Purgative Activities of Securidaca Longepedunculata Root Bark Aqueous Extract in Loperamide-Induced Constipated Wistar Rats

S.L. Mangbon, BSc., MSc., PhD[1], Prof. M.I.A Saleh, MBBS, MSc., PhD.[2], Prof. A. Abdul Wahab, BSc., MBBS, MSc., PhD.[3], R.L. Mangbon BSc., MSc., PhD[4]

[1,2,3]Department of Human Physiology, Ahmadu Bello University, Zaria, Nigeria

[4]Department of Geography, Ahmadu Bello University, Zaria, Nigeria,

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ABSTRACT

Constipation is a digestive tract disorder that can cause painful, stiff, and infrequent stools as well as difficulty in passage of the stool. The intestines may close as a result of acute constipation, necessitating surgery. Constipation is one of several ailments that plants have long been used as a source of medicine. In loperamide-induced constipated wistar rats, the current study evaluated the purgative activity of Securidaca longepedunculata root bark aqueous extract by measuring the peristaltic index after 30 minutes of meal administration. The gastric emptying effect of the extract was also evaluated by determining the weight of the meal emptied by the rat within 1 hour period after meal administration. For each objective, twenty-five animals (5 constipated and 20 non-constipated) were selected and randomly divided into five groups of five rats each. They were treated with 5, 10, and 20 mg/kg of the aqueous extract via i.p. injections, and 5 ml/kg of normal saline was administered to normal and constipated control groups. The study revealed a significant ($p<0.05$) increase in intestinal length covered by administered meal in the S. longepedunculata extract treated group at 5 mg/kg (65.00±1.58cm), 10 mg/kg (59.80 ± 3.24cm) as compared to the constipated group (14.80 ± 1.77cm). Similarly, there was a significant increase in intestinal length covered by administered meal at 20 mg/kg (73.80 ± 1.53) as compared to normal (61.00 ± 3.93cm) and constipated control groups (14.80 ± 1.77cm) respectively. The percentage intestinal length covered by administered meal was also significantly ($p<0.05$) increased in the S. longepedunculata extract treated group at 5 mg/kg (74.60 ± 2.78%), 10 mg/kg (67.63 ± 1.06%) as compared to constipated group (17.40 ±2.33%). Similarly, there was also a significant increase at 20 mg/kg (83.20 ± 2.95%) compared to normal (70.00 ± 4. 60%) and constipated control groups (17.40 ±2.33%).

Gastric meal emptied was significantly ($p<0.05$) increased in the S. longepedunculata extract treated group at 5 mg/kg (5.42±0.11g), 10 mg/kg (5.10 ± 0.20g) compared to normal (3.48 ± 0.18g) and constipated control groups (2.18 ± 0.22g); and the 20 mg/kg (3.88±0.17) as compared to constipated control group (2.18 ± 0.22g). Meal weight in stomach was significantly ($p<0.05$) decreased in the S. longepedunculata root-bark aqueous extract treated group at 5 mg/kg (1.78±0.11g), 10 mg/kg (2.10±0.20g) compared to normal (3. 62±0.16g) and constipated control groups (5. 02±0.22g); and 20 mg/kg (3.42±0.16) as compared to constipated control group. (5.02±0.22g). It was therefore concluded that graded doses (5 mg/kg, 10 mg/kg, and 20 mg/kg) of S. longepedunculata aqueous root-bark extracts are effective purgatives in albino Wistar rats and might have therapeutic potential in the management of bowel emptying disorders.

Keywords—laxative, purgative, S. longependunculata, aqueous, extract, loperamide, constipation, wistar, rats.

INTRODUCTION

The Study Background

Constipation is the delayed transit of faeces through the large intestine, which is frequently accompanied by an accumulation of large amounts of dry, hard feces in the descending colon as a result of excessive fluid absorption (Anthony, 2014). According to Benninga et al. (2005), acute constipation can lead to intestinal closure that may possibly necessitate surgery. According to Wintola et al. (2010) and Meite et al. (2010), 3–15% of the general population suffers from constipation, a very common and frequently chronic functional gastrointestinal disorder.

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Constipation is a common clinical issue with a constellation of symptoms including excessive straining, hard stools, a sense of incomplete evacuation or infrequent defaecation. Constipation can be brought on by a number of conditions, including drug use, fiber deficiency, metabolic issues, and anorectal issues. It is well known that loperamide can cause constipation. According to Akapa et al. (2014) and Ashafa et al. (2011), the medication is an opioid agonist anti-diarrheal agent that reduces intestinal water secretion and colonic peristalsis. This inhibition slows intestinal luminal transit and increases the time needed for faecal evacuation (Akapa et al., 2014; Ashafa et al., 2011).

Laxatives are substances that either stimulate intestinal secretion or motility to increase the frequency and ease of defaecation, or they add bulk to the intestinal contents by retaining water within the bowel lumen as a result of their osmotic effects (Ashafa et al., 2011).

In Nigeria, the plant Securidaca longepedunculata Fres. (Polygalaceae) is frequently used as a purgative (Us et al., 2019). Its common names include violet tree, Fibre tree, wild vesteria, and Rhodesian violet. It is also referred to locally as Uwar magunguna or Sanya (Hausa), Ipeta (Yoruba), Alali (Arabic), and Umfufu, mzigi (Swahili). Based on the traditional use of S. longepedunculata extracts as a purgative and laxative, this study scientifically investigated its laxative and purgative effects on the gastrointestinal tract using experimental animal models to confirm the claim of traditional healers.

Statement of the Problem

Constipation is a common gastrointestinal condition that costs communities a lot of expenses, with a prevalence range of 1% to 80% worldwide (Sanchez and Bercik, 2011). A wide geographic variation in the condition is one of its defining features. Older people who experience chronic constipation often struggle to pass stool (Suares and Ford, 2011). Accordingly, this condition has a close connection to patients' quality of life and the use of healthcare resources (Rajindrajith and Devanarayana, 2020). Constipation has serious negative effects on both one's personal and societal health (Rajindrajith and Devanarayana, 2020). Physical, social, academic, and emotional well-being are all negatively impacted by constipation in children (Vriesman et al., 2019). According to Youssef et al. (2005), children with constipation have a lower health-related quality of life than kids with severe organic gastrointestinal diseases like inflammatory bowel disease. Children with constipation also showed high rates of absenteeism from school and poor academic performance, which has serious consequences for their future as adults (Olaru et al., 2016). Constipation is regarded as a serious health issue in children, with an estimated global prevalence of 9.5% (Koppen et al., 2018).

The Study Justification

For the treatment of constipation, affected people frequently use chemical medications like Senna®, Correctol®, Exlax®, Senokot®, and Gaviscon®, which have sennosides as active ingredients. Ashafa et al. (2011) note that using these conventional medications has drawbacks including high cost, unfavorable side effects (such as stomach pain and cramps), and slow activity (up to 8 h) in treating constipation. As a result, almost half of patients with constipation are dissatisfied with how well traditional laxatives work at enhancing quality of life (Ashafa et al., 2011).

As a result, focus has shifted to the use of medicinal plants, particularly in Nigeria, for the treatment of constipation (Ashafa et al., 2011). Users generally believe that plant extracts are affordable, fast acting, and easily accessible, and there are many options available (Ashafa et al., 2011). This research was therefore necessary as a result of the ongoing search for a laxative and purgative of plant origin that is more natural, potent, affordable, and accessible.

Study Aim

The present study assessed the purgative activities of Securidaca longepedunculata root bark aqueous extracts in loperamide-induced constipated wistar rats.

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Specific Objectives

I. To determine the Lethal dose LD_{50} of S. longepedunculata root-bark aqueous extracts via the acute toxicity test

II. To assess the effects of S. longepedunculata root bark aqueous extracts on intestinal motility by determining the percentage distance covered by intestinal charcoal meal (peristaltic index) after 30 minutes of charcoal meal administration.

III. To assess the effects of S. longepedunculata root bark aqueous extracts on gastric emptying by determining the weight of the meal emptied by the rat within 1 hour period after meal administration.

Null Hypothesis (H_0)

Securidaca longepedunculata root bark aqueous extract has no purgative effect in loperamide-induced constipated wistar rats.

MATERIALS AND METHODS

Collection of Plant Materials

The S. longepedunculata root bark was collected from the Department of Botany, Ahmadu Bello University Zaria. Identification and authentication were completed in the same herbarium area of the Department of Botany at Ahmadu Bello University Zaria where a voucher number was provided.

Aqueous Extraction of Plant Materials

The root bark was carefully collected, washed in clean water, and allowed to air dry. They were then ground into a rough powder. 16g of the powdered root bark was placed in a conical flask along with 120cm^3 of distilled water. After shaking vigorously, the flask's contents were kept for 48 hours at room temperature with the top covered with aluminum foil. After filtering it through Whatman's No. 1 filter paper, the crude extract was then concentrated and obtained using a vacuum evaporator (Auwal et al., 2012).

Materials and Drugs

Male Albino wistar rats weighing 140-170 g, standard laboratory rodent feeds and drinking water, normal saline, digital weighing balance, loperamide hydrochloride a carboxymethyl-cellulose (products of BDH Chemicals Ltd. Poole, England), cages, S. longepedunculata aqueous extracts, 5ml and 1ml syringe, stomach tube or a suitable intubation cannula, activated charcoal, distilled water, dissecting kits, meter rule, universal bottles, corn starch flour, bottled water, Maggi cubes, gastric tube.

Formal Ethical Approval

An ethical approval and clearance for performing the experiment was sought from the Committee on Animal Use and Care of the Ahmadu Bello University, Zaria (ABUCAUC) an approval number ABUCAUC/2022/048 was given.

Lethal Dose Determination

The Lorke (1982) method was used to determine the acute toxicity LD_{50}. Eighteen rats were used for acute toxicity testing for the determination of LD_{50} in two phases (Lorke, 1982), and Lorke's method was used because less than half of the grouped rats dosed at 2000 mg/kg survived (Oecd, 2008). Nine rats were divided into three groups (A, B, and C) of three rats each for the first phase. They received oral treatments with extract doses of 20 mg/kg, 200 mg/kg, and 2000 mg/kg. The rats were monitored for any mortality for 24 hours. The rats were divided into three groups (A, B, and C) of three rats each, and they were given oral treatments with the extract at different doses (250 mg/kg, 500 mg/kg, and 750 mg/kg) during the second phase. The final LD_{50} value was

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calculated using the highest dose that results in no mortality and the lowest dose that results in mortality in both phases after 24 hours of observation of the animals. The following formula (Oecd, 2008) describes the lethal dose anticipated to result in 50% mortality in the population of the rats:

$LD_{50} = \sqrt{500 \times 750} = 612mg/kg$

Doses of 5 mg/kg, 10 mg/kg and 20 mg/kg of S. longipedunculata as adopted from Olumayokun et al. (1999) were used in the experiment since it's below the LD_{50} and has been confirmed safe.

Intestinal Motility Effect Determination

The Obidike (2012) method with minor modification was applied. Twenty-five male wistar rats (5 constipated and 20 non-constipated) were divided into five groups, each with five animals (n=5), and were fasted for 12 hours the night before treatment.

The average weight of the rats was 160g. They received i.p. injections of 5 mg/kg, 10 mg/kg, and 20 mg/kg of the aqueous extract of S. longepedunculata, and 5 ml/kg of normal saline was given to the normal control and constipated control groups. Each animal received 1.3 ml of charcoal meal (100 ml of distilled water with 10% gum acacia mixed with 5g activated charcoal) orally after 15 minutes. The gastrointestinal tract was quickly removed from each animal after 30 minutes, and the small intestine was stretched out and closely observed. Each animal's small intestine was measured using a thread/meter rule, and the distance (in cm) that the charcoal meal in the small intestine traveled from the pylorus was measured.

This distance was expressed as the percentage of the total length of the small intestine (cm) from the gastropyloric to the ileocaecal junction (Olumayokun et al., 1999). Distance covered by the intestinal charcoal meal is directly proportional to intestinal motility. Hence, percentage motility (peristaltic index) was determined.

Peristaltic index = (distance travelled by charcoal meal/length of small intestine) x 100

Gastric Emptying Determination

The Olumayokun et al., (1999) method with minor modifications was employed. Using corn starch and boiling water to create a smooth paste, a special test meal was made. The paste was mixed with Maggi® cubes (Nestle Plc, Nigeria) for seasoning before being cooked for three minutes to thicken as the test food, pap (also known as ogi or akamu locally). Five groups of five rats each were used to group the rats (n=5 groups). The groups were given 5 mg/kg, 10 mg/kg, and 20 mg/kg of the extract, as well as 5 ml/kg of normal saline for the constipated normal control group, which was given by intravenous injection. Ten minutes after drug administration, each rat was given a weighed amount (7.2g) of the test meal by gastric tube and the animals were anaesthesized and euthanized 1 hr later. The stomachs were taken out, weighed, and cut open along the greater curvature to gently rinse them with sponges. The stomachs were then put back together and reweighed to determine the weight of the meal that the rats had emptied within the 1-hour time frame. Weight of the gastric meal emptied is directly proportional to gastric emptying. Gastric Emptying was determined as follows:

Weight of the gastric meal emptied = initial weight of meal – final weight of meal in stomach after gastric emptying in 1hr

Data Analysis

Data from this research were summarized and analyzed statistically with one-way analysis of variance (ANOVA) using SPSS 25.0 and were expressed as mean ± standard error of mean (M±SEM), followed by Tukey's post hoc test of multiple comparisons to compare the effects between control and test groups. Values with $P< 0.05$ were considered statistically significant.

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RESULTS

Acute Toxicity Test of S. longepedunculata Root-Bark Aqueous Extracts

Table 4.2 shows acute toxicity test results of S. longepedunculata extracts. At phase one of the experiment, three mortalities were recorded at 2000mg/kg dose of the extract administered, whereas, at phase two only a single mortality was recorded at 750mg/kg dose of the extract administered. The LD_{50} was calculated as thus:

$LD_{50} = \sqrt{500 \times 750} = 612mg/kg$

Table 3.2: Acute Toxicity Test of S. longepedunculata Root-Bark Aqueous Extracts

Phases	Doses (mg/kg)	Rats	Survivors	Mortality
Phase One				
Group A	20	3	3	0
Group B	200	3	3	0
Group C	2000	3	0	3
Phase Two				
Group A	250	3	3	0
Group B	500	3	3	0
Group C	750	3	2	1

$LD_{50} = \sqrt{500 \times 750} = 612mg/kg$

Intestinal Motility Effect of S. longepedunculata Root-Bark Aqueous Extracts

Figure 3.6 shows a significant decrease ($p<0.05$) in intestinal length covered by administered meal in the constipated group (14.80 ± 1.77cm) compared to normal control group (61.00 ± 3.93cm). The percentage (%) intestinal length covered was also significantly decreased ($p<0.05$) in the constipated group (17.40 ± 2.33%) compared to normal control (70.00±4.60%). Intestinal length covered by administered meal was significantly ($p<0.05$) increased in the S. longepedunculata extract treated group at 5 mg/kg (65.00±1.58cm), 10 mg/kg (59.80 ± 3.24cm). Similarly, there was a significant increase in intestinal length covered by administered meal at 20 mg/kg (73.80 ± 1.53)) as compared to normal (61.00 ± 3.93cm) and constipated control groups (14.80 ± 1.77cm) respectively. The Percentage intestinal length covered by administered meal was also significantly ($p<0.05$) increased in the S. longepedunculata extract treated group at 5 mg/kg (74.60 ± 2.78%), 10 mg/kg (67.63 ± 1.06%). as compared to constipated group (17.40 ±2.33%). Similarly, there was also a significant increase at 20 mg/kg (83.20 ± 2.95%) compared to normal (70.00 ± 4. 60%) and constipated control groups (17.40 ±2.33%).

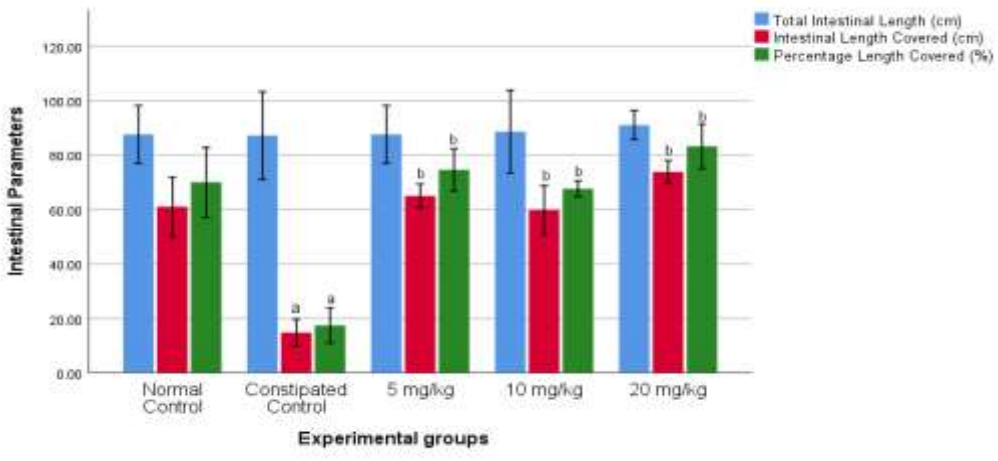

Figure 3.6: Effect of S. longepedunculata Root-Bark Aqueous Extracts on Intestinal Parameters

Key: Bars with superscript letter **"a"** show significant decrease ($p<0.05$) as compared to normal control. Bars with superscript letter **"b"** show significant increase ($p<0.05$) as compared to constipated control.

GASTRIC EMPTYING EFFECT OF S. LONGEPEDUNCULATA ROOT-BARK AQUEOUS EXTRACTS

Figure 3.7 shows a significant decrease ($p<0.05$) in gastric meal emptied in the constipated group (2.18±0.22g) compared to normal control group (3.48 ± 0.18g). Meal weight in stomach increased significantly ($p<0.05$) in the constipated group (5.02 ± 0.22g) compared to normal control group (3.62±0.16g). Gastric meal emptied was significantly ($p<0.05$) increased in the S. longepedunculata extract treated group at 5 mg/kg (5.42±0.11g), 10 mg/kg (5.10 ± 0.20g) compared to normal (3.48 ± 0.18g) and constipated control groups (2.18 ± 0.22g); and the 20 mg/kg (3.88±0.17) compared to constipated control group (2.18 ± 0.22g). Meal weight in stomach was significantly ($p<0.05$) decreased in the S. longepedunculata root-bark aqueous extract treated group at 5 mg/kg (1.78±0.11g), 10 mg/kg (2.10±0.20g) compared to normal (3. 62±0.16g) and constipated control groups (5. 02±0.22g); and 20 mg/kg (3.42±0.16) compared to constipated control group. (5. 02±0.22g).

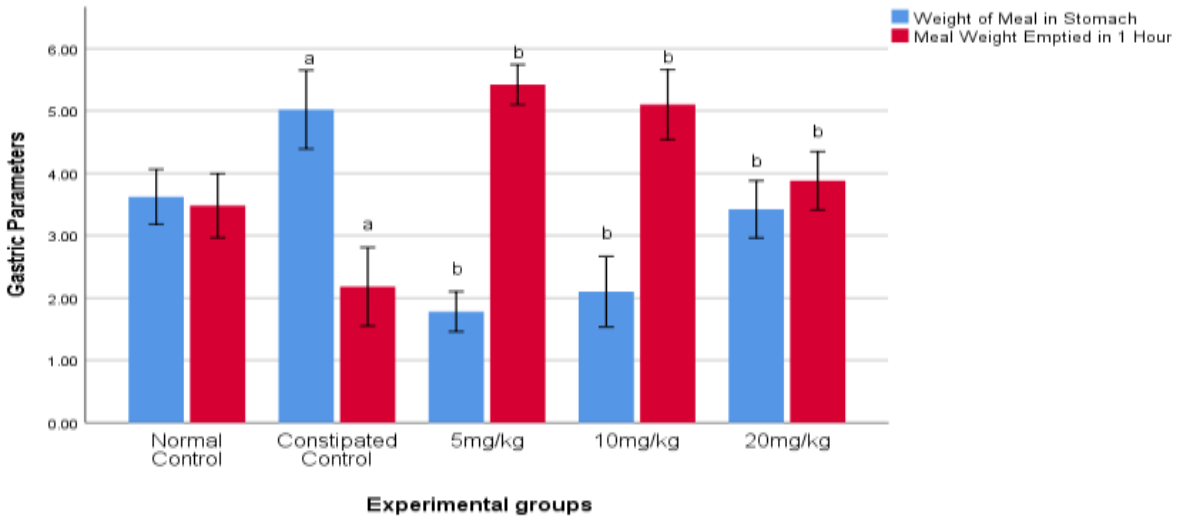

Figure 3.7: Effect of S. longepedunculata Root-Bark Aqueous Extracts on Gastric Parameters

Key: Bar with superscript letter **"a"** shows significant decrease ($p<0.05$) as compared to the normal control. Bars with superscript letter **"b"** show a significant increase ($p<0.05$) as compared to the constipated control.

DISCUSSION

Phytochemical is a term used to describe plant secondary metabolite. Plants naturally produce chemicals called phytochemicals, which are not necessary for the majority of the metabolic processes that take place within them. According to Srivastava et al. (2012), phytochemicals are primarily produced in response to environmental pressures such as unfavorable climatic conditions, immune responses to infectious agents,

The LD_{50} for oral administration of S. longepedunculata root-bark aqueous extract was determined in the current study to be 612 mg/kg. However, in the constipated test group III that received 20 mg/kg of the extract via intraperitoneal route, acute toxicological effects including reduced feeding, weight loss, single mortality, reduced urination, and reduced activity were observed. Similar observations was reported by Adeyemi et al., (2010) who reported LD_{50} values of 740 mg/kg and 20 mg/kg body weight for oral and intraperitoneal application routes of aqueous root-bark extract of the plant respectively, while Dapar et al., (2007) and Keshebo et al., (2014) reported LD_{50} values 547 mg/kg and 37 mg/kg LD_{50} values for aqueous and ethanol S. longepedunculata root-bark extracts via oral and intraperitoneal route respectively. The aqueous extracts of S. longepedunculata had an LD_{50} of 771 mg/kg, according to Auwal et al. (2012). However, Etuk et al. (2006) found that when various doses (300, 900, and 2700 mg/kg body weight) of the aqueous root extract were given orally once daily for 28 days, no

deaths were reported. The graded doses of S. longepedunculata extract administered at 5 mg/kg, 10 mg/kg, and 20 mg/kg were toxicologically safe, according to the LD_{50} value of 612 mg/kg recorded in this study.

The study revealed that S. longepedunculata root-bark aqeuous extracts significantly ($p<0.05$) increased intestinal motility (% distance covered by the charcoal meal) at doses of 5 mg/kg and 10 mg/kg 20 mg/kg respectively as compared with normal and constipated control groups in the present study. This might be due to its antagonistic action on opioid receptors. The deactivation of potassium (K^+) channels in the intestine and the disinhibition of calcium (Ca^{2+}) channels, adenylyl cyclase, and calmodulin in intestinal smooth muscle may be the cause of its antagonistic action on opioid receptors. The increased peristaltic movement in the rat gastrointestinal tract via cholinergic receptors stimulation brought on by the secondary metabolites of S. longepedunculata extracts is likely what propelled the charcoal meal in the extracts treated group. Similar findings were reported by Nafiu et al. (2015), who found that giving rats with constipation L. cupanioides extract can effectively normalize their defecation frequency, weight gain, faecal volume, and colon motility. This could be as a result of the natural anthraquinone derivatives that are present in the root extract and have been linked to laxative effects (Nweje et al., 2019). According to Nweje et al. (2019), this substance may work by upsetting the balance between water secretion into the intestinal lumen and water absorption from the lumen via an active sodium transport mechanism.

Furthermore, in the present study, S. longepedunculata root-bark aqeuous extracts significantly ($p<0.05$) increased gastric emptying (meal weight emptied) at doses of 5 mg/kg, 10 mg/kg and 20 mg/kg respectively as compared with the constipated control group. According to Meite et al. (2010), both neural and myogenic mechanisms control gastrointestinal transit. The secondary metabolites of the extract might have increased the contractile activity of the smooth muscle layers of the stomach, which has speeded-up the gastric emptying processes. These motor patterns are controlled by a number of mediators and neurotransmitters. Since acetylcholine is the primary neurotransmitter in the enteric nervous system, the presence of cholinimetric constituents in the plant extract can account for the ethnobotanical information's claim that S. longepedunculata is useful in treating constipation (Meite et al., 2010). Similar results were noted by Olumayokun et al. (1999), who found that a methanol extract of the root of S. longepedunculata significantly ($p<0.05$) increased gastric emptying and the propulsive movement of the intestinal contents.

The results demonstrate a dose-dependent pattern, indicating that higher doses of 10 mg/kg and 20 mg/kg had more purgative effects. The secondary metabolites (flavonoids, glycosides) of the extract may have an antagonistic effect on loperamide, which lowers colonic reabsorption of water and electrolytes and increases colonic peristalsis. This is one potential mechanism for the laxative effect of the extract. According to well-established research, loperamide eliminates experimental osmotic diarrhea by affecting intestinal motility and, as a result, lowering the flow of faecal matter into the colon (Meite et al., 2010). The polyphenol (Flavonoids) in the extract may have had a purgative effect by stimulating peristalsis and, like other purgatives, water reabsorption reduction, which softens stools (Meite et al., 2010). The majority of natural purgatives work by stimulating Cl^- secretion and/or inhibiting Na^+ reabsorption, which causes fluid to accumulate and be retained while also increasing colonic motility (Meite et al., 2010).

SUMMARY, CONCLUSION AND RECOMMENDATIONS

Summary

The present study has established that graded doses of S. longepedunculata root-bark aqeuous extracts at 5 mg/kg, 10 mg/kg, 20 mg/kg significantly ($p<0.05$) increased intestinal motility and gastric emptying when compared to the normal and constipated control groups, thereby causing good purgative effect.

Conclusion

Therefore, from the findings of this study, it was concluded: graded doses of S. longepedunculata aqueous root-bark extracts at 5 mg/kg, 10 mg/kg and 20 mg/kg have effective purgative effects in Wistar rats. Lower doses of 5 mg/kg and 10 mg/kg have effective purgative principles by increasing intestinal motility and gastric emptying.

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Recommendations

Based on the findings of this study, we therefore make the following recommendations:

(i) Graded doses (5 mg/kg, 10 mg/kg and 20 mg/kg) of S. longepedunculata root-bark aqueous extracts might have therapeutic potential in the management of constipation.

(ii) Further studies should be conducted to determine the effect of S. longepedunculata root-bark aqueous extracts on intestinal and gastric contractility rate.

(iii) Further studies should be conducted to determine the histopathological effects S. longepedunculata root-bark aqueous extract on the GIT to ascertain its anti-ulcerative potentials.

(iv) Further studies should be conducted to determine the mechanism(s) of action of S. longepedunculata on GIT secretions and contractility as compared to standard stimulant laxative drug.

Contributions to Knowledge

1. Graded doses of S. longepedunculata extracts at 5 mg/kg, 10 mg/kg and 20 mg/kg significantly ($p<0.05$) increased intestinal motility (length covered by administered meal in 30 minutes) in wistar rats when compared to normal and constipated controls. Therefore, it can be used for the development of purgatives of plant origin.

2. Lower doses of 5 mg/kg and 10 mg/kg of S. longepedunculata root-bark aqeuous extracts significantly ($p<0.05$) increased gastric emptying processes (gastric meal emptied in 1 hour of meal administration) in wistar rats when compared to normal and constipated controls. Therefore, it can be used for the development of purgatives of plant origin.

Conflict of Interest

None declared

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