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Antipyretic Properties of Methanol Stem Bark Extracts of *Acacia hockii* De Wild and *Kigelia africana* (Lam) Benth in Wistar Rats

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Abstract

Synthetic antipyretic drugs are not readily accessible and have adverse side effects. Herbal medicines possess bioactive compounds that are safer and efficient in the management of various diseases and disorders. *Acacia hockii* and *Kigelia africana* are traditionally used to manage pyrexia among the Embu and Mbeere communities in Kenya but lack scientific data to validate their use. The present study evaluated for the antipyretic activity of the *A. hockii* and *K. africana* in rat models to scientifically validate their traditional use. The plant samples were collected with the help of local herbalists in Embu County, Kenya and transported to Kenyatta University for cleaning, air drying, milling, and extraction. Adult male Wistar rats were randomly divided into six groups of 5 animals each; normal control, positive control, negative control, and three experimental groups. The antipyretic effect was assessed using turpentine-induced pyrexia method. The antipyretic activities of the extracts were compared to reference drug aspirin. The stem bark extract of *A. hockii* reduced the raised rectal temperature by between 0.62-3.88% while the stem bark extract of *K. africana* reduced the elevated rectal temperature by between 0.06-3.07%. The reference drug aspirin reduced the rectal temperature of pyretic rats by between 0.63-3.1%. The qualitative phytochemical screening of the two extracts indicated the presence of flavonoid, alkaloids, steroids, saponins, terpenoids which are associated with the antipyretic activity. The present study demonstrated potent antipyretic activities of methanolic extracts of *A. hockii* and *K. africana* in a dose-dependent manner after the second hour of the treatment period, which supports their traditional use. The present study, therefore, recommends the ethnomedicinal use of *K. africana* and *A. hockii* in the management of pyrexia.

Keywords: *Kigelia africana*; *Acacia hockii*; Pyrexia; Turpentine; PGE₂

Introduction

Pyrexia, also known as fever [1], is a medical sign associated with the elevation of body temperature above the normal range (36.5-37.5°C), due to the cytokine-induced upward displacement of the thermoregulatory set-point of the hypothalamus [2]. The elevation of the body temperature occurs when prostaglandin E₂ (PGE₂) increases within the pre-optic region of the hypothalamus and changes the firing rate of neurons in the thermoregulatory center [3]. Symptoms of fever include shivering, sweating, headache, dehydration, muscle aches and general weakness [4].

The impacts of secondary infection, tissue damage, neoplasm or other diseased states induce fever. The infectious causes of pyrexia include viral, bacterial, parasitic infections, common cold, malaria, and meningitis among others while the non-infectious causes of fever include deep vein thrombosis, cancer, and side effects of medication among others [4]. Infected or damaged tissue produces cytokines such as interleukins 1 (β and α), tumor necrosis factor (β and α) and interleukin-6 which triggers the arachidonic acid pathway to initiate the synthesis of PGE₂ in the hypothalamus. The increased production of PGE₂ stimulates the hypothalamus to generate responses to raise the body temperature [5].

Most of the conventional antipyretic drugs such as ibuprofen, paracetamol, aspirin, and naproxen inhibit cyclooxygenase 2 (COX-2) expression [6]. The inhibition of COX-2 lowers the production of PGE₂ necessary for pyrexia induction. However, they are toxic to hepatic cells, glomeruli and heart muscle [7].

The World Health Organization estimates that 80% of populations in developing countries depend on herbal preparations for their health care [8]. The demand for ethnomedicine is raising due to the

growing recognition of herbal medicine having fewer side effects, better compatibility with the human body, easily available and being comparatively affordable [9]. Herbal preparations have become the subject of extensive recent studies regarding whether their traditional uses can be scientifically validated [10].

Traditionally, *A. hockii* and *K. africana* are used in management of pyrexia among Embu community in Kenya, but lacks scientifically validated data [11]. This study was, therefore, designed to test for the antipyretic activity of the two extracts to act as a preliminary step towards the development of alternative antipyretic agents.

Materials and Method

Plant sample collection and preparation

Fresh stem bark of *A. hockii* and *K. africana* were collected in Embu County, Kenya with the help of traditional herbalist in September, 2015. Some of the information obtained from local herbalist included vernacular names, plant parts used in the management of various ailments and other cultural uses. The plant samples were provided to an acknowledged taxonomist in Kenyatta University for botanical authentication and a sample voucher deposited at National Museums

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of Kenya herbarium. The plant samples were sorted out, cleaned with distilled water and transported to biochemistry and biotechnology laboratories at Kenyatta University. The plant samples were chopped into small pieces, and air dried at room temperature until dry. The dried plant samples were ground into homogenous fine powder using an electric mill.

Extraction

To 400 grams of plant sample powder, 2 litre of methanol was added, stirred for four hours and left for two days for the bioactive compounds to dissolve. The extract was filtered using Whatman's No.1 filter paper and then the filtrate concentrated to dryness under reduced pressure using rotary evaporator at a maximum temperature of 64°C. The concentrate was then put in an airtight container and stored at 4°C until utilized.

Laboratory animals

Male Wistar rats aged 3 months and weighing between 140-160 grams were used in the present study. The animals were acquired from animal breeding and experimentation facility in Kenyatta University and were allowed to acclimatize for seven days before testing. The experimental animals were kept in the standard cages in animal experimental facility maintained under standard condition of an ambient temperature of 20-25°C with 12 hours darkness and 12 hours day light cycles. The male Wistar rats were provided water and fed on standard rodent pellets *ad libitum* [12].

Evaluation of antipyretic activity

The animals were fasted during the experiment but were given water *ad libitum*. Before fever induction, rats were weighed and their basal rectal temperature measured and recorded. Steam distilled turpentine (20 ml/kg bw) was injected intraperitoneally to induce pyrexia [13]. Rats whose rectal temperatures rose by 0.8°C after one hour were termed pyretic and used for studies. The extract was dissolved in Dimethyl Sulfoxide (DMSO) solvent and a vehicle normal saline (0.9% sodium chloride solution) added before treatment. The extracts and aspirin (0.5 ml) were administered intraperitoneally one hour after fever induction.

Thirty male Wistar rats were divided randomly into six groups of five rats each and treated as follows; normal control (Group I) was not induced with fever but administered DMSO. Negative control (Group II) was induced with fever and received DMSO. Positive control (Group III) was induced with fever and received aspirin (standard drug) at a dosage of 100 mg/kg body weight. Experimental groups (Group IV, V and VI) were induced with fever and received extract at a dose levels of 50 mg/kg, 100 mg/kg and 150 mg/kg body weight. This design is summarized in Table 1.

The rectal temperatures were taken by inserting a well-lubricated thermistor probe of a digital thermometer in the rectum [13]. The digital

Group	Status	Treatment
I	Control	DMSO
II	Negative control	Turpentine+DMSO
III	Positive control	Turpentine+100 mg/kg bw Aspirin
IV	Experimental group A	Turpentine+50 mg/kg bw extract+DMSO
V	Experimental group B	Turpentine+100 mg/kg bw extract+DMSO
VI	Experimental group C	Turpentine+150 mg/kg bw extract+DMSO

Steam distilled turpentine, DMSO=4%

Table 1: Treatment protocol for evaluation of antipyretic activities of methanolic extracts of *Kigelia africana* (Lam) benth and *Acacia hockii* de wild in male Wistar rats.

thermometer was calibrated against a mercury thermometer before recording rectal temperature. The mean temperature was measured at 15 minutes intervals for one hour prior to pyrexia induction, and this was termed as baseline temperature.

The rectal temperatures were measured and recorded at 1, 2, 3, and 4 hours after treatments. Rectal temperature at the first hour after turpentine administration and after treatments was compared and their percentage inhibition calculated using formula as follow [14];

$$\text{Inhibition (\%)} = \frac{B - C_n}{B} \times 100$$

Where,

B - Rectal temperature at 1 hour after turpentine administration

C_n - Rectal temperature after treatment

Phytochemical screening

The extracts were subjected to standard qualitative phytochemical screening to identify the absence or the presence of various phytochemicals according to methods as described by Harbone [15] and Kotake [16]. Some of the phytochemicals tested are associated with antipyretic properties and they include alkaloids, steroids, terpenoids, saponins and flavonoids [17]. Alkaloids were tested using Dragendroff's test, sodium hydroxide test was used for flavonoids, Salkowski test was used for terpenoids, sulfuric acid steroidal ring test was used for steroids and froth test was used for saponins.

Data management and statistical analysis

Recorded rectal temperature were tabulated on the spread sheet in Microsoft excel. The tabulated data was exported to Minitab statistical software version 17.0 (State College, Pennsylvania) for statistical analysis. Descriptive statistics was expressed as mean ± standard error of mean. One-way Analysis of Variance (ANOVA) was used to determine the significant difference between the means of different treatment groups followed by Tukey's post hoc tests for pairwise comparison among the various treatment groups. The mean activity of the two extracts was compared using unpaired student t-test. The values of p ≤ 0.05 were considered significant. The data was presented in tables and graphs.

Results

Antipyretic activity of stem extract of *Acacia hockii* de wild on turpentine-induced pyrexia

The methanol stem bark extract of *A. hockii* demonstrated antipyretic effect on turpentine-induced pyrexia by lowering rectal temperature of pyretic rats (Figure 1; Table 2). In the first hour after treatment, only the group of rats treated with aspirin (reference drug) at the dosage of 100 mg/kg body weight showed antipyretic activity by reducing the elevated rectal temperature of pyretic rats by 1.7% (Figure 1; Table 2). However, the group of rats treated with extract at the dose levels of 50 mg/kg, 100 mg/kg and 150 mg/kg body weight never demonstrated antipyretic effects at this hour (Figure 1; Table 2). The antipyretic effects of the extract at all dose levels showed no significant difference and were comparable to the negative control (p>0.05; Table 2).

In the second hour after extract administration, the extract at the dosage of 100 mg/kg and 150 mg/kg body weight as well as the aspirin demonstrated antipyretic effect by reducing elevated rectal temperature by 0.68%, 0.72% and 2.47% respectively (Figure 1; Table 2). However, the group of rats treated with extract at the dose level of 50 mg/kg body

Group	Treatment	% change in rectal temperature (°C) after treatment				
		0 hr	1 hr	2 hr	3 hr	4 hr
Normal control	DMSO	100 ± 0.00 (0.00)	99.89 ± 0.11 ^a (0.11)	100.27 ± 0.09 ^{ab} (-0.27)	100.32 ± 0.10 ^b (-0.32)	100.27 ± 0.09 ^b (-0.27)
Negative control	Turpentine+DMSO	100 ± 0.00 (0.00)	101.00 ± 0.10 ^a (-1.00)	101.83 ± 0.19 ^a (-1.83)	102.67 ± 0.34 ^a (-2.67)	102.67 ± 0.26 ^a (-2.67)
Positive control	Turpentine+Aspirin	100 ± 0.00 (0.00)	98.30 ± 0.52 ^b (1.70)	97.53 ± 0.66 ^c (2.47)	96.85 ± 0.52 ^e (3.16)	96.90 ± 0.32 ^{de} (3.10)
Methanolic Extracts	Turpentine+50 mg/kgbw+DMSO	100 ± 0.00 (0.00)	100.58 ± 0.40 ^a (-0.58)	100.22 ± 0.60 ^{ab} (-0.22)	99.38 ± 0.34 ^{bc} (0.62)	98.39 ± 0.22 ^c (1.61)
	Turpentine+100mg/kgbw+DMSO	100 ± 0.00 (0.00)	100.05 ± 0.31 ^a (-0.05)	99.32 ± 0.36 ^{bc} (0.68)	98.54 ± 0.24 ^{cd} (1.46)	97.86 ± 0.21 ^{cd} (2.14)
	Turpentine+150mg/kgbw+DMSO	100 ± 0.00 (0.00)	100.11 ± 0.28 ^a (-0.11)	99.28 ± 0.25 ^{bc} (0.73)	97.72 ± 0.27 ^{de} (2.28)	96.12 ± 0.34 ^e (3.88)

Values expressed as Mean ± SEM for five animals per group. Values with the same superscript letter are not significantly different by one-way ANOVA followed by Tukey's test ($p > 0.05$). Percentage reduction in rectal temperature is given within parentheses. Steam distilled turpentine=20 mg/kg bw; 100 mg/kg aspirin; 4% DMSO.

Table 2: Effects of intraperitoneal administration of methanolic stem bark extract of *Acacia hockii* de wild on turpentine-induced pyrexia in male Wistar rats.

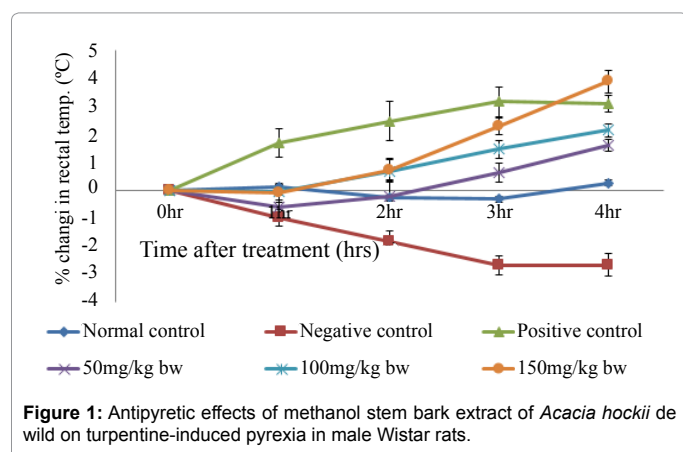


Figure 1: Antipyretic effects of methanol stem bark extract of *Acacia hockii* de wild on turpentine-induced pyrexia in male Wistar rats.

weight never showed antipyretic effect at this hour (Figure 1; Table 2). The antipyretic activity of extract at the three dose levels showed no significant difference and were comparable to normal control ($p > 0.05$; Table 2). Besides, the antipyretic activity of extract at the dose levels of 100 mg/kg and 150 mg/kg body weight were comparable to aspirin ($p > 0.05$; Table 2).

In the third hour, the group of rats treated with extract at the dosages of 50 mg/kg, 100 mg/kg, and 150 mg/kg body weight showed antipyretic effect by lowering the elevated rectal temperatures by 0.62%, 1.46% and 2.28% respectively (Figure 1; Table 2). In addition, the rats treated with aspirin (reference drug) reduced rectal temperature by 3.16% (Figure 1; Table 2). The antipyretic effect of extract at the dose levels of 50 mg/kg and 100 mg/kg body weight showed no significant difference ($p > 0.05$; Table 2). Besides, the antipyretic activity of the extract at the dose levels of 100 mg/kg and 150 mg/kg body weight demonstrated no significant difference ($p > 0.05$; Table 2). Moreover, the antipyretic activity of the extract at the dose level of 150 mg/kg was comparable to the aspirin ($p > 0.05$; Table 2).

In the fourth hour, the group of rat treated with extract at the dosage of 50 mg/kg, 100 mg/kg and 150 mg/kg body weight as well as aspirin lowered the elevated rectal temperatures by 1.61%, 2.41%, 3.88% and 3.1% respectively (Figure 1; Table 2). The antipyretic activity of the extract at the dose level of 150 mg/kg body weight was significantly different from the extract at the dose levels of 50 mg/kg and 100 mg/kg body weight ($p < 0.05$; Table 2). The antipyretic activity of the extract at the dosage of 100 mg/kg and 150 mg/kg body weight was comparable to aspirin (reference drug) ($p > 0.05$; Table 2).

Antipyretic activity of stem bark *Kigelia africana* (Lam) benth on turpentine-induced pyrexia

The methanol stem bark extract of *K. africana* showed antipyretic activity on turpentine-induced pyrexia in male Wistar rats, which was demonstrated by decreased elevated rectal temperature after extract administration (Figure 2; Table 3). In the first hour after extract administration, the stem bark extract of *K. africana* at the dosage of 150 mg/kg body weight and aspirin (reference drug) at the dose level of 100 mg/kg body weight reduced temperature of pyretic rats by 0.31% and 0.63% respectively (Figure 2; Table 3). However, the extract at the dosage of 50 mg/kg and 100 mg/kg body weight never demonstrated antipyretic activity at this hour (Figure 2; Table 3). The antipyretic activity of the extract at the dosage of 50 mg/kg, 100 mg/kg and 150 mg/kg demonstrated no significant difference and were comparable to aspirin and normal control ($p > 0.05$; Table 3).

In the second hour after extract administration, the group of rats treated with extract at the dose levels of 50 mg/kg, 100 mg/kg, and 150 mg/kg body weight demonstrated antipyretic activity by decreasing the raised rectal temperature by 0.06%, 0.11% and 1.20% respectively (Figure 2; Table 3). Similarly, the rats treated with aspirin (reference drug) showed antipyretic activity by lowering the elevated rectal temperature by 1.25% (Figure 2; Table 3). The antipyretic activity of extract at the dose level of 150 mg/kg body weight was significantly different from 50 mg/kg and 100 mg/kg body weight ($p < 0.05$; Table 3). Besides, the extract at the dosage of 150 mg/kg body weight was comparable to aspirin ($p > 0.05$; Table 3).

In the third hour after treatment, the group of rats administered with extract at the dosage of 50 mg/kg, 100 mg/kg, and 150 mg/kg body weight reduced rectal temperature of pyretic rat by 0.58%, 1.30% and 2.41% respectively (Figure 2; Table 3). Similarly, the rats treated with aspirin reduced elevated rectal temperature by 1.88% (Figure 2; Table 3). The antipyretic activity of the extract at the dosage of 100 mg/kg and 150 mg/kg body weight showed no significant difference and were comparable to the aspirin ($p > 0.05$; Table 3). Besides, the antipyretic activity of the extract at the dosages 50 mg/kg and 100 mg/kg was not significantly different ($p > 0.005$; Table 3).

In the fourth hour after extract administration, the group treated rats with extract at the dose levels of 50 mg/kg, 100 mg/kg and 150 mg/kg body weight as well as the aspirin reduced elevated rectal temperature by 1.41%, 2.09%, 3.07% and 2.40% respectively (Figure 2; Table 3). The antipyretic activity of the extract at the dosages of 50 mg/kg and 100 mg/kg body weight showed no significant difference ($p > 0.005$; Table 3).

Group	Treatment	% change in rectal temperature (°C) after treatment				
		0hr	1hr	2hr	3hr	4hr
Normal control	DMSO	100 ± 0.00 (0.00)	100.11 ± 0.28 ^b (-0.11)	100.06 ± 0.23 ^b (-0.06)	100.11 ± 0.28 ^b (-0.11)	100.22 ± 0.18 ^b (-0.22)
Negative control	Turpentine+DMSO	100 ± 0.00 (0.00)	101.47 ± 0.20 ^a (-1.47)	102.25 ± 0.13 ^a (-2.25)	102.94 ± 0.16 ^a (-2.94)	103.04 ± 0.14 ^a (-3.04)
Positive control	Turpentine+Aspirin	100 ± 0.00 (0.00)	99.37 ± 0.26 ^b (0.63)	98.75 ± 0.23 ^c (1.25)	98.12 ± 0.13 ^d (1.88)	97.60 ± 0.15 ^{de} (2.40)
Methanolic extracts	Turpentine+50 mg/kg bw+DMSO	100 ± 0.00 (0.00)	100.42 ± 0.24 ^{ab} (-0.42)	99.95 ± 0.30 ^b (0.06)	99.42 ± 0.30 ^{bc} (0.58)	98.59 ± 0.24 ^c (1.41)
	Turpentine+100 mg/kgbw+DMSO	100 ± 0.00 (0.00)	100.06 ± 0.29 ^b (-0.06)	99.89 ± 0.23 ^b (0.11)	98.70 ± 0.08 ^{cd} (1.30)	97.91 ± 0.16 ^{cd} (2.09)
	Turpentine+150 mg/kgbw+DMSO	100 ± 0.00 (0.00)	99.69 ± 0.22 ^b (0.31)	98.80 ± 0.15 ^c (1.20)	97.97 ± 0.10 ^d (2.41)	96.93 ± 0.10 ^e (3.07)

Values expressed as Mean ± SEM for five animals per group. Values with the same superscript letter are not significantly different by one-way ANOVA followed by Tukey's test ($p > 0.05$). Percentage reduction in rectal temperature is given within parentheses. Steam distilled turpentine=20 mg/kg bw; 100 mg/kg bw aspirin and 4% DMSO.

Table 3: Effects of intraperitoneal administration of methanolic stem bark extract of *Kigelia africana* (Lam) benth on turpentine-induced pyrexia in male Wistar rat.

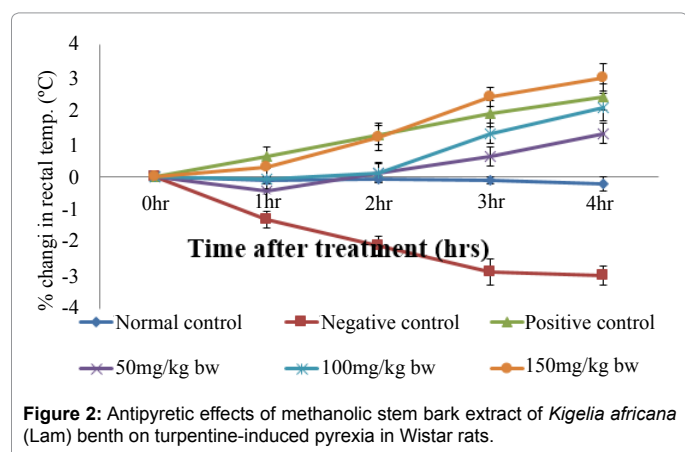


Figure 2: Antipyretic effects of methanolic stem bark extract of *Kigelia africana* (Lam) benth on turpentine-induced pyrexia in Wistar rats.

3). However, the group of rats administered with extract at the dosage of 150 mg/kg body weight was comparable to the group of rats treated aspirin ($p > 0.05$; Table 3).

Comparison between the antipyretic activities of *Acacia hockii* and *Kigelia africana* on turpentine-induced pyrexia

In comparison, the antipyretic activity of the two extract was not significantly different at the dose level of 50 mg/kg body weight in the 1, 2, 3 and 4 hours of the test period with p values of 0.75, 0.70, 0.93, and 0.56 respectively ($p > 0.05$). Similarly, the antipyretic effect of the two extracts at the dose level of 100 mg/kg body weight was not significantly different in the 1,2,3 and 4 hours of the test period with p values of 0.9, 0.23, 0.58, and 0.86 respectively ($p > 0.05$). Besides, the antipyretic activity of the two extracts was not significantly different at the dosage of 150 mg/kg body weight in the 1,2,3 and 4 hours of test period with p values of 0.28, 0.16, 0.42 and 0.08 respectively ($p > 0.05$). The antipyretic activity of both extracts was best active at the dosage of 150 mg/kg in fourth hour after extract administration (Figure 3).

Phytochemical screening

The qualitative phytochemical screening of the methanolic stem bark extracts of *K. africana* and *A. hockii* indicated the presence of alkaloids, cardiac glycosides, flavonoids, phenolics, saponin, steroids, and terpenoids.

Discussion

Although there is a considerable progress in the treatment of diseases and disorders using modern therapeutic drugs, search for

alternative medication continues due to the existing association of synthetic drugs with several limitations. The long-term use of NSAIDs in the management of pyrexia and inflammation may result in severe complications such as renal damage, cardiac abnormalities and gastric ulcers [18]. Herbal preparations possess a wealthy of secondary metabolites that can manage various disease and disorders. In addition, herbal preparations have shown potent antipyretic activities in experimental animals [19].

The present study was designed to determine the antipyretic effects of methanol extracts of *A. hockii* and *K. africana* in male Wistar rats. Exogenous pyrogens such as Lipopolysaccharides (LPS), steam distilled turpentine, brewer's yeast, Muramyl Dipeptide (MDP) and polyinosinic: polycytidylic acid (poly I: C) are used to induce pyrexia in experimental animals [20,21].

The exogenous pyrogens produce fever by their ability to stimulate the synthesis and release of endogenous pyrogens from the host phagocytic cells. Moreover, it is the circulating endogenous pyrogens rather than circulating exogenous pyrogens which act on the thermoregulatory center to raise the thermostatic set-point in the hypothalamus and produce fever [22]. Fever is mediated by the release of endogenous pyrogenic cytokines such as tumor necrosis- α , interleukins (IL-1 α , IL-1 β , and IL-6), and interferons (β and α) which are synthesized and released by activated phagocytes in response to exogenous pyrogens. These mediators stimulate the synthesis of PGE₂, which are the primary mediators of the well-coordinated fever response [23].

Turpentine is a fluid obtained by the distillation of resin from pine. Subcutaneous injection of steam distilled turpentine causes pyrexia by enhancing the production of PGE₂, which ultimately increase the body temperature [24]. The turpentine-induced pyrexia has been established to be fast, has persistent fever pattern and experimental animals have a high tolerance to turpentine compared to other exogenous pyrogens [21,25]. Steam distilled turpentine was, therefore, selected to induce pyrexia in this study.

The present study demonstrated significant antipyretic activity of methanol stem bark extracts of *A. hockii* and *K. africana* on turpentine-induced pyrexia in rats (Figures 1 and 2; Tables 2 and 3). These findings were in agreement with other study carried out on herbal preparation using experimental animals. The study carried out on dichloromethane: methanolic leaf and root bark extracts of *Carissa edulis* (Forssk.) Vahl showed antipyretic activity on turpentine-induced pyrexia in rats [26]. Similarly, the root extract of *Solanum incanum*

(Linnaeus) demonstrated antipyretic activity on lipopolysaccharides-induced pyrexia in male Wistar rats [27]. Besides, according to [28] the methanolic leaf extract of *Vernonia cineral* showed antipyretic activity on brewer's yeast induced pyrexia in Wistar rats.

Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, acetaminophen, diclofenac and ibuprofen are the commonly used in the medication of fever [29]. The NSAIDs manage pyrexia through inhibition of the Cyclooxygenase (COX) enzyme that stimulates the production of PGE₂ responsible for fever induction [30]. Studies have established that at least two COX isoenzyme exist; COX-1 and COX-2. The COX-1 synthesizes prostaglandins that protect the stomach and the kidney from damage while the COX-2 stimulates PGE₂ production that contributes to fever induction [31]. It was therefore believed that the methanolic stem bark extracts of *K. africana* and *A. hockii* reduced the elevated rectal temperatures of rats by inhibiting the enzyme COX-2 responsible for the production of PGE₂.

The antipyretic activity of methanol stem bark extracts of *K. africana* and *A. hockii* demonstrated a dose-dependent response after the second hour of the test period, with the dose level of 150 mg/kg body weight producing greater antipyretic activity (Figures 1 and 2; Tables 2 and 3). These findings were consistent with the study carried out on the antipyretic activity of methanol extracts of aerial parts of *Costus speciosus* Koen in experimental animals [32]. Similarly, a study conducted on the antipyretic activity of ethyl acetate roots extracts of *Ocimum sanctum* demonstrated a dose dependent response in laboratory animals [33].

The aspirin (reference drug) achieved its maximum antipyretic activity in the third hour (Figures 1 and 2; Tables 2 and 3). Its activity decreased subsequently probably due to metabolism and elimination of the drug. The maximum antipyretic activity of the stem bark extracts of *A. hockii* and *K. africana* occurred in the fourth hour, indicating slow but steady passive diffusion of the bioactive compounds across the cell membrane [34]. The stem bark extracts of *A. hockii* and *K. africana* at the dose level of 150 mg/kg body weight were more active in the fourth hour of treatment compared to aspirin (reference drug) (Figures 1 and 2; Tables 2 and 3). These findings indicated that stem bark extracts of *K. africana* and *A. hockii* were able to inhibit the synthesis of prostaglandins more than the reference drug (aspirin). However, the aspirin showed a sudden decrease in elevated rectal temperatures as compared to the extracts of *A. hockii* and *K. africana* (Figures 1 and 2; Tables 2 and 3).

The antipyretic activity of methanolic stem bark extracts of *K. africana* and *A. hockii* could be due to the ability of herbal preparations to possess a wealth of secondary metabolites required in the management of various diseases and disorders [19]. The qualitative phytochemical screening of methanolic stem bark extracts of *A. hockii* and *K. africana* indicated the presence of alkaloids, flavonoids, steroids, saponins and terpenoids (Table 4). The presence of these bioactive constituents such

Phytochemical	Stem bark <i>Kigelia africana</i>	Stem bark <i>Acacia hockii</i>
Alkaloids	+	+
Flavonoids	+	+
Steroids	+	+
Saponins	+	+
Terpenoids	+	+

Present phytochemical is denoted by (+) sign; absent phytochemical is denoted by (-) sign

Table 4: Qualitative phytochemical composition of methanolic stem bark and leaf extracts of *Kigelia africana* and methanolic stem bark extracts of *Acacia hockii*.

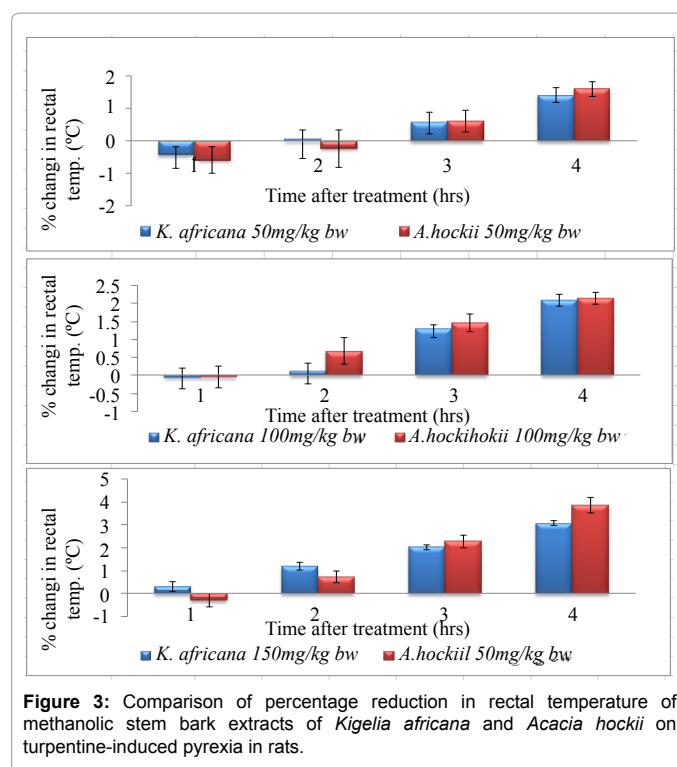


Figure 3: Comparison of percentage reduction in rectal temperature of methanolic stem bark extracts of *Kigelia africana* and *Acacia hockii* on turpentine-induced pyrexia in rats.

as steroids, terpenoids, saponins, alkaloids and flavonoids have shown to exhibit antipyretic activity in experimental animals [35].

Flavonoids exhibit inhibition of arachidonic acid peroxidation, which results in the reduction of prostaglandins levels thus managing fever [36]. Flavonoids also inhibit the synthesis of tumor necrosis factor- α which stimulates the production of PGE₂ necessary for fever induction [37]. Alkaloids, terpenoids and steroids inhibit the synthesis of prostaglandins synthase which stimulates the production of PGE₂ [36]. Steroids have also been reported to inhibit the conversion of linoleic acid to arachidonic acid, a substrate required for PGE₂ synthesis [38]. The antipyretic activity exhibited by methanolic stem bark extracts of *K. africana* and *A. hockii* was therefore believed to be associated with the presence of flavonoids, terpenoids, alkaloids and steroids in the extracts.

Conclusion

The methanolic stem bark extracts of *K. africana* and *A. hockii* demonstrated significant antipyretic effects on turpentine-induced pyrexia in rats. The antipyretic activity of the two extracts showed a dose-dependent response and were comparable to aspirin (reference drug). Besides, the extracts of *K. africana* and *A. hockii* at the dose level of 150 mg/kg body weight were more active in the fourth hour after treatment.

The extracts of *K. africana* and *A. hockii* could, therefore, can be an alternative bio-resource for generating antipyretic agents which are efficient and with less side effects. Besides, further studies should be carried out to elucidate the mechanism behind these effects. The present study, therefore, scientifically confirm and supports the ethnomedicinal use of *K. africana* and *A. hockii* in the management of pyrexia.

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