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Antipyretic, Anti-inflammatory and Analgesic Activities of Aqueous Leaf Extract of *Aloe volkensii* in Albino Mice

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Abstract

Aloe volkensii has been used to manage several diseases including pain, inflammation and fever. However, its efficacy has not been scientifically validated. The aim of this study therefore is to investigate the analgesic, antipyretic and anti-inflammatory activities of its aqueous extracts. The plant was collected from Loita division, Narok County in Kenya. A total of 96 albino mice with an average weight of 20 g were used for this study. Analgesic activity was determined by use of 0.05 ml of 2.5% formalin−induced writhing test. A writhe was recorded by a stopwatch following the stretching of the abdomen and/or stretching of at least one hind limb. Anti-inflammatory activity was established by a formalin induced inflammation test. Hourly changes in paw sizes and reduction of edema around the paw was determined using a vernier calipers. Antipyretic activity was carried out using 0.03 g of 10 ml/kg of 15% w/v Brewer's yeast-induced pyrexia. Temperature of each mouse was determined rectally by thermal probe thermometer. The aqueous leaf extracts of *Aloe volkensii* reduced pain, inflammation and fever mostly at dose 150 mg/kg body weight compared to dose of 50 mg/kg and 100 mg/kg body weight. The results support the traditional use of *A. volkensii* in the treatment of various diseases associated with pain, fever and inflammation.

Keywords: *Aloe volkensii*; Pyrexia; Antinociceptive activity; Antiinflammatory activity

Introduction

Non-steroidal anti-inflammatory drugs (NSAID) are used worldwide for the treatment of inflammation, pain and fever. However, they often produce significant side-effects, which include gastric ulcer, renal damage, bronchospasm and cardiac abnormalities, thus limiting their use [1]. Drugs of natural origin are an important source for the treatment of many diseases worldwide [2]. The research and analysis of plants employed as pain-relievers and anti-inflammatory agents in traditional ethnomedicine is one of the productive and logical strategies in the search for new drugs [3,4]. *Aloe volkensii* (family Asphodeteceae) is of great utility and bio-cultural value worldwide occurring as a succulent-leaved shrub [5]. The plant is mainly found in Africa, western India and the Arabian Peninsula [6]. The cultivated species in this family such as *A. vera* are mainly used as a source of natural products for industries [5]. The Aloe spp has been extensively documented for its medicinal value against infectious parasites [7], digestion problems [8], treatment of injuries [9] and skin diseases [10]. Particularly, *Aloe volkensii* has been shown to be effective against whooping cough in children [11]. This species is however no commonly used for treatment of illnesses due to the nature of its exudates that are considered unsuitable. For instance, Olembo et al. [11] reported the use of *A. volkensii* in preparation of rodentiles used to kill moles. Similarly, Rood [9] reported that the exudates from this shrub were painted on children's fingers to discourage nail biting and also painted on structures to discourage gnawing by animals. The objective of this study therefore was to determine the analgesic, anti-inflammatory and antipyretic activities of *Aloe volkensii* in albino mice.

Materials and Methods

Collection and preparation of plant materials

Fresh leaf material of *A. volkensii* was collected from Loita division, Narok County in Kenya where it is used by the locals to treat wounds and diabetes. The plant material was identified and authenticated with the help of Mr. Karimi, a laboratory technician from the Department of Botany, Kenyatta University. Preparation of plant extract was carried out using a protocol as described by Nostro et al. [12]. The powdered materials were kept at room temperature away from direct sunlight in closed dry khaki paper bags.

Extraction

The powdered material was separately extracted with single distilled water at 125 g/L on a 60°C water bath for 6 hours. The solvent extract was then concentrated to dryness under reduced pressure and the residue preserved at 4°C for future use. About 400 g of *Aloe volkensii* was therefore dissolved in 3.2 L of single distilled water in a conical flask and the mixture put on the water bath. Decantation and filtration processes through a No.1 Whattman filter paper were repeated until the sample became clear. The filtrate was freeze-dried, weighed and stored in an airtight plastic bag and refrigerated until it was used for bioassay. This procedure yielded 60 g of freeze-dried *Aloe volkensii*.

Preparation of reagents and extracts used for bioassay

The plant extract for determination of analgesic, anti-inflammatory and antipyretic activities were prepared in the following manner (Tables 1, 2 and 3).

Animal models

Swiss albino mice of average weight of 20 g were used in this study. These animals were maintained in the experimental room at the Animal House, Department of Biochemistry and Biotechnology, Kenyatta University. The room was set at controlled conditions of 25 ± 2°C

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Group	Status	Treatment
I	Control	Normal saline (0.1 ml) + Formalin (0.05 ml of 2.5% formalin)
II	Baseline	Formalin (0.05 ml of 2.5% formalin)
III	Standard	Diclofenac (12 µl of 75 mg/3 ml diclofenac sodium + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
IV	Test-1	50 mg/kg extract (0.001 g + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
V	Test-2	100 mg/kg extract (0.002 g + 0.1ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
VI	Test-3	150 mg/kg extract (0.003 g + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)

Table 1: Treatment protocol for the determination of analgesic activity for the aqueous leaf extract of *Aloe volkensii*.

Group	Status	Treatment
I	Control	Normal saline (0.1 ml) + Formalin (0.05 ml of 2.5% formalin)
II	Baseline	Formalin (0.05 ml of 2.5% formalin) + Formalin (0.05 ml of 2.5% formalin)
III	Standard	Diclofenac (10 µl of 75 mg/3 ml diclofenac sodium + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
IV	Test-1	50 mg/kg extract (0.001 g + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
V	Test-2	100 mg/kg extract (0.002 g + 0.1ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)
VI	Test-3	150 mg/kg extract (0.003 g + 0.1 ml Normal saline) + Formalin (0.05 ml of 2.5% formalin)

Table 2: Treatment protocol for the determination of anti-inflammatory activity for the aqueous leaf extract of *Aloe volkensii*.

Group	Status	Treatment
I	Control	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline) + Normal saline (0.1 ml)
II	Baseline	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline)
III	Standard	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline) + Paracetamol (0.286 mg in 0.1 ml normal saline)
IV	Test-1	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline) + 50 mg/kg extract (0.001 g + 0.1 ml Normal saline)
V	Test-2	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline) + 100 mg/kg extract (0.002 g + 0.1ml Normal saline)
VI	Test-3	Yeast (0.03 g of 10 ml/kg of 15% w/v yeast + 0.2 Normal saline) + 150 mg/kg extract (0.003 g + 0.1 ml Normal saline)

Table 3: Treatment protocol for the determination of antipyretic activity for the aqueous exctract of *Aloe volkensii*.

temperature, 55% humidity and 12 hr light/12 hr darkness photoperiod regime to acclimatize the animals. The mice were kept in a cage and fed with standard laboratory food and water *ad libitum*.

Experimental design

Determination of analgesic activity: To determine the analgesic activity of the plant extract, a formalin–induced writhing test was carried out using a method described by Ref. [13]. Groups of 5 mice were used for test and for control specimen (Table 1). The mice were individually placed in a glass beaker and observed for writhing. The number of stretches per animal was recorded for the following 30 minutes. A writhe was recorded following the stretching of the abdomen and/or stretching of at least one hind limb according to Ref. [14].

Determination of anti-inflammatory activity: To determine the anti-inflammatory effect of the extract in mice, a formalin induced inflammation test was carried out as described by Ref. [14]. Hourly changes in paw sizes and reduction of edema around the paw was determined using a vernier calipers.

Determination of antipyretic activity: The antipyretic activity of the plant extract was evaluated using Brewer's yeast induced pyrexia as described by Ref. [15]. According to the protocol, 15% aqueous suspension of Brewer's yeast was first prepared using normal saline (Table 3). Temperatures of each mouse was then determined by thermal probe thermometer rectally before the extract and drug administration and at hourly interval for three hours after extract and drug administration.

Results

Analgesic activity

In this early phase, aqueous leaf extracts of *Aloe volkensii* reduced formalin induced pain in mice but not in a dose dependent manner (Figure 1, Table 4). At the dose level of 50 mg/kg body weight, the aqueous leaf extracts exhibited significant analgesic effect compared with control and baseline groups ($p< 0.05$; Table 4). Diclofenac (reference drug), showed a significant reduction in pain. This study showed that the aqueous leaf extract of *Aloe volkensii* did not exert analgesic activity against formalin-induced chronic pain (Figure 2, Table 5). The group treated with the drug of reference showed greater analgesic activity.

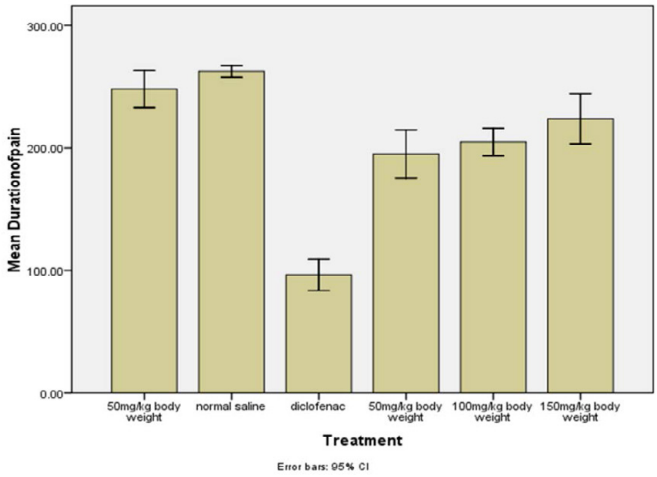

Figure 1: Analgesic effect of *Aloe volkensii* aqueous extract on acute pain.

Group	Treatment	Mean paw-licking time (sec) ± SD
1 Control	Normal saline	262.4 ± 3.84^{d}
2 Baseline	Formalin	248.0 ± 12.20^{d}
3 Standard	Diclofenac	96.4 ± 10.35^{a}
4 Test-1	50 mg/kg	195.0 ± 15.81^{b}
5 Test-2	100 mg/kg	204.8 ± 9.01^{bc}
6 Test-3	150 mg/kg	223.8± 16.52^{c}

Mean values ± SD with the same letters are not statistically different from one another by ANOVA followed by Tukey's post hoc test ($p > 0.05$). n=5

Table 4: Analgesic effect of *Aloe volkensii* aqueous extract on acute pain.

Group	Treatment	Mean paw-licking time(sec) ± SD
1 Control	Normal saline	347.4 ± 4.39^{c}
2 Baseline	Formalin	444.4 ± 8.50^{d}
3 Standard	Diclofenac	203.6 ± 9.86^{a}
4 Test-1	50 mg/kg	341.0 ± 8.33^{c}
5 Test-2	100 mg/kg	287.0 ± 15.31^{b}
6 Test-3	150 mg/kg	340.0 ± 16.94^{c}

Mean values ± SD with the same letters are not statistically different from one another by ANOVA followed by Tukey's post hoc test ($p > 0.05$). n=5

Table 5: Analgesic effect of *Aloe volkensii* aqueous extract on chronic pain.

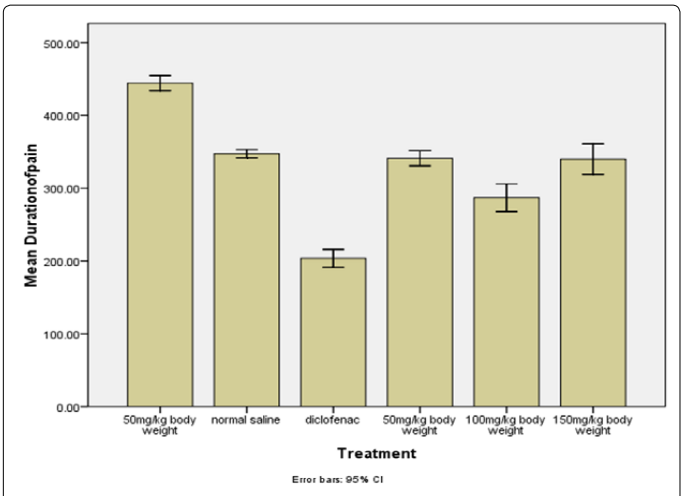

Figure 2: Analgesic effect of *Aloe volkensii* aqueous extract on chronic pain.

Anti-inflammatory activity

Treatment of mice with leaf extracts of *Aloe volkensii* showed some anti-inflammatory activity against formalin-induced edema, which was indicated by reduction in paw edema (Figure 3, Table 6). The initial paw diameter of the albino mice was 2 mm. In the first hour, the group treated with plant extract at dose of 50 mg/kg body showed greater inhibition of inflammation and this was indicated by a reduction to 88.54% (Table 6). Aqueous leaf extract of *Aloe volkensii* showed anti-inflammatory effect though not in a dose dependent manner with 50 mg/kg body weight inhibiting inflammation more compared to the control and the reference drug (p> 0.05; Table 6). In the second hour, all mice treated with the leaf extracts of *A. volkensii* at doses of 50, 100 and 150 mg/kg body weight recorded a reduction in paw diameter (Figure 3, Table 6). The anti-inflammatory effectiveness at dose level of 50 mg/kg had greater inhibition of inflammation by 76.49% compared to diclofenac which reduced inflammation by 84.45% (Table 6). In the third hour, *A. volkensii* at all dose levels (50, 100 and 150 mg/kg body weight) was found to lower the elevated paw diameter (Table 6). At this hour, the mice treated with 100 mg/kg of the herbal extract exhibited the highest anti-inflammatory effect of 66.75% (Table 6). Four hours after drug administration, *A. volkensii* at all dose levels (50, 100 and 150 mg/kg body weight) was found to lower the formalin-induced inflammation (Figure 3, Table 6). The group of mice treated with 100 mg/kg was even better than the other dose levels for it lowered the inflammatory activity to 57.14% (Table 6).

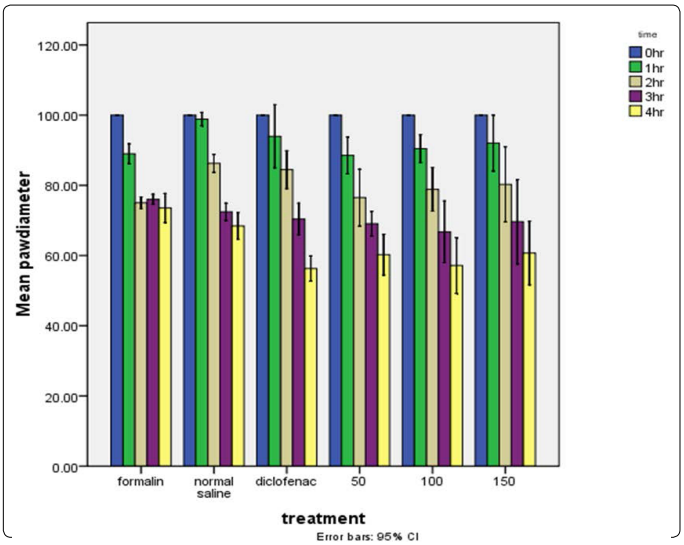

Figure 3: Anti-inflammatory effect of *Aloe volkensii* aqueous extract on albino mice.

Antipyretic activity

Treatment of mice with leaf extracts of *Aloe volkensii* showed some antipyretic activity against brewer's yeast induced pyrexia, which was indicated by reduction in rectal temperature (Figure 4, Table 7). The average initial rectal temperature of the albino mice was 36°C. In the first hour after treatment, plant extract at dose of 150 mg/kg body weight showed the highest antipyretic activity by reducing fever to 97.83% among the extract dosages and the reference drug (Figure 4, Table 7). Aqueous extract of *A. volkensii* exhibited antipyretic activities in a non-dose dependent manner (Figure 4, Table 7). In the second hour, plant extract at dose of 50 mg/kg body weight showed better effectiveness in reducing the rectal temperature to 96.05% (Table 7). Rectal temperature of the group treated with herbal medicine at dose 150 mg/kg exhibited a pyretic effect as the fever increased to 100.48% (Table 7). In the third hour, plant extract at dose of 150 mg/kg showed a greater antipyretic activity as the rectal temperature reduced to 97.55% compared to the reference drug. The dose level of 100 mg/kg body weight did not perform better than the reference drug (Figure 4, Table 7).

Discussion

This study was oriented to evaluate the curative capacity of aqueous leaf extract of *Aloe volkensii* against pain, inflammation and fever. The evaluation of analgesic, anti-inflammatory and antipyretic properties of the leaf extracts was done by formalin induced pain and inflammation and brewer's yeast induced pyrexia in albino mice. Subcutaneous injection of a dilute aqueous formalin (formaldehyde) solution into the dorsal surface of the rat or mouse hind paw elicits two distinct quantifiable nociceptive behaviors, i.e., flinching / shaking and licking / biting of the injected paw [16]. This formalin-induced

Percent change in paw diameter (mm) after drug administration						
Group	**Treatment**	0 hr	1 hr	2 hr	3 hr	4 hr
Control	Normal saline	100.00 ± 0.00^{Ec}	98.87 ± 1.54^{Dc}	86.24 ± 2.06^{Cc}	72.44 ± 1.98^{Bc}	68.42 ± 3.04^{Ac}
Baseline	Formalin	100.00 ± 0.00^{Ebc}	88.98 ± 2.28^{Dbc}	75.01 ± 1.32^{Cbc}	76.00 ± 1.14^{Bbc}	73.54 ± 3.32^{Abc}
Standard	Diclofenac	100.00 ± 0.00^{Eab}	93.96 ± 7.23^{Dab}	84.45 ± 4.35^{Cab}	70.38 ± 3.62^{Bab}	56.30 ± 2.9^{Aab}
Test-1	50 mg/kg	100.00 ± 0.00^{Ea}	88.54 ± 4.21^{Da}	76.49 ± 6.52^{Ca}	69.06 ± 2.83^{Ba}	60.24 ± 4.67^{Aa}
Test-2	100 mg/kg	100.00 ± 0.00^{Ea}	90.43 ± 3.21^{Da}	78.83 ± 4.99^{Ca}	66.75 ± 7.07^{Ba}	57.14 ± 6.39^{Aa}
Test-3	150 mg/kg	100.00 ± 0.00^{Eab}	92.04 ± 6.42^{Dab}	80.26 ± 8.59^{Cab}	69.63 ± 9.65^{Bab}	60.71 ± 7.29^{Aab}
Mean values ± SD with the same capital letters down the columns and same small letters across the rows are not statistically different from one another by ANOVA followed by Tukey's post hoc test (p>0.05). n=5						

Table 6: Anti-inflammatory effect of *Aloe volkensii* aqueous extract on albino mice.

Percent change in rectal temperature (°C) after drug administration					
Group	**Treatment**	0 hr	1 hr	2 hr	3 hr
Control	Normal saline	100.0 ± 0.00^{Ba}	94.49 ± 0.55^{Aa}	93.70 ± 0.84^{Aa}	95.28 ± 0.85^{Aa}
Baseline	Yeast	100.0 ± 0.00^{Bc}	98.10 ± 0.01^{Ac}	99.09 ± 0.21^{Ac}	99.91 ± 0.70^{Ac}
Standard	Paracetamol	100.0 ± 0.00^{Bab}	98.50 ± 0.61^{Aab}	98.96 ± 2.04^{Aab}	99.03 ± 2.20^{Aab}
Test-1	50 mg/kg	100.0 ± 0.00^{Bb}	98.20 ± 0.51^{Ab}	96.05 ± 0.68^{Ab}	97.94 ± 0.67^{Ab}
Test-2	100 mg/kg	100.0 ± 0.00^{Bbc}	98.39 ± 0.00^{Abc}	97.86 ± 0.00^{Abc}	99.33 ± 0.65^{Abc}
Test-3	150 mg/kg	100.0 ± 0.00^{Bbc}	97.83 ± 5.26^{Abc}	100.48 ± 1.73^{Abc}	97.55 ± 2.32^{Abc}

Mean values ± SD with the same capital letters down the columns and same small letters across the rows are not statistically different from one another by ANOVA followed by Tukey's post hoc test (p>0.05) n=6

Table 7: Antipyretic effect of *Aloe volkensii* aqueous extract on albino mice.

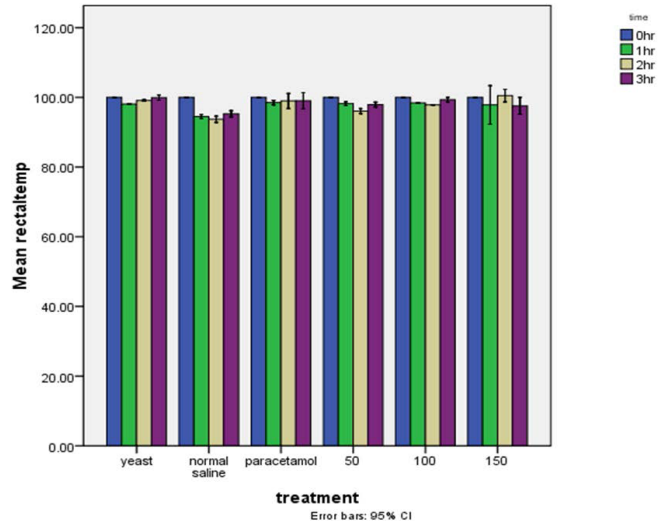

Figure 4: Antipyretic effect of *Aloe volkensii* aqueous extract on albino mice.

nociceptive behavior shows an early and a late phase. The early phase, which starts immediately following injection of formalin, only lasts approximately 5 min and is probably due to direct chemical stimulation of nociceptors (acute pain). The second phase, which lasts 20 to 40 min, starts approximately 15 to 30 min following formalin injection and experimental data suggest that peripheral, inflammatory processes are involved [17]. The formalin test differs from most other nociceptive tests, such as the hot plate, tail flick and tail pinch tests, in that it enables evaluation of analgesic activity towards moderate, continuous pain generated by injured tissue. As a result, it has been suggested that this test provides a more valid model been suggested that this test provides a more valid model such as the hot plate and tail flinch tests [16,18,19]. The two distinct phases in formalin test are due to direct effect of formalin on nociception and due to inflammation with the release of serotonin, histamine, bradykinin and prostaglandins and at least to some degree, the sensitization of central nociceptive neurons [16,20,21]. Stimulation of opioid receptors has also been suggested as a possible mechanism of action against neurogenic pain [22]. In this study, aqueous leaf extract of *Aloe volkensii* showed the highest analgesic effect at dose 50 mg/kg dose level for both early and late phases. These findings suggest both direct analgesic effects on the nociceptor blockage and an inhibition of the synthesis and/or release of inflammatory pain mediators such as prostaglandins.

These results are similar to other previous studies on evaluation of analgesic activities of medicinal plant extracts. That the aqueous leaf extract of *Aloe volkensii* demonstrated a reduction in the formalin-induced paw licking time in both phases is consistent with [23] who observed analgesic activity of hydroalcoholic extract of *Marrrubium parviflorum* against formalin-induced pain in mice. Similarly, the methanolic leaf extract of *Securinega virosa* demonstrated related analgesic effect in acetic acid induced writhing test and formalin test models [24]. That the aqueous extracts of *Aloe volkensii* produced non-dose dependent analgesic activity is related to studies by Ref. [25] who observed the analgesic activities of *Melissa officinalis* leaf extracts in laboratory animals. The dose ranges used in this study were within the dose ranges used by Ref. [26-28]. The aqueous leaf extract of *Aloe volkensii* showed the highest analgesic effect at lower dose of 50 mg/kg body weight in early and late phases. This may be due to the fact that the high dose takes longer to be absorbed across the peritoneum cavity.

The analgesic effect of *Aloe volkensii* can be attributed to one or more groups of the phytoconstituents observed in the extracts. Several studies have shown the analgesic activity of such compounds. Phytochemical screening of methanolic leaf extract of *Securinaga virosa* revealed the presence of flavonoids, saponins, tannins, glycosides, alkaloids and steroids [24]. A study on the phtochemical composition of *Aloe volkensii* has revealed presence of saponins, tannins, flavonoids, alkaloids and phenols [29]. Analgesic and anti-inflammatory effects have been observed in flavonoids as well as tannins [30]. Flavonoids such as quercetin are known to be effective in acute inflammation [31]. There are also reports on the analgesics effects of alkaloids, essential oils and saponins [32-34]. The analgesic and anti-inflammatory effect of the extracts in this study may therefore, be due to the presence of flavonoids, tannins, alkaloid or saponins. Flavonoids are widely shown to target prostaglandins which are involved in the pain perception through moderating opioidergic mechanism. These findings strongly recommend that these medicinal plants have peripheral analgesic activity and their mechanisms of action may be mediated through inhibition of local peritoneal receptors which may be the involvement of cyclooxygenase inhibition potential. The profound analgesic activity of these medicinal plants may be due to the interference of their active principle(s) with the release of pain mediators. Tissue damage and injury are always associated with pain and inflammation. In this formalin test, the mice used were treated with several treatments to reduce inflammation. Formalin test is a biphasic response where first phase is the direct effect of formalin which involves neurogenic pain. The pain is usually initiated when harmful mechanical, thermal or chemical stimuli agitate the peripheral terminals of particular main afferent neuron named nociceptors [35].

The second phase is involved in the inflammatory reactions. In this study, it was noticed that exposure of formalin induced inflammation to various treatments resulted in a significant inhibition of inflammation. The aqueous leaf extract of *Aloe volkensii* was found to significantly suppress the inflammation when treated with different concentrations. After five hours of the test period, the aqueous leaf extract of *Aloe volkensii* showed the highest effectiveness against inflammation at dose

50 mg/kg indicating a possibility that maybe the high dose takes longer to be absorbed across the peritoneum cavity. This was as effective as the reference drug, diclofenac. The association of both analgesic activity and moderate anti-inflammatory effect observed with the extracts has also been shown in non-steroidal anti-inflammatory drugs (NSAIDs). It is a well-established fact that NSAIDs exert their analgesic and anti-inflammatory activity by the inhibition of cyclo-oxygenase activity [36]. The anti-inflammatory effects of the extracts may be due to their content of flavonoids, tannins, alkaloids and saponins. Several studies have shown the analgesic activity of such compounds. A study by Muhammad et al. [37] showed that the *Viola betonicifolia* methanolic extract was found to contain alkaloids, saponins, flavonoids, tannins, proteins, and phenolic compounds where the anti-inflammatory activity of *V. betonicifolia* was attributed to these groups of chemical compounds. The anti-inflammatory effect of *Aloe volkensii* was not evident in every concentration of the extracts as early as the first hour of formalin injection but maximum inhibition was during the fifth hour. They did not maintain the suppression of the inhibition throughout the duration of the study. These findings could have been due to the fact that the active principles in the extracts required biotransformation so as to have an anti-inflammatory effect.

Brewer's yeast was used to induce fever in albino mice. Fever was recorded 19 hrs after yeast injection since yeast takes a total of about 19 hrs to cause the elevation of body temperature [38]. Subcutaneous injection of Brewer's yeast induces pyrexia by increasing the synthesis of prostaglandin. It is considered as a useful test for the screening of plants materials as well as synthetic drugs for their antipyretic effect [39,40]. Yeast induced pyrexia is called pathogenic fever and its etiology could be the production of prostaglandins [41]. The inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol and the inhibition of prostaglandin can be achieved by blocking the cyclo-oxygenase enzyme activity. There are several mediators for pyrexia and the inhibitions of these mediators are responsible for the antipyretic effect [42]. The oral administration of *Aloe volkensii* significantly attenuated rectal temperature of yeast induced albino mice. Thus it can be postulated that *Aloe volkensii* contained pharmacologically active principle(s) that interfere with the release of prostaglandins. After three hours of the test period, the aqueous leaf extract of *Aloe volkensii* produced appreciable antipyretic activity against brewer's yeast induced pyrexia in albino mice. Dose of 150 mg/kg body weight demonstrated the greatest rectal temperature lowering activity for this medicinal plant. These findings were in agreement with the effects of other medicinal plants in laboratory animals. Similar work carried out by Ref. [43] showed that the hydro alcoholic extract of *Rosa alba* plant possessed a significant antipyretic effect in yeast induced elevation of body temperature in experimental rats. It was revealed that the extract showed dose dependent antipyretic activity. At a dose of 200 mg/kg it showed significant antipyretic activity. Non-steroidal anti-inflammatory drugs produce their antipyretic action through the inhibition of prostaglandin synthetase within the hypothalamus. Work done by Ref. [43] showed that the antipyretic activity of hydro alcoholic extract of *Rosa alba* is probably by inhibition of prostaglandin synthesis in hypothalamus. Therefore it is possible that the antipyretic action of aqueous extract of *Aloe volkensi* was related to the inhibition of prostaglandin synthesis in hypothalamus. However, other alternative mechanisms for blocking fever cannot be ruled out. Further hydro alcoholic extract of *Rosa alba* was found to contain carbohydrates, alkaloids, glycosides, flavonoids and tannins, through preliminary photochemical screening. Qualitative phytochemical screening in this study revealed that the aqueous leaf extract of *Aloe volkensii* contain tannins, saponins, phenolics, alkaloids and flavonoids. A number of these phytochemicals have been shown to exhibit inhibitory action on cyclooxygenase enzyme and, as a result, produce antipyretic activity by preventing the formation of prostaglandins or by increasing the concentration of body's own antipyretic components [44]. Flavonoids are known to target prostaglandins which are involved in the pyrexia. Hence the presence of flavonoids in the aqueous leaf extract of *Aloe volkensii* plant may be contributory to its antipyretic activity. The presence of alkaloids in these extracts could also be responsible for the antipyretic activity. For instance, according to Ref. [45] while evaluating on antipyretic effects of alkaloids extracted from the stem bark of *Hunteria zeylanica,* reported that alkaloids also possesses antipyretic effects. The antipyretic activity of the aqueous leaf extract of *Aloe volkensii* may also be attributed to the presence of saponins, which are involved in inhibition of prostaglandin synthesis. According to the study of [46] saponins are suggested to act synergistically to exert antipyretic activity. In a related study, the antipyretic effect of ethanolic root extracts of *Asparagus racemosus* on yeast-induced hyperthermia in rats was attributed to the saponins in the extracts [47]. It was observed that aqueous leaf extract of *Aloe volkensii* at lower dose levels of 50 and 100 mg/kg body weight were not as effective as the higher dose of 150 mg/kg body weight, and thus may be explained by the fast metabolism, clearance and inactivation of the lower concentration of the active principles. It's also likely that at the lower dose there is simply not a sufficient concentration of the active principle(s).

The aqueous leaf extract of *Aloe volkensii* at all the dose levels did not lower rectal temperature in the first and second hours as effectively as in the third hour. These findings could have been due to the fact that the active principles in the extracts required biotransformation so as to become antipyretic. That the dose level of 150 mg/kg body weight of the aqueous leaf extract of *Aloe volkensii* was marginally effective than paracetamol, suggests a possibly better blockage of prostaglandins biosynthesis or mimicry of paracetamol action by the active principles in the extract. It is also possible that the herbal extracts were efficiently inhibiting alternative mechanisms for blocking fever. The decline in rectal temperature in case of treatment with the medicinal plants extracts was not as sudden as that of paracetamol administration. Therefore, the extracts offer some advantage over the standard drug (paracetamol) [48].

Conclusion

This study confirms the analgesic, anti-inflammatory and antipyretic potential of aqueous leaf extracts of *Aloe volkensii* in albino mice. It was able to inhibit pain sensation in the acute phase. Possibly, opioids present in the aqueous leaf extracts of *Aloe volkensii* may have contributed to the analgesic effects. Furthermore, the phytochemicals present may have contributed to the anti-inflammatory and antipyretic activities as established in this study. A dose of 150 mg/kg, 100 mg/kg and 50 mg/kg body weight of *Aloe volkensii* aqueous extract is more effective in the management of fever, inflammation and pain respectively. The present study, therefore, scientifically confirms and supports the traditional use of aqueous leaf extract of *Aloe volkensii* for management of fever, inflammation and pain.

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