results of this study demonstrated that the leaf extract of *A. comosus*possibly possesses considerable antiplasmodial and antipyretic properties. These confirm its use in the treatment of malaria and fever in folkloric medicine.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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