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The Journal of Phytopharmacology 2026; 15(3):203-210
Online at: www.phytopharmajournal.com

Research Article

ISSN 2320-480X
JPHYTO 2026; 15(3): 203-210
May- June
Received: 09-01-2026
Accepted: 23-05-2026
Published: 24-06-2026

doi: 10.31254/phyto.2026.15301

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Evaluation of the antidiarrheal effects of freeze-dried bark extract of *Warburgia ugandensis* in experimental animals

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ABSTRACT

Background: Diarrheal diseases remain a major global public health concern and are an important cause of morbidity and mortality, especially among children. Current therapies for diarrhoea management are often limited by poor availability, low acceptability, and adverse effects. Traditional herbal remedies such as *Warburgia ugandensis*, widely used in African traditional medicine, may provide a useful alternative. **Objective:** To investigate the antidiarrheal effects of freeze-dried bark extract of *W. ugandensis* and explore its possible mechanism of action. **Materials and Methods:** Freeze-dried bark extract of *W. ugandensis* was prepared and evaluated using experimental animal models. Thirty rats were randomly assigned to six groups (n=5): negative control (normal saline, 5 mL/kg), positive control (loperamide, 5 mg/kg), and four test groups receiving extract doses of 200, 400, 800, and 1200 mg/kg orally. Diarrhoea was induced using castor oil, and faecal output was monitored for 6 h. Intestinal motility was assessed using the charcoal meal test, while antisecretory activity was evaluated by prostaglandin E-induced enteropooling. The effect on smooth muscle contractility was studied using isolated rabbit jejunum preparations. To investigate the mechanism of action, tissues were pretreated with tamsulosin (α-antagonist), yohimbine (α-antagonist), propranolol (β-antagonist), naloxone (opioid antagonist), and acetylcholine before administration of the extract. **Results:** The extract reduced faecal output in a dose-dependent manner, with significant inhibition observed at 800 mg/kg ($p<0.01$). In the charcoal meal test, the same dose significantly reduced intestinal transit ($p<0.001$). The extract also significantly inhibited prostaglandin E_2-induced intestinal fluid accumulation ($p<0.001$). In isolated rabbit jejunum, the extract produced a dose-dependent reduction in the force of spontaneous contractions up to 5.0 mg/mL. The relaxant effect of 1.0 mg/mL extract was attenuated by acetylcholine, tamsulosin, yohimbine, and naloxone, but was unaffected by propranolol. **Conclusion:** Freeze-dried bark extract of *W. ugandensis* exhibited significant antidiarrheal activity through inhibition of intestinal motility and secretion. Its antimotility effect may involve activation of α-adrenergic and μ-opioid receptors, supporting its traditional use in the management of diarrhoea.

Keywords: *W. ugandensis*, Antidiarrheal activity, Castor oil-induced diarrhea, Intestinal motility, Enteropooling assay, Traditional medicine.

INTRODUCTION

Diarrheal diseases are a global problem affecting both developed countries and the developing world. However, the economic and social burden is felt more in poorer countries due to inadequate resources, poor sanitation, and congestion [1]. Those who are at risk of diarrhoeal diseases include preschool children, the elderly, those with acquired and congenital immunodeficiencies, and those on cancer chemotherapy. Globally, there are 1.7 billion childhood cases of diarrhoea annually, and 525,000 children under-five die yearly as a result [1]. In the developing world especially sub-Saharan Africa, the Indian sub-continent, and South East Asia, children experience 2.9 cases episodes of diarrhoea a year [2]. Intestinal infection is the most common cause of diarrhoea worldwide. Diarrheal diseases are the leading causes of malnutrition in children [1]. The relationship between diarrhoea and malnutrition is a bidirectional one [3]. Mortality results from excessive loss of fluid and electrolytes leading to dehydration and acidosis.

Oral Rehydration solutions (ORS) remain the mainstay of treatment due to its availability and simplicity of use. ORS is used mainly in infectious diarrhoea to replace fluid loss and promote fluid absorption in the intestine. ORS have proven to be effective and have reduced morbidity and mortality [4]. However, ORS fail to reduce the volume of watery stool, and to limit the duration of diarrhoea [5]. Therefore, there remains an unmet need to offer complementary, and/or alternative therapy due to, in part, unavailability, limited acceptability and shortfalls of ORS. Alternative options to ORS include anti-motility drugs (e.g. loperamide hydrochloride, diphenoxylate), adsorbents (e.g. kaolin, attapulgite), bismuth subsalicylate, enkephalinase inhibitor (i.e. racecadotril), and antibiotics such as quinolone, azithromycin etc [6]. These agents are associated with a good prognosis. However, they possess an adverse drug profile that includes: sedation, constipation, dizziness, nausea, and vomiting [7,8]. In addition, most anti-diarrhoeal agents are contraindicated in children under the age of 4. Therefore development, and/or discovery of new agents is important

Most herbal medicine have synergistic properties, and/or side effect neutralizing properties [9]. They are readily accessible, cheaper and in some instances have efficacy similar to that of standard treatments [6]. Some of the plants that have demonstrated antidiarrheal properties include *Bidens biternata* [10], *Mangifera indica* [11], *Punica granatum* [12], and *Psidium guajava* [13]. *W. ugandensis* has been used in traditional African medicine to treat a number of diseases such as gastrointestinal disorders, cold, cough, fever and malaria [14]. The plant extracts have antimicrobial activities due to the presence of a variety of phytochemicals that include drimane sesquiterpenoids such as warburganal, polygoidal, muzigadial, mukaadial, ugandenisal, and flavonoids and other miscellaneous phytochemicals [15]. However, there are no documented scientific studies that have investigated its antidiarrheal properties. The aim of this experiment was to evaluate the antidiarrhoeal effects of freeze-dried extracts of *W. Ugandensis.*

MATERIAL AND METHODS

Chemicals and reagents

Loperamide (Nila Pharmaceuticals Ltd, Kenya) was suspended in 0.9% normal saline and administered orally at a dose of 2 mg/kg body weight. Activated charcoal (10%; Sigma Chemical Co., St. Louis, MO, USA) was suspended in 0.9% normal saline (Hartman's Solution B.P.; Kemia International, Nairobi, Kenya), and 2 mL was administered orally. Acetylcholine, tamsulosin, yohimbine, propranolol, and naloxone (Kobian Chemicals, Kenya) were administered intraperitoneally for mechanistic studies. All solutions were freshly prepared immediately before use and administered intraperitoneally in a fixed volume of 1 mL per mouse using 25 G × 0.625-inch needles.

Collection and preparation of extracts

Fresh bark was obtained from *W. ugandensis* trees in the forest at Chiromo campus of the University of Nairobi. A specimen was deposited at the University of Nairobi herbarium for identification and allocated voucher specimen number SOUON2023/012. The bark was then air dried for 4 weeks. It was then milled using a blender and the dry powder weighed 400 g. Aqueous extracts were obtained from the extract using a freeze-drier. The final weight of the extract was 54 g.

Experimental animals

Thirty (30) Sprague Dawley rats of both sexes, weighing 120-400 g, were used for the *in vivo* study. The animals were randomized into six groups (n = 5 per group). Additionally, five New Zealand rabbits were used for the *ex-vivo* study. Ethical approval for the study was obtained from the Biosafety, Animal Use, Care and Ethics Committee, Faculty of Veterinary Medicine, University of Nairobi (REF: FVM BAUEC/2023/478). All experimental procedures were conducted in accordance with the Guidelines for Ethical Conduct in the Care and Use of Animals (APA Council of Representatives, 2012).

All animals were housed in the animal facility of the Department of Medical Physiology, University of Nairobi, under standard laboratory conditions with a 12 h light/dark cycle, controlled room temperature, and appropriate humidity. Food and water were provided *ad libitum*, and the animals were allowed to acclimatize for one week prior to the commencement of the experiments.

Castor oil induced diarrhoea

Rats of either sex (150-250 g) were randomized into 6 groups (n = 5). They were fasted for 12 h. They received treatments, with the control group receiving 2mL of 0.9% normal saline and the positive control group receiving Loperamide (2 mg/kg) orally as suspension. The extract was given orally to four other groups at 200 mg/kg, 400 mg/kg, 800 mg/kg or 1200 mg/kg as a suspension. After 30 min, the animals in each group received 2mL of castor oil orally. The character and mass of faecal output was noted up to 6 h with the filter paper at the base of the cages. The weight of the filter paper before and after the experiment was noted [16].

Charcoal meal test

Rats of either sex (150-250 g) were randomized into 4 groups (n = 5). They were fasted overnight. The first group received the vehicle 2mL of 0.9% normal saline, the second group received Loperamide 2 mg/kg orally as a suspension. The extracts were administered orally to two groups, 800 mg/kg to the third group and 1200 mg/kg to the fourth group. 30 min after treatment, the rats were given 2 mL of 10% activated charcoal suspended in 0.9% normal saline p.o. The animals were euthanized 30 min after charcoal administration. The abdomen was opened and the small intestine removed from the pylorus to the caecum. The distance travelled from the pylorus to the caecum was measured and represented as a percentage of the whole length of the intestine from the pylorus to the caecum for each of the rats [16].

Castor oil induced enter pooling

Rats of either sex (150-250 g) were fasted for 18 h and randomized into 3 groups (n=5). The first group received normal saline (2 mg/kg). The second group received Loperamide (2 mg/kg) by oral route. The third group was administered extract orally at 800 mg/kg as oral suspension. One h later, 2mL of castor oil was administered. After 2 h following administration of castor oil each rat was sacrificed by cervical dislocation and the whole length of the intestine from pylorus to caecum was dissected out, its content collected in measuring cylinder and volume measured [16].

Isolated rabbit jejunum motility

Five rabbits were fasted for 18 h. The rabbits were sacrificed via cervical dislocation. The abdomen was cut open and a 10 cm of the jejunum was dissected out from the mesentery. The jejunum was placed in a beaker containing the cold physiological salt solution (PSS) Tyrode's solution. The contents of the jejunum were flushed twice using PSS and placed in a beaker containing warm PSS. A 2 cm segment of the jejunum was mounted on an organ bath containing the PSS solution at 37±1 °C and aerated with carbogen gas (95% oxygen and 5% carbon dioxide). The upper end of the segment was hooked to an isometric force transducer (ML500/A, AD Instruments) connected to a Power Lab data acquisition system (Power Lab 8/30, AD Instruments).

The segment was first allowed to equilibrate for a period of 60 minutes with the PSS being changed every 15 min as a precaution against metabolites [16]. Effects of different concentrations of extracts on the intrinsic contractions of jejunum were tested. A record of 2 minutes of normal activity was recorded before administering each treatment. Each dose of the extract was added to the organ bath and

its effect recorded for 5 min before washing out. The organ was then rinsed twice with fresh PSS before testing the next concentration. The force and rate of concentration were recorded and analysed using Chart software (AD Instrument). Rate is the number of cycles per minute (cpm) while force is measured in grams (g). The values were expressed as a percentage of control (values before treatment) [16].

To investigate the possible mechanisms of action, the effect of 1 mg/mL *W. ugandensis* extracts was tested in the presence of agonists and antagonists of the autonomic nervous system and opiate system: acetylcholine, tamsulosin (α1 adrenergic blocker), yohimbine (α2 adrenergic blocker), propranolol (β adrenergic blocker) and naloxone (μ opioid blocker). A record of 2 min was taken before adding the antagonist (10^{-6} M). The extract was then added, and its effect was recorded for (3-5 minutes) before washing out.

Statistical analysis

The data was expressed as mean ± standard error of mean (SEM). GraphPad software v 8.0.1 was used to analyse the data. The data was analysed using one way ANOVA followed by Tukey's post hoc test. Statistical significance was set at $p < 0.05$.

RESULTS

Castor oil induced diarrhoea

There was a significant difference in the mean mass of faecal output between the treatment groups as determined by one-way ANOVA (F [4; 30] = 145.348, P=0.000). Post hoc analysis showed that the mean mass of faecal output in the group that received normal saline (4.151 ± 0.1253 g) was significantly increased compared to the groups that received 800 mg/kg of WUG (0.6761 ± 0.5238 g; P = 0.004) and 1200 mg/kg of WUG (0.4956 ± 0.2243 g; P = 0.002) and loperamide 5 mg/kg (0.3192 ± 0.1089 g; P = 0.002). There was no statistical difference between the groups that received high dose WUG; 0.6761 ± 0.5238 g (800 mg/kg of WUG), 0.4956 ± 0.2243 g (1200 mg/kg) or 0.3192 ± 0.1089 g (Loperamide 5 mg/kg).

Castor oil induced enter pooling

There was a significant difference in the mean volume of intestinal contents between the treatment groups as determined by one-way ANOVA (F [4; 30] = 145.348, P=0.000). Post hoc analysis showed that the mean volume of intestinal contents in the group that received normal saline (2.959 ± 0.2149 cm^3) was significantly high compared to the groups that received 800 mg/kg of WUG (1.811 ± 0.2992 cm^3; P = 0.001) and loperamide 5 mg/kg (0.3086 ± 0.1209 cm^3; P = 0.002). The group that received 800 mg/kg WUG 1.811 ± 0.2992 cm^3 had a significantly higher mean volume of intestinal contents compared to the group that received loperamide 0.3086 ± 0.1209 cm^3; P = 0.002.

Charcoal meal test

There was a significant difference in the mean distance travelled by the charcoal pellet between the treatment groups as determined by one-way ANOVA (F [4; 30] = 145.348, P=0.000). The charcoal pellet in the normal saline group travelled a mean distance equal to the 84.96 ± 3.118% of the small intestine. In the group administered with 800 mg/kg of WUG, it travelled 57.51 ± 2.597% of the small intestine, and the atropine sulphate group, 38.57 ± 4.393% of the small intestine. Post hoc analysis showed that the mean distance travelled by the charcoal pellet in normal saline group (84.96 ± 3.118%) was significantly higher compared to the treatment groups that received 800 mg/kg WUG or Atropine Sulphate i.e., 57.51 ± 2.597% and.38.57 ± 4.393% respectively (p value <0.001). There was also a statistically significant difference between the group administered with WUG and atropine sulphate; 57.51 ± 2.597% (800 mg/kg WUG) vs. 38.57 ± 4.393% (Atropine Sulphate) (p value <0.01).

Isolated jejunum motility

The extracts of *W. ugandensis* had a statistically significant effect on both the force and cycles of contractions of the isolated jejunum. The extracts had a dose dependent effect on the both the force and cycles of contractions with maximal inhibition at the highest dose of 5 mg/kg.

Effect of the extracts on cycles of contractions

There was a dose dependent significant difference between the treatment groups (Table 1). There was a significant difference between 0.5 mg/mL (85.84 ± 1.121%) and 1 mg/mL (73.94 ± 1.942%) (p value = 0.002). There was also a significant difference between 1 mg/mL (73.94 ± 1.942%) and 2 mg/mL (59.78 ± 2.388%) (p value = <0.001). There was also significant difference between 2 mg/mL (59.78 ± 2.388%) and the dose that produced the highest inhibition 5 mg/mL (39.64 ± 1.975%) (p value = < 0.001)

Effect of the extracts on force of contractions

There was no statistical difference between 0.5 mg/mL (76.65 ± 2.667%) and 1 mg/mL (61.60 ± 6.169%) (p value = 0.072). There was no significant difference between 1 mg/mL (61.60 ± 6.169%) and 2 mg/mL (58.38 ± 2.734%) (p value = 0.942). However, there was a statistically significant difference between 2 mg/mL (58.38 ± 2.734%) and 5 mg/mL (37.29 ± 3.321%) (p value = 0.009).

The relaxant effect of 1.0 mg/mL *W. ugandensis* (61.60 ± 13.79% of control) was significantly reduced in the presence of acetylcholine (89.23 ± 2.826% of control) (p value = <0.001), tamsulosin (87.37 ± 2.615% of control) (p value = <0.001), naloxone (85.59 ± 2.066% of control) (p value = 0.05), and yohimbine (77.48 ± 1.475% of control) (p value = 0.048). The relaxant effect was not affected by propranolol (70.30 ± 5.253% of control) (p value = 0.541).

There was no significant difference between the preparations pre-treated with tamsulosin and those pre-treated with yohimbine (p value = 0.405), or propranolol (p value = 0.029). There was no significant difference between preparations pre-treated with naloxone and those pre-treated with yohimbine (p value = 0.612) or propranolol (p value = 0.061). None of the antagonists completely inhibited the relaxant effect of 1.0 mg/mL *W. ugandensis* as compared to the control (Table 2).

Table 1: Effects of *W. ugandensis* extract on cycles and force of contraction in isolated rabbit ileum

W. ugandensis **(mg/mL)**	**% of Control (Mean ± SEM)**	
	Rate of contraction	**Force of contraction**
0.5	85.84 ± 1.121%	76.65 ± 2.667%
1.0	73.94 ± 1.942%*	61.60 ± 6.169%
2.0	59.78 ± 2.388%***	58.38 ± 2.734%*
5.0	39.64 ± 1.975%***	37.29 ± 3.321%***

*P < 0.05, **P < 0.01, ***P < 0.001 vs. control.

Table 2: Illustrating effects of preparation incubated with selected agonist

Treatment	**% of Control (Mean ± SEM)**
1.0 mg/ml *W. ugandensis*	61.60 ± 13.79%
Tamsulosin + 1.0 mg/mL *W. ugandensis*	87.37 ± 2.615%***
Yohimbine + 1.0 mg/mL *W. ugandensis*	77.48 ± 1.475%*
Propranolol + 1.0 mg/mL *W. ugandensis*	70.30 ± 5.253%
Naloxone + 1.0 mg/mL *W. ugandensis*	85.59 ± 2.066%*
Acetylcholine + 1.0 mg/mL *W. ugandensis*	89.23 ± 2.826%***

*P < 0.05, **P < 0.01, *P < 0.001 vs. 1.0 mg/mL *W. ugandensis* alone.

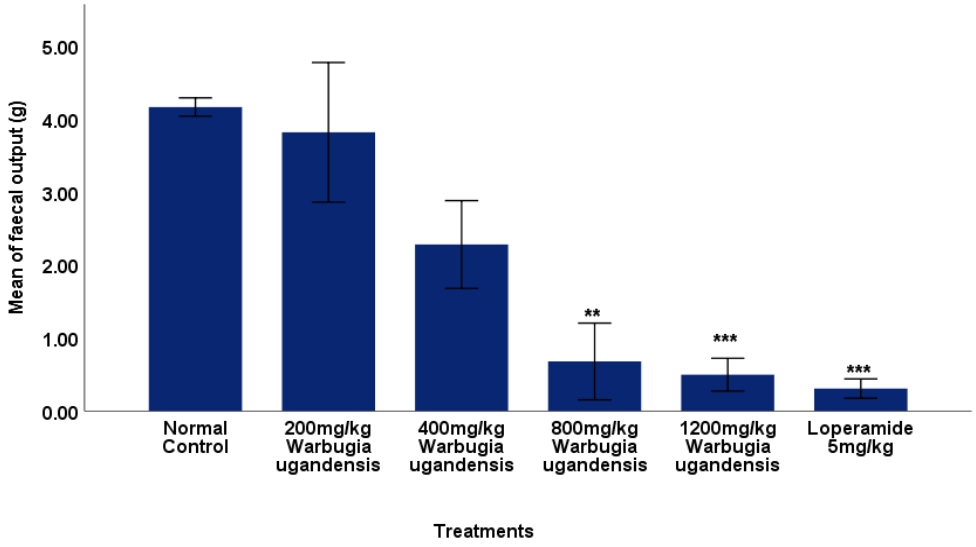

Figure 1: A bar graph showing the average mass of faecal output
*p < 0.05, **p < 0.01, ***p < 0.001 vs. normal control

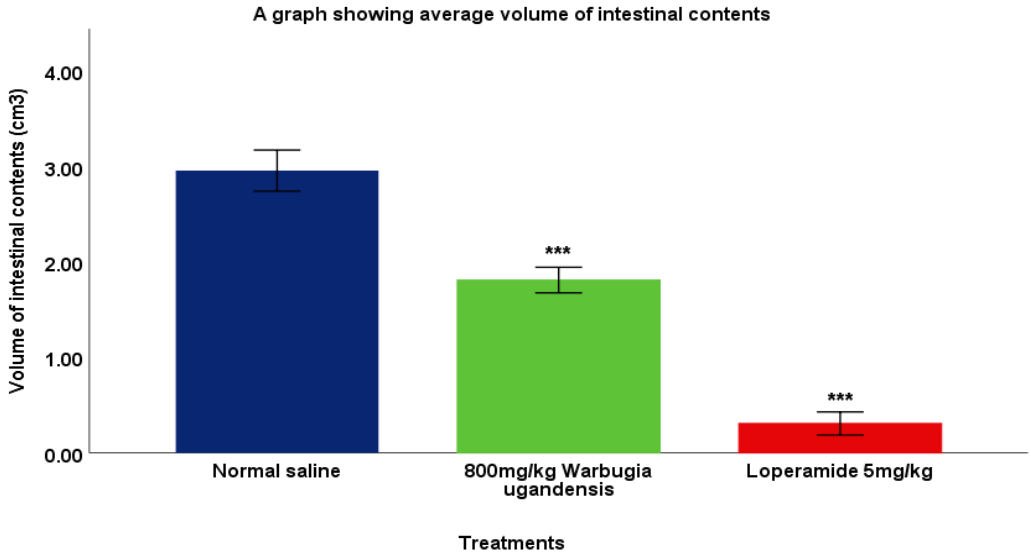

Figure 2: Showing the average volume of intestinal contents
*p < 0.05, **p < 0.01, ***p < 0.001 vs. normal saline

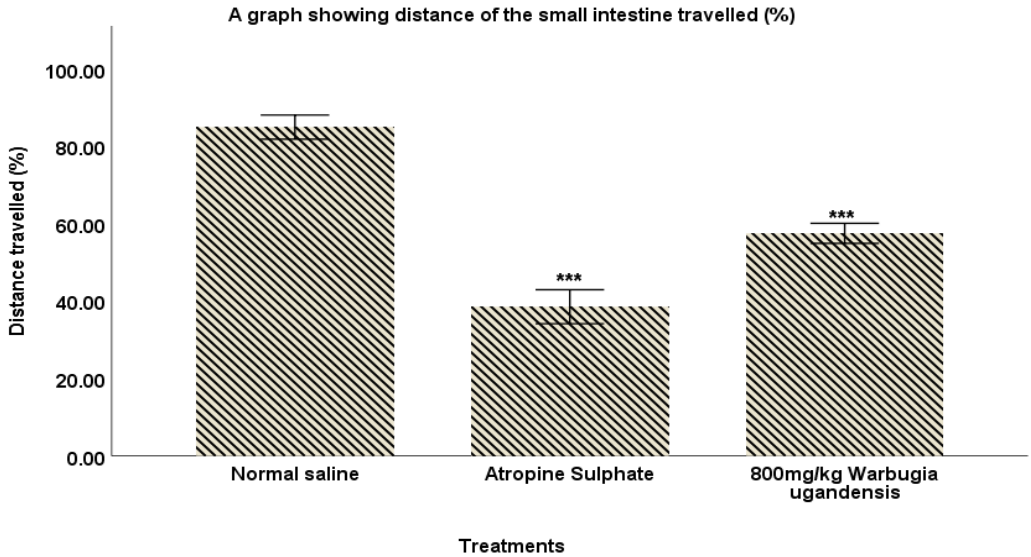

Figure 1: Bar chart for distance travelled by pellet
*p < 0.05, **p < 0.01, ***p < 0.001 vs. normal saline

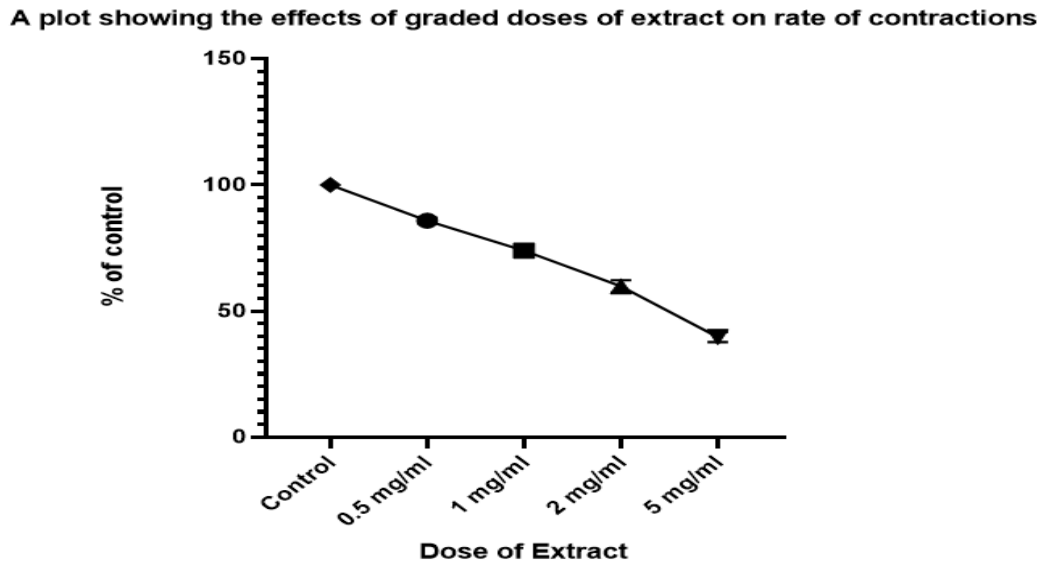

Figure 4a: A line plot illustrating the effects of graded doses on rate of contractions

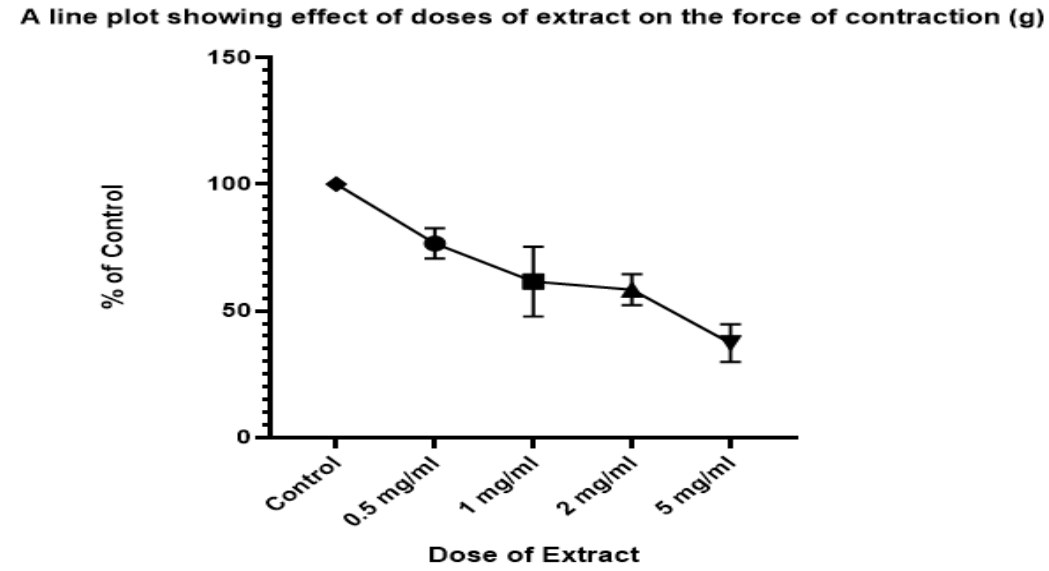

Figure 4b: A line plot illustrating the effect of doses of extract on the force of contraction

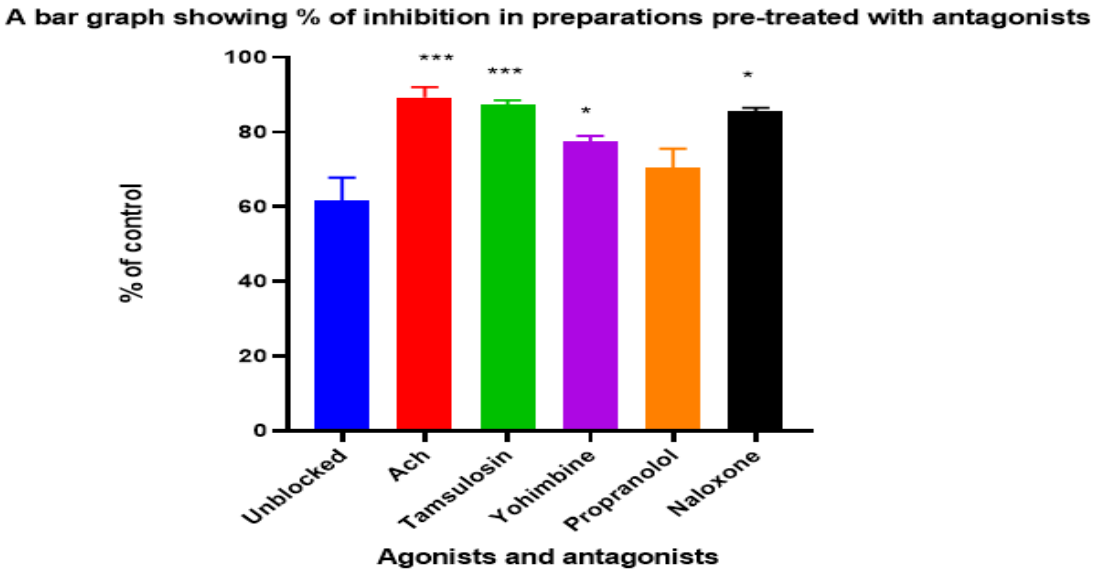

Figure 5: A bar graph showing % of inhibition in preparations pre-treated with antagonists. *p value < 0.05, **p value < 0.01, *** p value < 0.001 vs. unblocked

DISCUSSION

The genus *Warburgia* is exclusively found in Africa, predominantly east, central and southern Africa. The genus consists of 5 taxa [17,18] that have an illustrious history of use in traditional medicine. They are used anecdotally in treating coughs, cold, venereal diseases, candidiasis, toothaches and gastrointestinal disorders [15]. The bark is the most commonly used part, while the leaves and roots are occasionally used. The bark is prepared as decoction and is sometimes infused, or used as snuff [19]. Non-medicinal uses of the family include use as mulch for soil, inciting aggression in dogs and bees, for crafting wooden ornaments, for firewood and timber, for shade and resin, to season food, and for antifeedant [17,18]. *W. ugandensis* is used for treatment of stomach-ache, constipation, toothache, venereal diseases, cough, and as preventative for diarrhoea [20]. The bark is chewed and the juice swallowed. The leaf decoction is used to treat skin diseases. Animals have been documented to use *W. ugandensis* for self-treatment. This includes elephants which travel long distances outside their habitat to consume the bark of *W. ugandensis* [21]. The tree is usually planted for aesthetic purposes, used as firewood due to its high oil content, making ornaments. Its resin is locally used as glue to fix tool handles. The leaves, pods and seeds are fed to livestock.

In this study, *W. ugandensis* inhibited castor oil induced diarrhoea dose dependently (Figure 1). The antidiarrheal effects of WUG may act through direct inhibition or via other antagonistic mechanisms. *W. ugandensis* significantly inhibited intestinal fluid secretion (Figure 2). Castor oil induces secretion in the intestine, decreases reabsorption of fluid [22,23]. Castor oil-induced diarrhoea in rats is an appropriate model of the complex prolonged processes of hypersecretion and accelerated transit that characterize secretory diarrhoea [24]. Castor oil contributes to diarrhoea by lubricating the intestinal mucosa, thus shortening the transit time of intestinal contents. This may contribute to the laxative effect seen in castor oil-induced diarrhoea [22].

Charcoal meal pellet is an indigestible material that distends the intestinal wall triggering reflex peristalsis. *W. ugandensis* inhibited the movement of the charcoal pellet significantly when compared with the normal saline (Figure 3). The degree of inhibition was comparable to the effect of loperamide on motility. Reduction in motility allows more time for reabsorption hence reducing fluid losses and faecal output. The experiments on isolated jejunum attempted to elucidate the probable mechanisms of action on motility. *Ex-vivo* motility test showed that *W. ugandensis* has effect on the intestinal motility. The tests showed that *W. ugandensis* inhibited activity with maximal inhibition at 5 mg/mL (Figure 4a and b). Pre-treatment with tamsulosin (α1 adrenoceptor blocker), yohimbine (α2 antagonist), and naloxone (opioid receptor blocker) decreased the relaxant effect of *W. ugandensis* significantly (Figure 5). The relaxant effect of *W. ugandensis* was not affected by pre-treatment with propranolol (β antagonist). Pre-treatment with acetylcholine (muscarinic receptor agonist) decreased the relaxant effect of *W. ugandensis*. This indicates that *W. ugandensis* exert their effects via parasympathetic, sympathetic and opiate mechanisms. An excitatory cholinergic pathway allows smooth muscle contraction via activation of G_q coupled muscarinic receptors, while a non-adrenergic non-cholinergic pathway acts to cause smooth muscle relaxation via the release of NO and/or vasoactive intestinal peptide (VIP) [25]. Administration of muscarinic receptor antagonist such as atropine has a significant effect on gastric tone and motility. The pre-treatment with acetylcholine reduced the relaxant effect of *W. ugandensis* indicating that the extract acted independently of mechanisms that are involved the parasympathetic pathway. Sympathetic preganglionic neurons innervating the GI tract arise from the thoracic and lumbar spinal cord. The sympathetic nervous system regulates the activity of the GIT via both alpha and beta adrenoceptors.

The relaxant effect of *W. ugandensis* was sensitive to naloxone (opioid receptor blocker) suggesting that *W. ugandensis* may also contain opiate like constituents. Opiates and opioid peptides have a universal action - supress neuronal excitability [26] Morphine and other μ-opioid agonists slow gastric emptying of liquids and solids in humans and animal models [27,28]. Naloxone reverses the effects of opiates on the neuronal system. Naloxone and other μ-antagonists reverse the slowing of gastric emptying by morphine. Opiate-induced slowing of gastric emptying is associated with elevated tonic contraction in the antrum and pylorus and decreased resting tone in the musculature of the gastric reservoir. Downstream effects of opioid signalling involve inhibition of adenylyl cyclase, inhibition of Ca^{2+} influx and activation of K^+ efflux. This leads to inhibition of neurotransmitter release and reduced neuronal excitability [26]. These actions lead to inhibition of propulsive motility and inhibition of mucosal Cl^- secretion. *W. ugandensis* may have acted synergistically through activation of alpha adrenoceptors and enteric opioid receptors to produce the observed changes in motor and secretory functions.

Diarrhoea is a symptom of either intestinal disorders, such as infection, or of a systemic issue. The mechanisms that drive diarrhoea can be osmotic, active secretion, motility disorders, and exudation. In specific diarrhoeal diseases, more than one mechanism is usually involved. Diarrhoea can result due to dysregulated motility with both increases and decreases in gut motility leading to diarrhoea. Increased motility decreases the time required for effective reabsorption of fluid in the intestine, this occurs in conditions such as thyrotoxicosis, and opiate withdrawal. Decreased motility leads to diarrhoea due to bacterial overgrowth in the GIT. This is found in conditions such as autonomic neuropathy due to diabetes, muscular dystrophy, or radiation injury. There are three clinical types of diarrhoea classified based on their duration, and contents i.e., acute watery diarrhoea, bloody diarrhoea, and persistent watery diarrhoea [1]. Infectious agents are the leading cause of diarrhoeal diseases in the world [5]. Non-infective causes of diarrhoea include inflammatory processes in the GIT due to milk protein intolerance, psychogenic, drug induced increases in motility, and typhlitis (inflammation of colon due to neutropenia) [29]. *W. ugandensis* effects on intestinal motility contribute to its antidiarrhoeal activity, the rapid response of the intestine to the administration of the extracts serve to indicate the quick therapeutic effects of the extracts. The isolated jejunum eventually recovered back to normal after a certain period of time, this shows the reversibility of its effects. This shows that in addition to the antidiarrhoeal effect, *W. ugandensis* has spasmolytic effects.

The mainstay of treatment has been ORS, which replace the fluid and electrolytes lost to prevent dehydration of patient due to the massive loss of fluid, and electrolytes. These solutions have significantly reduced mortality due to diarrhoea since they were formulated [5]. Though ORS therapy reduces mortality, they don't reduce stool volume or the duration of diarrhoea [30]. This can prolong the suffering of the diseased individual. Alternative remedies such as *W. ugandensis* that have antidiarrheal effects are worth investigation. Phytochemical analysis of *W. ugandensis* has identified certain classes of compounds that may explain some of the observed effects on the intestine. Some of these include glycosides, flavonoids, sesquiterpenes, tannins and free fatty acids [15]. Tannins have been shown to enhance mucosal barrier leading to decreased permeability and fluid secretion. Gallo tannins have been shown to inhibit CaCC, believed to mediate the therapeutic benefits of certain red wines and green teas, in managing secretory diarrhoea and cardiovascular disease [31]. Certain classes of phenols have also been shown to modulate intestinal fluid transport. Flavonoids are polyphenols found in almost every plant and have been found to mediate the pharmacological properties of most herbal remedies [32]. A good number of flavonoids have also been shown to modulate the activity of the CFTR Cl^- channel, including quercetin, luteolin, apigenin and kaempferol [33]. It has been suggested that flavonoids may not only prove useful in the management of secretory diarrhoea, but also in the management of cystic fibrosis and polycystic kidney disease [33,34]. It appears likely that in this study, several compounds including flavonoids and tannins caused the antidiarrheal effects observed in the rat models.

CONCLUSION

The results of this study showed that *W. ugandensis* has potential as an antidiarrheal herbal remedy and merits further exploration. Additional investigations are recommended to evaluate the effects of individual compounds isolated from *W. ugandensis* on intestinal motility and secretion. Furthermore, studies on its influence on the gut microbiome, which plays a crucial role in gut function and immunity, are warranted. The widespread distribution of this herb in sub-Saharan Africa could make it a readily accessible remedy in a region where diarrheal diseases remain highly prevalent.

Acknowledgements

We would like to thank Dr. Peter Waweru and Mr. Boniface Chege of the Department of Human Anatomy and Medical physiology, University of Nairobi for the technical support and advice rendered during the course of the research work.

Author Contributions

Rugut C. Kiprop was involved in concept, design, literature review and execution of research work; Charles G. Githinji and Anne W. Muriithi conceptualised the manuscript; Charles G. Githinji was involved in statistical analysis and in data acquisition. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data that support the findings of this study are available and will be made available upon request.

Use of AI in Drafting of Manuscript

The authors declare that they have not used any generative AI/AI-assisted technologies in the writing of this manuscript.

Conflict of interest

The authors declared no conflict of interest.

Financial Support

None declared.

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HOW TO CITE THIS ARTICLE
Kiprop RC, Githinji CG, Murithi AW. Evaluation of the antidiarrheal effects of freeze-dried bark extract of *W. ugandensis* in experimental animals. J Phytopharmacol 2026; 15(3):203-210. doi: 10.31254/phyto.2026.15301