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Original Research Article

Homogenized Pulp and Peel Extracts of Unripe *Musa paradisiaca* Mitigates Castor Oil-induced Diarrhea in Rats

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ABSTRACT

Traditionally, *Musa paradisiaca* (plantain) plant parts are used for the treatment of various health disorder including diarrhoea. The study determined the effects of unripe *Musa paradisiaca* pulp and peel homogenates on castor oil-induced diarrhoea in Wistar rats. Twenty-eight (28) Wistar rats (100-130 g) divided into 7 groups of 4 rats each and pre-administered with the extracts prior to diarrheal induction with castor oil. Groups 1 and 2 represented the normal and standard control and received 1 mL normal saline and 3 mg/kg b.wt. of Lomotil respectively. Groups 3 and 4 were administered 200 and 400 mg/kg b.wt. of the pulp extract respectively. Groups 5 and 6 were administered 200 and 400 mg/kg b.wt. of the peel extract respectively, while rats in Group 7 received a dose of 400 mg/kg b.wt of the combined extracts. The acute toxicity result showed neither death nor toxic signs on administration of both extracts. The result also showed significant inhibition of castor oil-induced defecation frequency and stool wetness in the treated groups relative to control. The extract-treated groups also had significant increases in Na^+ and K^+ concentrations and a significant decrease in HCO_3^- concentration compared to the normal control. The result of this study affirms the antidiarrheal activity of *Musa paradisiaca* peels and pulp.

Keywords: *Musa paradisiaca*, Electrolytes, Antidiarrhoea, Lomotil, Wistar rats.

Introduction

The act of using different plant parts for therapeutic purpose is as old as man. Plants play an indispensable role in human existence.[1-5] Scientific research reveals that the therapeutic power of herbal plant is as a result of the vast phytochemical properties inherent in them and not just because of the plants shapes as claimed by traditional users.[6,7] Global herbal products are becoming the hub of research in treatment of diseases because of its little or no side effects.[8]

Diarrhoea has been described as a state of one having abnormal frequent bowel movement or passing loose fluid stool. This can be as a result of bacterial, parasitic or viral attack.[9] The resultant effects of diarrhoea due to the excessive passing of fluid leads to electrolyte imbalance and dehydration.[9] Diarrhoea case is more prevalent in developing countries as a result of poor hygiene, unsafe drinking water and nutrition. Diarrhoea occurs when the rate of fluid secretion is more than the rate of fluid absorption in the gastrointestinal tract, resulting to hyper motility and excessive fluid loss in faeces.[10] Castor oil, which is used to induce diarrhoea, is hydrolysed in the jejunum to ricin oleic acid generating irritating and inflammatory actions on the intestinal mucosa.

The effect of the oleic acid stimulates the formation and release of autacoids and prostaglandins.[11-13] The autacoids and prostaglandins formed induces increase in membrane permeability and changes in electrolyte transport. This changes results in a hyper-secretory response (decreasing Na^+ and K^+ absorption and reducing Na^+ / K^+ ATPase activity in the small intestine and colon) stimulating peristaltic activity and diarrhoea.[14-17] Other mechanisms that have been proposed to explain the diarrhoeal effect of castor oil include activation of adenylyl cyclase or mucosal cAMP mediated active secretion, platelet activating factor and recently nitric oxide.[16,18] The castor oil model incorporates both secretory and motility diarrhoea.[11]

M. paradisiaca (plantain)[19,20] is a perennial monocotyledonous plant of the family Musaceae and genus (Musa) with desert bananas.[21-23] *M. paradisiaca* is a tree like herb that grows in the tropic with a height range of 3-15 m. It has aerial pseudo stem with submerged rhizome producing a large pulpy and starchy fruit.[24] *M. paradisiaca* which is believed to originate from Southeast Asia is now widely grown across tropical and subtropical region.[25,26] The fruits and pulp are rich source of diverse phytochemicals and nutrients.[25] This work is aimed to determine the effects of unripe *Musa paradisiaca* pulp and peel homogenates on castor oil-induced diarrhoea in Wistar rats.

Materials and Methods

Plant collection and identification

Freshly harvested *M. paradisiaca* fruits were gotten from Nsukka in Enugu State Nigeria on 16 June 2016 and identified at the Bioresources Development and Conservation Programme (BDCP) Research Centre by Mr A. Ozioko with voucher number: Inter CEDD/790.

Preparation of plant materials

Freshly unripe *M. paradisiaca* fruits were properly washed and peeled. The peels and the pulp were diced and oven-dried for 48 hrs at 60°C to a constant weight. The dry samples were grounded into

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powder and mixed with normal saline to form homogenates to be given to the experimental animals.

Experimental animals

A total of 28 Wistar rats weighing 100-130g were used for the antidiarrheal study while eighteen (18) adult mice were used for acute toxicity (LD_{50}) study. The experimental rats were acclimatized to laboratory conditions for one week under standard conditions and allowed free access to water and feed. The study was approved by the Ethical Committee of the Faculty of Biological Sciences, University of Nigeria, Nsukka with approval number (UNN/FBS/EC/1060).

Qualitative and quantitative phytochemical analysis of unripe Musa paradisiaca pulp and peel

These were done according to the methods of Harborne[27] and Trease and Evans[28] to identify their active constituents.

Acute toxicity test of the homogenates of Musa paradisiaca pulp and peel

The method of Lorke.[29] was used for the acute toxicity test. This test involved two stages. In stage one, the animals were grouped into three (3) groups of three (3) mice each and were given 10, 100 and 1000 mg/kg body weight of the extract respectively, while in the second stage the animals were also grouped into three (3) groups of three (3) mice each and given 1600, 2900 and 5000 mg/kg body weight of the extract. Oral method of administration was used.

Experimental design

A total of 28 adult Wistar rats were fasted for 18 hrs with free access to water. The experimental rats were divided into 7 groups of 4 rats each.

Group 1: Received 0.2 mL of normal saline (control).

Group 2: Administered 3 mg/kg of a standard drug, Lomotil (atropine).

Group 3: Rats treated with 200 mg/kg body weight of unripe *M. paradisiaca* pulp homogenate.

Group 4: Rats treated with 400 mg/kg body weight of unripe *M. paradisiaca* pulp homogenate.

Group 5: Rats received 200 mg/kg body weight of unripe *M. paradisiaca* peel homogenate. Group 6: Rats administered with 400 mg/kg body weight of unripe *M. paradisiaca* peel homogenate.

Group 7: Rats given 200/400 mg/kg body weight of unripe *M. paradisiaca* peel and pulp homogenates.

After 1 hr of treatments, each of the rats in group 1-7 were given 1 mL of castor oil orally and then separated into their respective metabolic cages and their faecal droppings and the frequency of defaecation observed. The Faeces were collected on a white sheet of paper placed beneath the cages. The number of both wet and dry droppings for each rat was counted every 1 hour for a period of 4 hours and the white papers were changed periodically for each evaluation.

Enteropooling test

As described by Robert *et al*., [30] the weights and volumes of small intestines of experimental rats were measured before and after emptying as well as the weights and contents of each intestine. The differences in weights and volumes pre- and post-emptying were calculated relative to the control group.

Gastro-intestinal motility test

Following the protocol described by Mascolo *et al*.[16], one-hour post-treatment, the rats were administered 0.2 mL of charcoal meal (10% activated charcoal suspended in 5g of gum acacia) and their small intestines collected after sacrifice. The small intestines were carefully separated from the mesentrum to prevent over-stretching. Measuring from the pyloric sphincter to the ileo-caecal junction, intestinal length and distance travelled by charcoal meal were measured and the values used to calculate gastro-intestinal motility as follows:

$$Gastro-intestinal\ Motility = \frac{distance\ travelled\ by\ charcoal\ meal}{length\ of\ the\ intestine}\ x\ 100\ \%$$

Electrolyte tests

Following the protocol of Tietz[31], two hours' post-treatment, the serosal solution from the intestinal loops of each rat was collected into a test tube and centrifuged for 30 minutes at 3000 rpm. Na^+, K^+, and HCO_3^- concentrations were determined from the supernatants of each intestinal content.

Statistical analysis

Data obtained from the study were analyzed by one-way analysis of variance (ANOVA) using the Statistical Package and Service Solutions (SPSS) software, version 18. Mean differences were considered statistically significant at $p < 0.05$.

Results and Discussion

The extracts of *M. paradisiaca* pulp and peel showed no toxicity up to 5000mg/kg body weight which suggested that they are safe for human consumption. The phytochemical analysis of aqueous extracts of *M. paradisiaca* pulp and peel revealed the presence of alkaloids, flavonoids, saponins, tannins and reducing sugars (Table 1).

Water is said to be the only transported material in the intestinal tract of diarrhoea patient when the volume and weight of the intestinal content are equal. However, when the weight is greater than the volume of the intestinal content, it means that other substances must have been secreted into the lumen in addition to water. The extracts were able to decrease the distance travelled by the charcoal meal (Figure 2)

Phytochemicals such flavonoids and reducing sugars found medicinal plants posseses antidiarrhoeal properties as reported by Rahman and Wilcock[32] and Perez *et al*.[33] Longanga *et al*.[34] in his work screened a number of medicinal plants and showed that antidiarrhoeal activities of these plants were due to presences of tannins, alkaloids, saponins, flavonoids, steroids, terpenes and glycosides contained in them. Several scientific researches have reported the therapeutic effects of tannins in having antidiarrhoeal property.[35,36] The mechanism of tannins exhibiting antidiarrhoeal properties lies in its ability to denature proteins and form protein tannate. The formed protein tannate regulates the intestinal mucosa membrane by reducing the rate of intestinal secretion and increase the membrane resistance to microbial attack.[35,36] The antidiarrhoeal activity of flavonoids has been linked to their ability to decrease intestinal motility and hydro-electrolytic secretion.[37,38,18] The presence of these phytochemical constituents in *M. paradisiaca* pulp and peel may therefore be responsible for their antidiarrhoeal effects.

Aqueous extracts of unripe *M. paradisiaca* pulp and peel successfully inhibited the castor oil-induced diarrhoea, therefore the extract might have exerted its antidiarrhoeal action through antisecretory mechanism (table 2).

This was evident from the reduction of total number of wet faeces in the test groups compared to the control group. Extracts of plants that contain flavonoid, are known to modify the production of cyclo-oxygenase 1 and 2 and lipo-oxygenase thereby inhibiting prostaglandin production.[39-43] Plant rich in flavonoid mediates diarrhoeal activity induced castor oil by decreasing intestinal motility and fluid secretion through autacoids inhibition. As reported for Eremomastax speciosa and Xylocarpus granatum, antidiarrhoeal plants are known to reduce the number of wet stools.[44,45] Infectious diarrhoea has been shown to be caused by micro-organisms; therefore, plants that have the potential to inhibit microbial growth could ameliorate diarrhoea.[44,45] Such phytoconstituents as saponin, phenolic compounds, flavonoids and glycosides present in the extracts have been reported to inhibit bacterial growth hence may reduce the frequency and number of wet stools.[46] More so, since lipid peroxidation has been implicated in the pathophysiology of diarrhoea, these extracts have antioxidant capacity as they contain phenol and poly-phenolic compounds. A direct correlation between antioxidant capacity and reducing power of certain plant extracts has been reported by Duh *et al*.[47] The reducing properties of plant with antidiarrhoeal activity are generally linked to the presence of reductones. Reductones executes its action by donating hydrogen atom which exert antioxidant action and cause the breakdown of the free

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radical chain[47] Scientific report has also shown that phenol and polyphenolic (flavonoids) constituents of plants used locally for treating diarrheal possess antioxidant properties mainly due to their redox properties. These properties could be the reason they act as reducing agents, hydrogen donors and singlet oxygen quenchers. These locally used plant is also reported to have metal chelation potential.[48] These observations suggest that the ability of unripe *M. paradisiaca* pulp and peel extracts to decrease the frequency of defecation may be due to their antioxidative, anti-secretory and anti-microbial properties. From the result obtained it seem the plant extracts contain pectin which is used in clinical trial to measure lactulose-mannitol intestinal permeability in children with diarrahoeal. Pectin is used because it is not susceptible to pancreatic amylase action.[49-51] Pectin's mechanism of action appears to be through its bacterial conversion short chain fatty acids such as into acetate, butyrate, and propionate in the large intestines.[52-55]

The phytochemical constituents of the extract stimulate pancreatic secretion and the flow of food substances through its indirect enterotrophic effect on the small bowel of the mucosal membrane as seen in figure 1, thereby leading to increase mucosal proliferation of the digestive tract.[52,53] Additional enterotrophic effects of Short Chain Fatty Acids (SCFAs) and other elements have also been described.[52,54] This mechanism could also be used to explain the improvement seen in the permeability and integrity of the small bowel mucosal membrane.[52,54] The unripe *M. paradisiaca* pulp and peel extracts significantly decreased the weight and volume of the intestinal contents. The observed effects are a direct consequence of decreased water and electrolyte secretion into the small intestine, suggesting that the plant extracts may enhance electrolyte and water absorption from the intestinal lumen. This is supported by the work of Duggan *et al*.[56], which states that electrolyte absorption determines the efficiency of nutrient absorption.

Previous studies revealed that activated charcoal enhanced drug and chemical absorption on the surface of the charcoal particles, preventing absorption.[57,58,59] Pre-treatment with the unripe *M. paradisiaca* pulp and peel extracts suppressed the propulsion of charcoal meal through the gastrointestinal tract. This delay in gastro intestinal transit allowed more time for further reabsorption of water from the faeces and may have additionally contributed to the reduction in the watery texture of the faeces.[59] They also possess anti-spasmolytic properties. The contraction of the muscles of the GIT in turn leads to increased propulsive movement of the intestinal content decreasing the intestinal transit time. This gives little or no time for nutrient, fluid or electrolyte reabsorption resulting in watery stool.[59]

Contraction is induced by acetylcholine binding to the parasympathetic receptors. The extracts may have been able to do this due to the presence of some phytochemicals like alkaloids which have a muscle relaxant and anti-cholinergic effects. It could also be as a result of phenolics such as tannins and flavonoids which inhibit histamine and acetylcholine induced contractile responses. The standard drug, atropine used is an anti-cholinergic or parasympatholytic drug which inhibits the parasympathetic nervous system. It performs this function by blocking the nicotinic and muscarinic receptors (M1 and M3), preventing acetylcholine from binding thereby decreasing contraction and consequently decreasing intestinal transit time. The effect of the standard drug (atropine) is supported by the findings of Brown and Taylor.[60] This states that atropine mediates the castor oil-induced gastrointestinal motility by regulating the cholinergic system.[60]

The extracts were able to enhance the reabsorption of electrolytes K^+ and Na^+ from the intestinal content or fluid.

This could be attributed to the ability of the extract to maintain intestinal membrane integrity, inhibit epithelial cell disruption thereby enhancing the absorption of these electrolytes. The extract could also have the ability to inhibit the destruction of brush border enzymes including the Na^+ /K^+ ATPase. This enzyme maintains the concentration gradient across the membrane by pumping $2K^+$ ions into the cell in exchange for $3Na^+$ ions pumped out.[61] There was a dose dependent decrease in the number of electrolytes secreted into the intestinal fluid. The high amount however of the electrolytes in the treated groups compared to the control could be attributed to the presence of Na^+ and K^+ ions in the extract. The unripe *M. paradisiaca* pulp and peel led to an increase in the influx of Na^+ ions from the mucosal compartment into the serosal compartment and K^+ efflux from the serosal to the mucosal compartment (Figure 4).

This indicates absorption of Na ions from the intestinal fluid to the blood and secretion of K^+ ions from the blood into the intestinal fluid. As sodium and glucose are drawn into the serosal membrane (absorption), water goes along with them due to the symport transport mechanism among them. On the other hand, potassium which exhibits an antiport mechanism of transport with sodium moves in the opposite direction (from the serosal to the mucosal compartment) that is secretion.[62] The extracts may have been able to exert this effect due to their ability to maintain the Na^+ /K^+ ATPase activity responsible for these transport mechanisms. These effects make the plant extracts able to ameliorate diarrhoea since as the water is absorbed alongside sodium and glucose; the volume of the stool is reduced thereby decreasing the watery nature of the faeces. The presences of K^+ channels in the epithelial cells of an organism's small intestine provide the driving force for electrogenic transport processes across the plasma membrane, and cell volume regulation. K^+ channels hyperpolarize the membrane voltage, thereby fueling electrogenic transport mechanisms such as Na^+ -coupled reabsorption of nutrients or luminal Cl^- secretion. Fine tuning of salt and water transport and of K^+ homeostasis occurs in colonic epithelia cells, where K^+ channels are involved in secretory and reabsorptive processes.[63]

Table 1: Quantitative phytochemical composition of unripe *M. paradisiaca* pulp and peel

Phytochemicals	Pulp (mg/100g)	Peel (mg/100g)
Flavonoids	4.44±0.001	5.44±0.005
Alkaloids	5.53±0.001	4.00±0.001
Saponins	2.33±0.002	2.63±0.002
Glycosides	0.19±0.002	2.59±0.001
Tannins	2.33±0.001	4.71±0.001
Reducing sugar	565.22±0.002	630.44±0.001
Steroids	1.47±0.002	1.24±0.001
Hydrogen cyanide	0.50±0.002	0.36±0.001

Results expressed in Mean ± SD; n = 3

Table 2: Inhibition of castor oil-induced frequency of defecation of unripe *Musa paradisiaca* pulp and peel homogenates in Wistar rats

Groups	Number of	Stools after			Mean value of defecation	Percentage of inhibition
	1st hour	2nd hour	3rd hour	4th hour		
1	7.00±2.3	7.25±1.9	2.50±0.9	4.00±0.4	5.18±1.4	-
2	2.75±1.7	1.25±0.7	3.00±1.2	0.75±0.5	1.90±1.0	63
3	7.75±2.1	0.75±0.5	2.25±1.9	0.25±0.2	2.75±1.2	47
4	5.25±1.4	8.00±5.2	1.75±1.4	1.00±1.0	2.17±2.3	58
5	7.75±4.6	2.25±1.6	1.00±0.0	4.75±2.0	4.90±2.0	5
6	6.50±0.5	4.25±1.8	2.00±1.2	3.00±3.0	3.90±1.6	25
7	7.00±1.0	4.75±2.1	2.25±0.7	2.25±1.0	4.06±1.2	22

Results expressed in Mean ± SD; n = 3.

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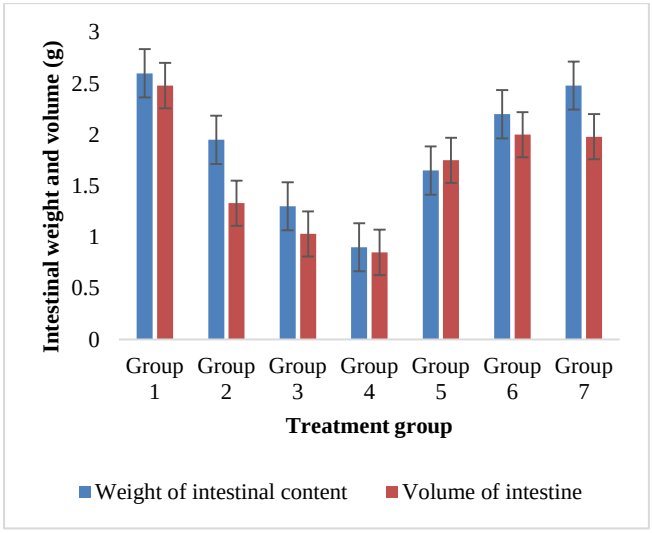


Figure 1: Effects of unripe *M. paradisiaca* pulp and homogenates on enteropooling of Wistar rats.

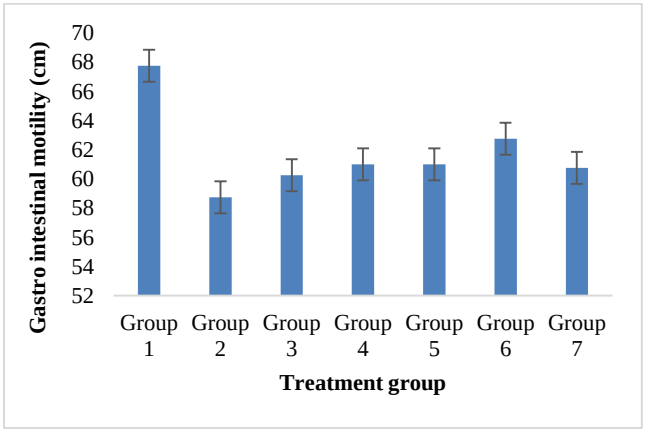


Figure 2: Effects of unripe *M. paradisiaca* pulp and homogenates on gastro-intestinal motility in Wistar rats.

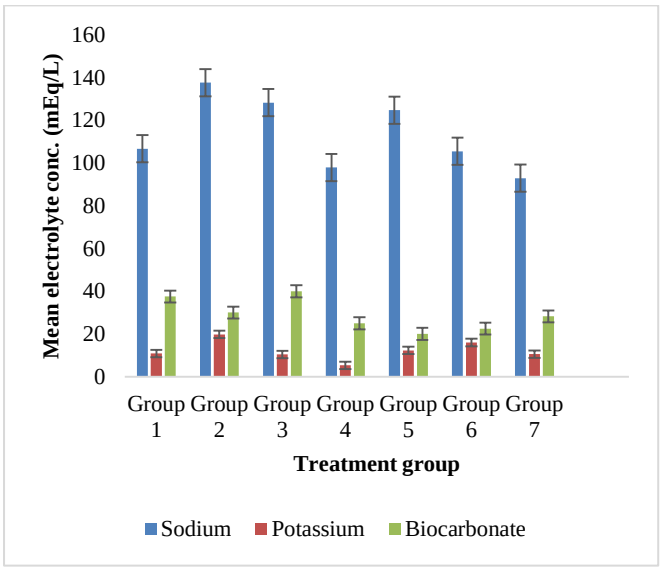
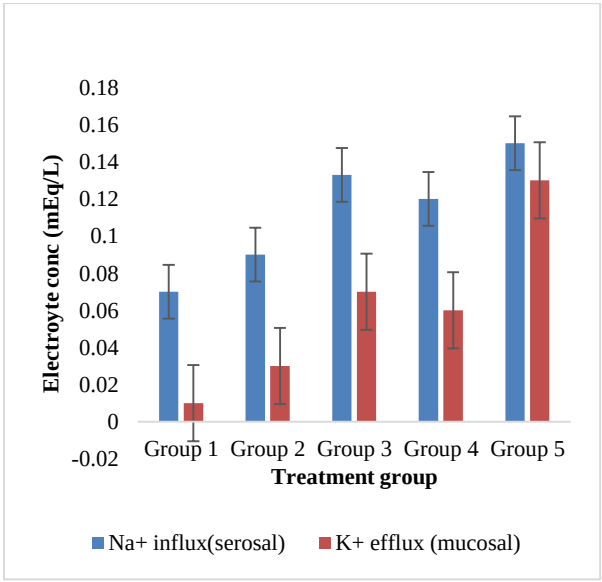


Figure 3: Effects of unripe *M. paradisiaca* pulp and homogenates on the electrolyte concentration of the small intestinal content in Wistar rats.



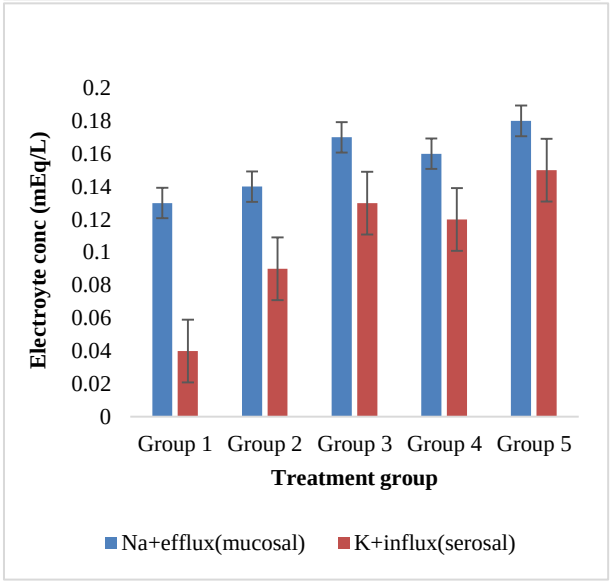


Figure 4: Electrolyte (Na^+ and K^+) transport into serosal and outside mucosal membrane of the small intestine of Wistar rats.

Conclusion

From the findings, unripe *M. paradisiaca* pulp and peel exhibited antidiarrhoeal properties by inhibiting gastro-intestinal motility, enteropooling, wetness and frequency of defecation. They also showed abilities to facilitate transport of electrolytes across the small intestinal membrane. This study therefore affirms the claims that unripe *M. paradisiaca* pulp and peel contain pharmacologically active substances effective for management of diarrhoea.

Conflict of Interest

The authors declare no conflict of interest

Authors Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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