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Evaluation of Analgesic Activities of Aqueous Leaf extract of *Adansonia digitata* L.(Malvaceae) in Mice

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ABSTRACT

Background: *Adansonia digitata* L. commonly known as African Baobab is widely used as food and in ethnomedicine for the treatment of various diseases. **Objective**: The aim of this study was to evaluate the analgesic properties of the aqueous leaf extract of the plant in mice.

Methodology: Phytochemical screening of the extract was carried out according to the methods of Trease and Evans. The LD_{50} of the extract was determined using OECD Guideline 425 . Acetic acid-induced writhing test as described by Koster *et al*. was used to investigate the peripheral analgesic activity of the extract, while the hot plate-induced pain model as described by Kumar *et al*. was used to evaluate central analgesic activity. In each of these models, twenty-five mice of both sexes weighing between 19-25 g were divided into five groups of five mice each. Group I (negative control) mice received 10 mL/kg normal saline, Group II (positive control) received 10 mg/kg diclofenac sodium (for acetic acid writhing test) or 10 mg/kg morphine sulfate (for hot plate-induced pain test), Groups III, IV and V received 125, 250 and 500 mg/kg doses of the extract respectively.

Results: Carbohydrates, flavonoids, saponins, tannins, steroids/terpenes, and cardiac glycosides were present while alkaloids and anthraquinones were absent in the extract. There were no signs of toxicity and mortality and the LD_{50} of the extract was estimated to be greater than 5000 mg/kg. The extract produced dose-dependent inhibition of abdominal writhing in mice with the 500 mg/kg dose showing a significantly higher ($p \leq 0.05$) analgesic activity than Diclofenac (62.5% inhibition Vs 45.8% inhibition). In the hot plate pain-induced model, the extract doses produced similar increases ($p > 0.05$) in reaction time when compared with morphine. **Conclusion:** The results of this study support the ethnomedicinal use of *Adansonia digitata* aqueous leaf extract as an analgesic.

INTRODUCTION

The International Association for the Study of Pain updated its definition of pain in 2020, (IASP)[1] as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage It is a universal human experience that in the short term serves to protect an individual from harm, but in the long term can become a debilitating condition[2]. Pain can be classified as nociceptive, neuropathic, acute or chronic. Nociceptive pain describes a normal physiological response to tissue damage resulting from trauma, non-healing injury or inflammatory processes[3]. Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system and occurs as a result of abnormal neural activity[4]. Neuropathic pain can be described as central or peripheral, depending on whether the lesion is in the central or peripheral nervous system[3]. Acute pain lasts for a short period of time, few minutes to about 3 months, sometimes up to 6 months and it tends to be related to a soft-tissue injury or a temporary illness, so it typically subsides after the injury heals or the illness subsides. Acute pain from an injury may evolve into chronic pain if the injury does not heal correctly or if the pain signals malfunction[3]. Chronic pain on the other hand lasts over many months or years – even if the pain isn't always present. It is often due to a health condition, like

arthritis, fibromyalgia or a spine condition[4]. Many orthodox medicines narcotic and non-opioid analgesics (acetaminophen, NSAIDs such as aspirin, ibuprofen, diclofenac, celecoxib) are used to treat mild, moderate and severe pain. However, many of these drugs are associated with side effects such as addiction potential, gastrointestinal disturbances, cardiovascular issues and renal impairment[5].

Medicinal plants have been used for many centuries throughout the world for the treatment of many disease conditions and they have also served as the sources of many orthodox medicines[6]. Medicinal plants that are used for the management of pain and whose analgesic properties have been scientifically evaluated and validated include: *Clutia abyssinia*[7], *Terminalia catappa* L. leaves[8], *Capparis spinosa* root powder[9] and *Terminalia chebula* fruit[10].

Adansonia digitata commonly known as African Baobab by both the English and the French[11] belongs to the family, Malvaceae, is a massive deciduous tree growing up to about 25 m tall with a diameter of 12 m[12], having a lifespan of up to 450 years[13]. Its common local names include; *Kuka* (Hausa), *Igi-Ose* (Yoruba) and *Kulambali* (Igbo). The Baobab tree occurs in the dry, hot savannah of sub-Saharan Africa and it is mainly found in countries such as Kenya, Nigeria, Sudan, South Africa and Zimbabwe[14,15]. Various parts *Adansonia digitata* are believed to be useful as a food source, medicine or for spiritual warfare[16-18]. In the Northern part of Nigeria, the leaves of *Adansonia digitata* are used in preparing soup (*miyan kuka* in Hausa). The pulp of the plant has been used locally as an immune-stimulant and an anti-inflammatory remedy[19] as well as an analgesic, anti-pyretic, febrifuge, astringent and in the treatment of diarrhoea and dysentery[11]. The oil from the seeds is used in the treatment of inflamed gums and diseased teeth[15]. The seeds are used in the treatment of hiccough and diarrhea[11]. Although a lot of pharmacological activities of the plant such as antioxidant capability of the fruit pulp[20], anti-inflammatory and antipyretic activities of the fruit pulp[21], antimicrobial activity of the petroleum ether, ethanol and aqueous extracts[22], there is a dearth of scientific studies on the analgesic activities of this plant. Therefore, this study aimed to evaluate the peripheral and central analgesic activities of the aqueous leaf extract of *Adansonia digitata* in mice.

MATERIALS AND METHODS

Experimental Animals: Albino mice weighing between 19 and 25 g of both sexes were obtained from the Animal House facility of the Department of Pharmacology and Toxicology, Kaduna State University, Kaduna. The animals were kept in clean, dry cages and maintained under ambient conditions of temperature and humidity, and 12h/12h light/darkness cycle in the Animal House. Standard feed (Vital Feed, Jos) and water *ad libitum* were provided for the animals, except when fasting was necessary in the course of the study.

The mice were acclimatized for five days in the laboratory prior to commencement of the experiment. The animals were handled in accordance with the Guidelines of the Ethics Committee of the Department of Pharmacology and Toxicology, Kaduna State University, Kaduna (Approval No: KASU/PT/2024/011) and the National Institute of Health (NIH) Guidelines for the care and use of laboratory animals[23]. All efforts were made to minimize the number of animals used for the study and their suffering. The minimum numbers of animals required to obtain reliable scientific data was used.

Drugs, Reagents and Equipment

All drugs and reagents used were obtained from representatives of reputable companies. They include: Diclofenac potassium, 50 mg (Cataflam®, Novartis Ltd, Lot KMC27), Morphine sulfate injection 10 mg/5ml (Martindale Pharma, UK, Lot 836131), Dragendorff's reagent (BDH, Poole Ltd, U.K), Concentrated Sulphuric acid, Concentrated Hydrochloric acid, Lead sub-acetate solution, Chloroform, 10% ammonium hydroxide solution, Glacial Acetic Acid containing traces of ferric chloride, 10% Sodium hydroxide, Ferric chloride solution, Acetic anhydride, 1% aqueous hydrochloric acid, Molisch's reagent (BDH, Poole Ltd, U.K), Wagner's reagent (BDH, Poole Ltd, U.K), Meyer's reagent (BDH, Poole Ltd, U.K), Sterile Syringes and Needles, Mixer, Whatman Filter Paper No 1, Stopwatch, Digital Weighing Balance, Animal Cages, Markers, Rotary Evaporator (Searchtech Instruments, England. RE 52-3), Water Bath (Model DK-420, No L-606382).

Plant collection and identification

Leaves of *Adansonia digitata* were collected on 19th May, 2024 at Nasfat village, Kaduna in Kaduna North Local Government Area, Kaduna State, Nigeria. The leaves were identified and authenticated by Mallam Umar Gallah, a taxonomist in the Department of Biological Sciences, Kaduna State University, Kaduna, Nigeria and was assigned a voucher specimen number: KASU/BSH/883.

Preparation of plant extract

Adansonia digitata leaves were air-dried under shade in the laboratory until a constant weight was achieved. The dried leaves were size reduced using a wooden pestle and mortar,

and then ground into fine powder using an electrical mixer (Binatone). Then 100g of the fine powder was weighed and macerated with 500 mL of water for 48 hours, with periodic shaking. The mixture was filtered using a Muslin cloth followed by Whatman filter paper No 1 and then dried on a water bath at a temperature of 60-70°C. The dried extract was transferred into an air-tight container for storage and labeled as *Adansonia digitata* aqueous leaf extract.
Percentage yield of the extract was calculated as follows;

$$\% \text{ Yield} = \frac{\text{Weight of dried extract (g)}}{\text{Weight of powdered plant material (g)}} \times 100$$

Qualitative phytochemical screening of plant extract
Qualitative phytochemical screening of the aqueous leaf extract of *Adansonia digitata* was carried out in the Department of Pharmacognosy and Drug Development, Kaduna State University, Kaduna. Nigeria. The standard methods of Trease and Evans[24] were used to screen for the presence or absence of alkaloids, flavonoids, saponins, tannins, glycosides, carbohydrates, steroids/triterpenes and anthraquinones.

Acute toxicity study (LD_{50} Determination) of plant extract
The acute toxicity study of the aqueous leaf extract of *Adansonia digitata* was carried out using OECD Guideline 425 (Limit Test Procedure)[25]. Five female nulliparous and non-pregnant mice were used and their weights fell within the interval of ±20% of the mean weight of the sample population obtained. The mice were housed individually in plastic cages in the laboratory at ambient temperature and humidity and 12 h light and 12 h dark cycle. The mice were fed with standard feed (Vital Feeds, Jos) and water *ad libitum*. The mice were kept in their cages for at least 5 days prior to dosing to allow for acclimatization to laboratory conditions.

The mice were deprived of food for 3-4 hours prior to dosing, but they were given water *ad libitum*. The mice were then weighed and the extract was administered orally in a single dose according to the body weight obtained after fasting. After the extract was administered, food (and not water) was withheld for another 1-2 hours. The extract was prepared shortly prior to administration to ensure the stability of the preparation. A Limit test dose of 5000 mg/kg body weight was used in the experiment.
One mouse was administered a single dose of 5000 mg/kg of the extract orally using an oral feeding cannula. After administration of the extract, food (and not water), was withheld for another 1-2 hours. The mouse was observed for any signs of toxicity or mortality in the first 4 hours and over a period of 24 hours . There was no mortality recorded after 24 hours, and two additional mice were administered with the extract at 5000 mg/kg body weight orally. The two mice were observed for any signs of toxicity or mortality for the first 4 hours and over the period of 24hours. Absence of mortality led to the termination of the Limit Test and all the three tested mice were observed for 14 days without further dosing with the extract.

EVALUATION OF ANALGESIC ACTIVITIES
Acetic acid-induced writhing test in mice
The acetic acid-induced writhing test was used to assess the peripheral analgesic effect of the aqueous leaf extract of *Adansonia digitata.* This test was done according to the method described by Koster *et al.*[26]. Twenty-five mice of both sexes were weighed and randomized into 5 groups of 5 mice each. Group I (Negative control) mice received 10 mL/kg body weight normal saline orally, Group II (Positive control) mice received diclofenac potassium, 10 mg/kg body weight orally, Groups III, IV and V mice received 125 mg/kg, 250 mg/kg and 500 mg/kg body weight of aqueous leaf extract of *Adansonia digitata* orally respectively. One hour after administration of normal saline, diclofenac potassium and the extract, each mouse was injected with 0.1% acetic acid at a dose of 10 mL/kg body weight intraperitoneally. The number of abdominal writhing produced by each mouse was counted for 15 minutes, beginning from 5 minutes after acetic acid injection[26]. Percentage inhibition of abdominal writhing was calculated thus;

$$\%\text{Inhibition of abdominal writhing} = \frac{Wc - Wt}{Wc} \times 100$$

Where;
Wc = Number of abdominal writhing in Control Group,
Wt = Number of abdominal writhing in Test Groups
Hot plate-induced pain test in mice
The hot plate-induced pain test is one of the most common methods used for evaluating central analgesic activity of a drug. This test was conducted according to the method described by Kumar *et al*.[27]. In this method, heat was used as a source of pain. Twenty-five mice were weighed and randomized into five groups of five mice each. Group I (Negative control) mice received normal saline 10 mL/kg (*p.o.*) body weight, Group II (Positive control) received morphine sulfate 10 mg/kg body weight, (*i.p.*), Groups III, IV and V mice received 125 mg/kg, (*p.o.*) 250 mg/kg (*p.o.*) and 500 mg/kg (*p.o.*) body weight of the aqueous leaf extract of *Adansonia digitata*, respectively. One hour after administration of normal saline, morphine and the extract, the mice were placed on a hot plate maintained at a

temperature of 55 ± 0.5°C. The cut-off time for the mice on the hot plate was 20 seconds, in order to avoid damage to their paws. The time taken to flick the hind paw or lick it or jump off the hot plate was considered as the reaction time of the particular mouse. The reaction time was recorded at 0, 30, 60, 90 and 120 minutes intervals. An analgesic activity increases the reaction time. Percentage increase in reaction time was taken as index of pain perception at each interval[28].

STATISTICAL ANALYSIS

Data were expressed as means ± SEM. The data were analyzed using one way analysis of variance (ANOVA) or repeated measures ANOVA followed by Bonferroni post-hoc test. p-values ≤0.05 were considered significant. SPSS Version 20.0 (IBM Corp., Armonk, NY, USA). Presented in tables, was the statistical software package used in analyzing the data.

RESULTS

Yield of Plant Extract

The percentage yield of the extract was 6.6%

Phytochemical constituents of aqueous leaf extract of *Adansonia digitata*

Phytochemical screening of the aqueous leaf extract of *Adansonia digitata* revealed the presence of carbohydrates, flavonoids, saponins, tannins, steroids/triterpenes and cardiac glycosides. Alkaloids and anthraquinones were absent (Table 1).

Table 1: Phytochemical constituents of aqueous leaf extract of *Adansonia digitata*

Phytochemical constituents	Test	Observation	Inference
Carbohydrates	Molisch's test	brownish or purple ring at the interface	+
Cardiac glycosides	Keller Killiani's test	A brown ring at the interface and a pale green colour at the upper layer	+
Alkaloids	Mayer's test	No formation of cream coloured Precipitate	-
Anthraquinones	Bontrager's test	No formation of bright pink colour in the aqueous upper layer	-
Flavonoids	Ferric chloride test	Greenish precipitate	+
Saponins	Froth test	Persistent honeycomb froth	+
Tannins	Lead sub-acetate test	Cream coloured precipitate	+
Steroids/Triterpenes	Liebermann-Buchard's test	Reddish pink or brown ring at the interphase and a bluish green or violet coloured upper layer	+

KEY
+ = Present
- = Absent

Acute toxicity test (LD_{50} Determination) of the aqueous leaf extract of *Adansonia digitata*

No signs of toxicity such as sedation, vomiting, diarrhoea, hyperactivity, piloerection or mortality were observed at a limit test dose of 5000 mg/kg. Therefore, the LD_{50} of the aqueous leaf extract of *Adansonia digitata* was estimated to be greater than 5000 mg/kg.

Evaluation of analgesic activities of aqueous leaf extract of *Adansonia digitata*

Analgesic activity of aqueous leaf extract of Adansonia digitata in acetic acid-induced abdominal writhing test in mice

The aqueous leaf extract of *Adansonia digitata* produced dose-dependent reductions in abdominal writhing in acetic acid-induced writhing in mice with the 500 mg/kg dose of the extract producing the highest inhibition of abdominal writhing (62.5%) compared to 47.7% inhibition of abdominal writhing produced by 125 mg/kg dose of the extract. The inhibition of abdominal writhing produced by 500 mg/kg dose of the extract was significantly ($p \leq 0.05$) higher than those produced by 125 mg/kg of the extract and diclofenac 10 mg/kg, but it was not significantly ($p > 0.05$) greater than that produced by 250 mg/kg dose of the extract (Table 1).

Table 2: Analgesic activity of aqueous leaf extract of *Adansonia digitata* in acetic acid-induced abdominal writhing test in mice

	Abdominal writhing	
Treatment	**Mean ± SEM**	**% Inhibition of writhing**
10 mL/ NS kg	31.80 ± 4.97^{c}	
Diclofenac 10 mg/kg	$16.80 + 5.62^{b}$	45.8
ADLE 125 mg/kg	$16.20 + 5.38^{b}$	47.7
ADLE 250 mg/kg	$14.80 + 4.61^{ab}$	52.2
ADLE 500 mg/kg	$11.60 + 3.30^{a}$	62.5

Values are Means ± SEM. one way ANOVA followed by Bonferroni post hoc test. Means with the same superscript in the column are not significantly different ($p > 0.05$), $n = 5$.
NS = Normal saline. ADLE = *Adansonia digitata* leaf extract.

Analgesic activity of aqueous leaf extract of Adansonia digitata in hot plate-induced pain test in mice

The effect of treatments with various doses of the extract and the standard drug, morphine was observed in the mice across different time points, 0, 30, 60, 90 and 120 minutes. At baseline (0 minute), there were observable responses across all groups, and all values were recorded. At 30 minutes, morphine produced the highest analgesic activity with a reaction time of 11.04 ± 3.12 seconds, which was significantly ($p \leq 0.05$) higher than the saline group (4.68 ± 1.94 seconds). The *Adansonia digitata* leaf extract (ADLE) groups at doses of 125 mg/kg, 250 mg/kg, and 500 mg/kg produced moderate responses, ranging between 7.72 ± 1.84 seconds and 8.50 ± 3.14 seconds. These values were not significantly ($p > 0.05$) different from either the morphine or saline groups, indicating similar analgesic effects. At 60 minutes, morphine produced strong analgesic activity with a reaction time of 10.62 ± 2.28 seconds, which was significantly higher ($p \leq 0.05$) than the saline group (5.84 ± 1.47 seconds). The analgesic responses of the ADLE groups (ranged from 7.84 ± 3.04 seconds to 8.88 ± 1.73 seconds) were significantly higher ($p \leq 0.05$) than saline but not significantly ($p > 0.05$) different from morphine, suggesting comparable effects to the standard analgesic. At 90 minutes, the analgesic effects of morphine decreased slightly to 8.00 ± 2.02 seconds but remained comparable to all ADLE groups, which showed response times of 9.88 ± 1.46 seconds (125 mg/kg), 9.12 ± 1.46 seconds (250 mg/kg), and 8.20 ± 1.60 seconds (500 mg/kg). All treatment groups showed significantly higher analgesic effect ($p \leq 0.05$) than the negative control group (normal saline), which had a response time of 3.72 ± 1.69 seconds. At 120 minutes after commencing the experiment, the ADLE group at 125 mg/kg produced the highest analgesic activity with a response time of 11.42 ± 1.31 seconds, while morphine showed a response of 9.16 ± 3.84 seconds with no significant ($p > 0.05$) difference in analgesic effect of 250 mg ADLE. The 250 mg/kg and 500 mg/kg ADLE groups also produced strong analgesic effects (10.16 ± 1.00 seconds and 9.66 ± 3.08 seconds, respectively). At this point, all treatments demonstrated significantly greater ($p \leq 0.05$) analgesic activity than the negative control (saline) group (4.44 ± 1.42 seconds).

Overall, significant differences were observed among the

treatment groups, with morphine consistently showing the strongest analgesic effect early on (30–60 minutes), while the *Adansonia digitata* extract displayed a dose-dependent and sustained analgesic activity, particularly at 125 mg/kg and 250 mg/kg. The extract's effects were comparable ($p > 0.05$) to morphine at later time points (90 and 120 minutes), confirming its potential as a natural analgesic.

Table 3: Effect of aqueous leaf extract of *Adansonia digitata* in mice using hot plate method

TREATMENT	0 MIN	30 MINS	60 MINS	90 MINS	120 MINS
Saline Group	3.50±1.00[a]	4.68±1.94[a]	5.84±1.47[a]	3.72±1.69[a]	4.44±1.42[a]
Morphine	4.80±1.10[a]	11.04±3.12[b]	10.62±2.28[b]	8.00±2.02[b]	9.16±3.84[b]
ADLE 125mg	4.25±2.03[a]	7.72±1.84[b]	8.88±1.73[b]	9.88±1.46[b]	11.42±1.31[b]
ADLE 250mg	4.40±3.20[a]	8.50±3.14[b]	7.84±3.04[b]	9.12±1.46[b]	10.16±1.00[b]
ADLE 500mg	4.68±2.41[a]	8.48±1.22[b]	8.10±2.70[b]	8.20±1.60[b]	9.66±3.08[b]

Values are mean ±SEM. One Way AANOVA followed by Turkey post hoc test. Means with the same superscript in the column are not significantly different ($p > 0.05$). ADLE = *Adansonia digitata* extract, n = 5

DISCUSSION

The phytochemical screening of the aqueous leaf extracts of *Adansonia digitata* indicated the presence of several bioactive compounds, including carbohydrates, flavonoids, saponins, tannins, steroids/terpenes, and cardiac glycosides, while alkaloids and anthraquinones were absent. Triterpenes, saponins, and sterols present in aqueous extracts have been reported for their complementary anti-inflammatory and analgesic effects [28]. The presence of flavonoids and tannins known for their antioxidant and anti-inflammatory properties, may further enhance the analgesic potential of the extract[29]. Flavonoids are critical in mitigating oxidative stress and inflammation, which are key factors in pain modulation[30]. Saponins are also known to exhibit analgesic properties by modulating inflammatory mediators[31]. Tannins act as astringents and contribute to reducing irritation and inflammation at injury sites[32]. Similarly, steroids/terpenes play a role in pain relief through the inhibition of pro-inflammatory pathways[33]. Flavonoids, tannins, saponins, steroids and terpenes found in this extract may have worked collectively to produce the analgesic activities of the aqueous leaf extract of *Adansonia digitata* observed in this study. The acute toxicity evaluation of the aqueous leaf extracts of *Adansonia digitata* in mice revealed that the LD_{50} was estimated to be greater than 5000 mg/kg and no mortality or observable toxic effects such as lethargy, reduced activity/hyperactivity, vomiting, diarrhoea, piloerection or weight loss, were observed at this dose over 14 days of monitoring and the extract can be classified as having a favorable safety profile[26]. This finding agrees with acute toxicity studies of Aworh *et al*.[34] and Odugbemi *et al*.[35] on *Adansonia digitata* extracts, where they also reported non-toxicity of this plant even at high doses. The non-toxic nature of *Adansonia digitata* leaf extract supports its long-standing use in traditional medicine as a remedy for various ailments, including pain, inflammation, and fever. However, further studies involving chronic toxicity and histopathological analysis are recommended to ensure comprehensive safety assessment[36].

The acetic acid-induced writhing test is a well-established model for assessing peripheral analgesic activity from natural sources[26]. This test is very sensitive and can detect anti-nociceptive effects of natural products and test compounds at dose levels which remain inactive for other methods[26]. Intraperitoneal injection of acetic acid causes irritation and stimulation of the peritoneal cavity that triggers the synthesis and release of various endogenous inflammatory mediators such as serotonin, histamine, bradykinin, substance P and prostaglandins[37]. These various endogenous inflammatory mediators elicited chemical-induced visceral pain which is characterized by constriction of abdominal muscles together with the extension of the forelimbs and elongation of the body[37]. This model has also been associated with increased level of prostaglandin within the peritoneal cavity which enhances inflammatory pain by increasing capillary permeability and activating peripheral nociceptors[38].

The results of the acetic acid-induced writhing test demonstrate a significant dose-dependent analgesic activity of *Adansonia digitata* aqueous leaf extract (ADE), with the highest dose (500 mg/kg) achieving a 62.5% inhibition of abdominal writhing which is significantly higher ($p \leq 0.05$) than the 45.8% inhibition produced by diclofenac (10

mg/kg). The result of this study showed that the peripheral analgesic effect may be mediated through suppression of inflammatory mediators such as prostaglandins[39]. Saka *et al*. [40] also observed a dose-dependent reduction in writhing behaviors in mice treated with *Adansonia digitata* fruit extracts, attributing the analgesic effects to the flavonoid content, which inhibits prostaglandin synthesis. Similarly, Ezeja *et al*. [41] evaluated the analgesic properties of *Euphorbia hirta*, a plant rich in flavonoids and saponins, and reported a writhing inhibition of up to 60% at higher doses similar to the 62.5% inhibition observed with ADE at 500 mg/kg in the current study. Akinmoladun *et al*. [42] who studied *Moringa oleifera*, another plant with a similar phytochemical profile, also found dose-dependent analgesic effects, with inhibition greater than 50%, similar to the results from this study, further highlighting the effectiveness of flavonoid-rich plants in pain management. Gwarzo *et al*. [43] in their study of *Adansonia digitata* seed extracts, found that the percentage writhing inhibition ranged from 40% to 60%, aligning with the results of the present study using leaf extracts. This supports the notion that *Adansonia digitata* contains bioactive compounds responsible for its analgesic effects. The results from this study also align with findings from research on synthetic analgesics, such as diclofenac, which are known to inhibit pain via COX-2 inhibition and reduce prostaglandin synthesis. The peripheral analgesic activity observed with this plant extract may have been mediated via COX-2 inhibition and a consequent reduction in prostaglandin synthesis. The hot plate test is a well-established method for evaluating central analgesic activity, as it measures the response time of animals to thermal pain stimuli. This model was used because of its sensitivity to strong analgesics and limited tissue damage with a cut off time of 20 seconds, which is usually applied to limit the time the mouse spends on the hot plate. The model also requires less time and measurements are usually accurate[37]. In this study, morphine produced significant ($p \leq 0.05$) analgesic activity throughout the period of the experiment compared to the negative control group (normal saline) with the highest reaction time achieved at 30 minutes. There was no significant ($p > 0.05$) difference in the analgesic activity of the extract doses tested when compared with the negative control (normal saline) in the first 60 minutes of the experiment. The delayed analgesic action of the leaf extract of *Adansonia digitata* in this study was similar to that reported for the fruit pulp extract of the plant by Aworh *et. al*. [44]. However, at 90 and 120 minutes, all the extract doses (125, 250 and 500 mg/kg) produced significant ($p \leq 0.05$) analgesic activities when compared to the negative control group, although these effects were not significantly ($p > 0.05$) different from those of the standard drug, morphine. Morphine produces its central analgesic activity by binding to μ receptors in the brain and spinal cord and this may suggest a similar pathway for the observed central analgesic activity of this plant. The phytochemical constituents of the leaf extract of *Adansonia digitata* such as flavonoids, saponins and tannins acting either singly or in combination may be responsible for the peripheral and central analgesic activities of the aqueous leaf extract of *Adansonia digitata* observed in this study.

CONCLUSION: The results of this study demonstrated that *Adansonia digitata* aqueous leaf extract possesses analgesic activity in mice and this plant may be a source of a new, more effective and safe analgesic.

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CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in the writing and publication of this manuscript.

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