Antidiarrheal Potentiality of Methanolic Extract of Different Parts of *Musa sapientum* Fruits

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Abstract: To investigate the antidiarrheal activities of the methanolic extract of peel (MSPL) and pulp (MSPP) of *Musa sapientum* fruits, the extract was studied for antidiarrheal property using castor oil and magnesium sulphate induced diarrheal model and charcoal induced gastrointestinal motility as well as PGE_2-induced enterolooping test in mice. In addition, activities against some causative diarrheal pathogenic bacteria were also determined. At the doses of 100 and 200 mg kg^{-1} body weight, both extracts significantly reduced the frequency and severity of diarrhea in test animals throughout the study period. Both extracts also showed a significant ($p < 0.001$, 0.05) reduction in the gastrointestinal motility in charcoal meal test, as well as PGE_2-induced intrafluid accumulation. MSPL extract also displayed strong antibacterial effect against against *Staphylococcus aureus*, *Salmonella typhi*, *Shigella dysenteriae* and *Escherichia coli*. Altogether, these results suggest that the *Musa sapientum* fruit extracts could be used as a potential antidiarrheal agent.

Key words: *Musa sapientum*, diarrhea, flavonoid, antibacterial, mice

INTRODUCTION

Diarrhea is an alteration in the normal bowel movement, characterized by increased frequency of bowel sound and movement, wet stool and abdominal pain (Guerrant *et al.*, 2001). Regardless of the understanding causes, treatment and prevention of diarrheal diseases, an estimated 4.6 million people with 2.5 million children, die from diarrhea every year, particularly in developing countries (Kosek *et al.*, 2003). Diarrhea may be acute or chronic. With acute diarrhea being the most common is usually caused by an infectious agent, even though drugs, poisons or acute inflammatory reactions can contribute a lot (Thapar and Sanderson, 2004). Now a days, rotavirus is the major causative agent for infectious diarrhea, particularly in young children, however other viral (adenovirus, enterovirus and norovirus), bacterial (*Escherichia coli*, *Salmonella* sp., *Shigella* sp., *Camphylobacter* and *Vibrio cholerae*) and parasitic (Cryptosporidium and Giardia) agents are important pathogens (Allen *et al.*, 2003). Oral Rehydration Therapy (ORT) has been identified as a key factor in the decline of child mortality rate due to diarrhea, although it does not reduce the volume or duration of diarrhea (Subbotina *et al.*, 2003). Likely, antibiotics and gut motility suppressing agents bid the other treatment option where

in reverse dehydration, shorten the length of illness and reduce the period of time when an individual is infected (Palombo, 2006). Treatment with pharmacological agents that are pathogen specific or that suppress severe symptoms would be of benefit to patients suffering from prolonged diarrhea (Takahashi *et al.*, 2001).

Medicinal herbs constitute an indispensable component of the traditional medicine practiced worldwide due to their economical viability, accessibility and ancestral experience. Despite the availability of a vast spectrum of approaches for diarrheal management, a vast majority of the people of Bangladesh have been known to treat diarrhea with a variety of medicinal plants one of which being *Musa sapientum* (Rahmatullah *et al.*, 2010). *Musa sapientum* L. (Family Musaceae) grows in humid lowland to upland tropical areas whose vernacular name is banana in Bengali. Agarwal *et al.* (2009) has studied the wound healing activity of plantain banana extracts. Plants parts like fruits, leaves, peels, root and stalks from banana plants have been utilized orally or topically as a medicine for treating diarrhoea and dysentery. It is also used in inflammation, pains and snakebite (Coe and Anderson, 1999) as well as it has antilithic (Prasad *et al.*, 1993), antiulcerogenic (Lewis *et al.*, 1999), hypoglycemic (Ojewole and Adewunmi, 2003), hypolipidemic and antioxidant actions (Krishnan and Vijayalakshmi, 2005).

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Houghton and Skari (1992) have also reported the antivenom action of the stem juice from banana plant. As a part of the ongoing research (Alam *et al.*, 2011; Jha *et al.*, 2010) on Bangladeshi medicinal plants, the present study aimed to evaluate the antidiarrheal activity of peel and pulp extracts of *Musa sapientum* fruits.

MATERIALS AND METHODS

Plant materials: The fruits of *Musa sapientum* were collected from the local market in Mirpur, Dhaka, Bangladesh in the month of April, 2010 and identified by experts in Bangladesh National Herbarium, Mirpur, Dhaka where the voucher specimen No: 38765 has been retained for future reference.

Preparation of plant extract: Around 250 g of powdered materials of both peel and pulp were taken in two different clean, flat bottomed glass containers and were immersed in 500 mL of 95% methanol. The containers with their contents were sealed and kept for a period of 7 days associated with occasional shaking and stirring. The two mixtures then underwent a coarse filtration by a piece of clean, white cotton material and were filtered through Whatman filter paper (Bibby 200, Sterilin Ltd., UK). The filtrates (methanolic extract) obtained were evaporated using rotary evaporator. The extracts were transferred to two different closed containers for further use and fortification.

Chemicals: Folin-chiocaltu phenol reagent were purchased from E. Merck (Germany). Galic acid and quercetin were purchased from Sigma Chemical Co., Ltd., (St. Louis, MO, USA). All other chemicals and reagents were of analytical grade.

The amount of phenolic compounds and flavonoids: The total phenolic content of extract was determined using Folin-Ciocalteu reagent (Yu *et al.*, 2002). Extracts (100 µL) were mixed with the Folin-Ciocalteu reagent (500 µL) and 20% sodium carbonate (1.5 mL). The mixture was shaken thoroughly and made up to 10 mL with distilled water. The mixture was allowed to stand for 2 h. Then the absorbance at 765 nm was determined with a Shimadzu UV-160A spectrophotometer (Kyoto, Japan). These data were used to estimate the phenolic contents using a standard curve obtained from various concentration of gallic acid.

The flavonoids content was determined by aluminium chloride colorimetric method (Chang *et al.*, 2002). The different concentration of extracts (0.5 mL) were separately mixed with 95% ethanol (1.5 mL), 10% aluminum chloride (0.1 mL), 1 M potassium acetate (0.1 mL) and distilled water (2.8 mL). After incubation at room temperature for 30 min, the absorbance of the reaction mixture was measured at 415 nm. The amount of 10% aluminum chloride was substituted by the same amount of distilled water in blank. All the determinations were carried out in duplicates. These data were used to estimate the flavonoid contents using a standard curve obtained from various concentration of quercetin.

Acute toxicity study: Animals were divided into groups of 5 mice each. The test was performed using increasing doses of both test extracts given orally, in a 10 mL kg^{-1} volume to different groups serving as test groups (Sanmugapriya and Venkataraman, 2006). Another group of mice was administered saline (10 mL kg^{-1}, p.o.) as negative control. The mice were allowed food *ad libitum* during the 24 h test and kept under regular observation for mortality.

Castor oil-induced diarrhea: The experiment was performed according to the method described by Shoba and Thomas (2001). Briefly, mice fasted for 24 h were randomly allocated to 6 groups of 5 animals each. The animals were all screened initially by giving 0.5 mL of castor oil. Only those showing diarrhea were selected for the final experiment. Group 1 received 1% tween 80 (10 mL kg^{-1}, p.o.), groups 3-6 received orally MSPL and MSPP extracts (100 and 200 mg kg^{-1}), respectively. Group 2 was given loperamide (3 mg kg^{-1}, p.o.) in suspension. After 60 min, each animal was given 0.5 mL of castor oil, each animal was placed in an individual cage, the floor of which was lined with blotting paper which was changed every hour, observed for 4 h and the characteristic diarrhoeal droppings were recorded.

Magnesium sulphate-induced diarrhea: Diarrhoea was induced by oral administration of magnesium sulphate at the dose of 2 g kg^{-1} to the animals 30 min after pre-treatment with vehicle (1% tween 80 in water, 10 mL kg^{-1}, p.o.) to the control group, loperamide (3 mg kg^{-1}) to the positive control group and the methanol extract (MSPL and MSPP) at the doses of 100 and 200 mg kg^{-1} to the test groups (Doherty, 1981).

Effect on gastrointestinal motility: Animals were divided into 6 groups of 5 mice each and each animal was given orally 1 mL of charcoal meal (5% activated charcoal suspended in 1% CMC) 60 min after an oral dose of drugs or vehicle. Group 1 was administered 1% CMC (10 mL kg^{-1}) and animals in groups 3-6 received extract of both MSPL and MSPP at the dose of 100 and 200 mg kg^{-1} body weight, respectively. Group 2 received atropine sulfate (0.1 mg kg^{-1}) as the standard drug. After 30 min,

animals were killed by light ether anaesthesia and the intestine was removed without stretching and placed lengthwise on moist filter paper. The intestinal transit was calculated as a percentage of the distance travelled by the charcoal meal compared to the length of the small intestine (Abdullahi *et al.*, 2001).

PGE₂-induced enteropooling: The method of Robert *et al.* (1976) was applied. Overnight fasted mice were divided into 7 groups of 5 animals each. Group 1 was given 2% gum acacia and kept as a control. Group 3-6 received 100 and 200 mg kg⁻¹ p.o. of MSPL and MSPP extracts, respectively. Group 2 served as a vehicle control and received 2% gum acacia plus PGE_2 (0.5 mL of 100 µg kg⁻¹, i.p). Group 7 received loperamide and kept as a positive control. Immediately afterwards, diarrhea was induced by 0.5 mL of 100 µg kg⁻¹, i.p., dose of PGE_2 (Sigma Aldrich, USA). After 30 min, the animals were sacrificed, small intestine was removed and intestinal contents were collected and measured in a syringe. The percentage inhibition in intestinal fluid was determined by comparing the values with vehicle control.

Antimicrobial activity: Sterile 6.0 mm diameter blank discs (BBL, Cocksville, USA) were impregnated with test substances of both MSPL and MSPP at the dose of 500 µg disc⁻¹. This disc, along with standard discs (Ciprofloxacin, Oxoid Ltd., UK) and control discs were placed in petri dishes containing a suitable agar medium seeded with the test organisms using sterile transfer loop and kept at 4°C to facilitate maximum diffusion. The plates then kept in an incubator (37°C) to allow the growth of the bacteria. The antibacterial activities of the test agents were determined by measuring the diameter of the zone of inhibition in terms of millimeter. Antimicrobial activity was tested against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonus aeruginosa*, *Salmonella typhi*, *Shigella boydii*, *Shigella flexneri* and *Shigella dysenteriae* were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) (Bauer *et al.*, 1966).

Statistical analysis: All values were expressed as the mean±Standard Error of the Mean (SEM) of three replicate experiments and were analyzed using the GraphPad program (GraphPad, San Diego, CA, USA). The analysis was performed by using student's t-test; $p < 0.001$ and < 0.05 were considered to be statistically significant.

RESULTS

Total phenolic and flavonoid contents: The total extractable phenolic contents of the peel and pulp of

Table 1: Yield, total amount of plant phenolic compounds and flavonoids of methanolic extract of *Musa sapientum* peel and pulp

Samples	Yield (%)	Total phenols mg g⁻¹ plant extract (in GAE)[a]	Total flavonoids mg g⁻¹ plant extract (in QA)[b]
MSPL	15.0	84.23±0.81	21.34±0.39
MSPP	12.1	21.95±0.12	8.23±0.19

[a]Gallic acid equivalents (GAE, mg g⁻¹ of each extract) for the total phenolic content; [b]Quercetin equivalents (mg g⁻¹ of each extract) for the total flavonoid content. The GAE and QA are expressed as means±SEM of triplicate experiments

Table 2: Effect of *M. sapientum* peel and pulp extracts on castor oil-induced diarrhea in mice

Groups	Onset of diarrhea (min)	Animals with diarrhea	No. of faeces in 4 h	Inhibition of defaecation (%)
1	25.45±1.19	5/5	22.6±0.68	-
2	160.00±0.13**	1/5	3.8±0.58**	83.18
3	38.67±2.73	4/5	20.2±1.05	10.62
4	51.23±3.03*	3/5	15.6±0.29*	30.97
5	48.67±2.73**	3/5	15.2±1.05**	32.74
6	64.23±3.03**	2/5	10.1±0.29**	55.30

Values are presented as mean±SEM (n = 5); **,*p<0.001 and <0.05, respectively compared to control by student's t-test. Group 1 animals received vehicle (1% tween 80 in water); group 2 received loperamide 10 mg kg⁻¹ body weight; group 3-6 were treated with 100 and 200 mg kg⁻¹ body weight (p.o.) of the MSPP and MSPL, respectively

M. sapientum were 84.23±0.81 and 21.95±0.12 mg g⁻¹ plant extract (GAE), respectively. As shown in Table 1, the polyphenol contents of MSPL extract was approximately 4 fold higher than the MSPP extract. In case of flavonoid, MSPL also displayed the highest flavonoid content (21.34±0.39 mg g⁻¹ plant extract in QA).

Acute toxicity studies: Methanolic extract of both peel and pulp of *Musa sapientum* (500-5000 mg kg⁻¹, body weight) given orally did not cause any death in the different dose groups. The LD_{50} values for oral administration of the plant extracts were found to be >5000 mg kg⁻¹ in both cases.

Effect on castor oil-induced diarrhea: The extracts significantly reduced the number of diarrheal episodes in a dose dependent manner when compared with the untreated controls. At 200 mg kg⁻¹ doses, MSPL showed 55.30% and MSPP 30.97% reduction in the number of fecal episodes whereas loperamide offered 83.18% protection (Table 2).

Effect on magnesium sulphate-induced diarrhea: Both extracts (MSPL and MSPP) exhibited significant antidiarrheal activity against magnesium sulphate-induced diarrhea (Table 3). The extracts at both dose levels significantly (p<0.001, 0.05) reduced the extent of diarrhea and also notably delayed the onset of diarrhea in a dose dependent manner.

Table 3: Effect of *M. sapientum* peel and pulp extract on magnesium sulphate-induced diarrhea in mice

Groups	Onset of diarrhea (min)	Animals with diarrhea	No. of faeces in 4 h	% inhibition of defaecation
Group 1	32.05±1.09	5/5	20.2±1.68	-
Group 2	160.00±0.10**	1/5	4.8±0.51**	76.23
Group 3	38.67±1.73	4/5	15.4±1.05	23.76
Group 4	45.23±1.03*	4/5	11.2±0.49*	44.55
Group 5	41.67±2.03**	3/5	10.4±1.15**	48.51
Group 6	59.23±2.03**	2/5	5.4±0.39**	73.27

Values are presented as mean±SEM (n = 5); **, *p<0.001 and <0.05, respectively compared to control by student's t-test. Group 1 animals received vehicle (1% tween 80 in water); group 2 received loperamide 10 mg kg^{-1} body weight; group 3-6 were treated with 100 and 200 mg kg^{-1} body weight (p.o.) of the MSPP and MSPL, respectively

Table 4: Effect of *M. sapientum* peel and pulp extract on charcoal meal stimulated gastrointestinal transit in mice

Treatments	Dose (p.o.)	Mean intestinal length (cm)	Mean distance traveled by charcoal (cm)	GI transit (%)
1% tween 80 in water	0.4 mL mouse^{-1}	69.6±0.91	52.0±1.08	75.00±1.57
Atropine	0.1 mg kg^{-1}	64.0±1.19	19.4±0.79**	30.27±0.80**
MSPP	100 mg kg^{-1}	68.8±1.11	50.6±1.06	73.73±2.32
	200 mg kg^{-1}	69.2±1.51	40.8±2.02*	59.26±3.82*
MSPL	100 mg kg^{-1}	67.2±1.23	30.2±0.83**	45.23±2.30**
	200 mg kg^{-1}	66.2±1.60	24.8±1.01**	37.82±1.04**

Values are presented as mean±SEM (n = 5); **, *p<0.001 and <0.05, respectively compared to control by student's t-test
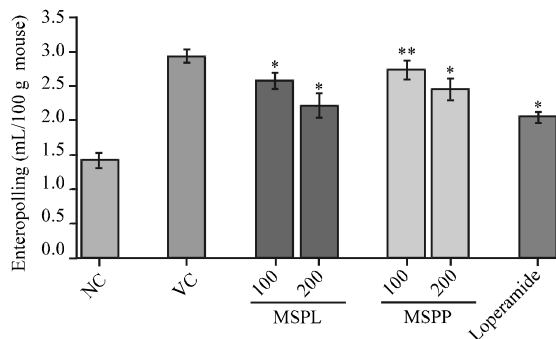

Fig. 1: Effect of the methanolic extract of peel and pulp of *M. sapientum* fruits on PGE$_2$-induced enteropooling in mice. Values are presented as mean±SEM (n = 5); **, *p<0.001 and <0.05, respectively compared to vehicle control by student's t-test; NC = Normal Control; VC = Vehicle Control

Effect on gastrointestinal motility: With the gastrointestinal transit experiment, the treated groups showed significant difference compared with control (p<0.001, <0.05). The intestinal transit of charcoal meal was 75.00% in the control group but at 200 mg kg^{-1} body weight dose 37.82% in MSPL and 59.26% in MSPP (Table 4).

PGE$_2$-induced enteropooling: The plant extracts reduced the intestinal fluid accumulation induced by PGE$_2$ in a

Table 5: Antibacterial activity of the methanolic extracts of *M. sapientum* peel and pulp

Bacterial strain	Diameter of zone of inhibition (mm)		
	Ciprofloxacin	MSPL	MSPP
Staphylococcus aureus	28.03±0.12	11.89±0.14	NA
Pseudomonas aeruginosa	29.13±0.21	NA	NA
Salmonella typhi	25.41±0.11	8.09±0.12	NA
Shigella flexneri	27.34±0.12	NA	NA
Shigella dysenteriae	28.01±0.11	9.02±0.62	10.02±0.02
Shigella boydii	29.39±0.14	NA	NA
Escherichia coli	30.23±0.18	10.59±0.22	7.09±0.12

Assay was performed in triplicate and results are the mean of three values±standard deviation; NA = Zone of inhibition <5 mm consider as no activity

dose dependent manner (Fig. 1). At 200 mg kg^{-1} body weight dose, MSPL showed a greater reduction (25.60%) than MSPP (16.04%) compared with the vehicle control.

Antibacterial activity: Table 5 expressed the antibacterial activity (zone of inhibitions) of the MSPL and MSPP extracts. The MSPL extract showed significant to moderate activity against *Staphylococcus aureus*, *Salmonella typhi*, *Shigella dysenteriae* and *Escherichia coli* whereas MSPP showed activity against *Shigella dysenteriae* and *Escherichia coli* only. Both extracts have not shown any activity against *Pseudomonas aeruginosa*, *Shigella flexneri* and *Shigella boydii*. The highest zone of inhibition was found against *Escherichia coli* (zone of inhibition 11.89±0.22 mm), followed by *Staphylococcus aureus* (zone of inhibition 10.59±0.14 mm) for MSPL.

DISCUSSION

Plants or plant derived preparations are used abundantly by mass population against diarrheal disorders without any scientific explanation. Imbalance between absorptive and secretary mechanisms in the GIT accompanied by intestinal hurry results in frequent loose stools or diarrhea (Yegnanarayan and Shrotri, 1982). Use of medicinal plants against diarrhea have been validated by several studies, i.e., antispasmodic effects, delay intestinal transit, suppress gut motility, stimulate water adsorption or reduce the intraluminal fluid accumulation (Almeida *et al.*, 1995; Atta and Mouneir, 2005). Those experimental procedures were therefore employed to judge the antidiarrheal efficacy of *Musa sapientum* peel and pulp in the current study.

In the present investigation, MSPL and MSPP at large dose (200 mg kg^{-1} body weight) exhibited significant antidiarrheal effects in one or the other experimental models. With respect to the castor oil induced diarrhea model, the results revealed that MSPL showed lightly better protection from diarrhea in the animals as compared

with MSPP and so was the case in PGE$_2$-induced enteropooling. It is likely that the extracts bring out the aforementioned action either through their proabsorbtive property that promotes faster fluid absorption in the intestine or through an anti-secretory mechanism. The first speculation gains support from the fact that castor oil which was used as a diarrhea inducing agent in the experimental protocol. Several mechanisms have been previously proposed to explain the diarrhoeal effect of castor oil including inhibition of intestinal Na$^+$, K$^+$-ATPase activity to reduce normal fluid absorption (Nell and Rummel, 1984), activation of adenylate cyclase or mucosal cAMP mediated active secretion (Capasso *et al.*, 1994), stimulation of prostaglandin formation (Galvez *et al.*, 1993), platelet activating factor and recently nitric oxide has been claimed to contribute to the diarrhoeal effect of castor oil (Mascolo *et al.*, 1996). However, it is well evident that castor oil produces diarrhea due to its most active component recinoleic acid which causes irritation and inflammation of the intestinal mucosa, leading to release of prostaglandins which results in stimulation of secretion (Gaginella *et al.*, 1975). The prostaglandins of the E series are considered to be good diarrheogenic agents in experimental animals as well as in human beings (Jaffe, 1979). The inhibitors of prostaglandins biosynthesis are therefore considered to delay the castor oil induced diarrhea (Pierce *et al.*, 1971).

On the other hand, magnesium sulphate has been reported to induce diarrhea by increasing the volume of intestinal content, through prevention of reabsorption of water. It has also been reported that it promotes the liberation of cholecystokinin from the duodenal mucosa which increases the secretion and motility of small intestine and thereby prevents the reabsorption of sodium chloride and water (Zavala *et al.*, 1998). Both MSPL and MSPP extracts were found to improve the diarrheal condition in this model. The extracts may increase the absorption of water and electrolyte from the gastrointestinal tract, since it delayed the gastrointestinal transit in mice as compared to the control. The delay in the gastrointestinal transit prompted by the extract might have contributed, at least to some extent to their antidiarrheal activity by allowing a greater time for absorption.

In the small intestinal transit test both extracts suppressed the propulsion of charcoal marker in a dose dependent manner. This finding suggests that the extracts act on all parts of the intestine. A decrease in the motility of gut muscles increases the stay of substances in the intestine (Tangpu and Yadav, 2004). This allows better water absorbtion. It is, therefore presumed that the reduction in the intestinal propulsive movement in the

charcoal meal model may be due to antispasmodic properties of the extracts. Salah *et al.* (2002) has reported that flavonoids inhibit the intestinal motility in experimental induced diarrhea in rats.

Flavonoids and sugars obtained from selected traditional medicinal plants in Bangladesh were reported by Rahman and Wilcock (1991) having antidiarrheal properties. Otshudi *et al.* (2000) screened a number of medicinal plants and showed that antidiarrheal activity of those plants were due to tannins, alkaloids, saponins, flavonoids, sterols, triterpenes and reducing sugars contained in them. The flavonoids presence of these types of compounds, such as kaemferol, myricetin, apigenin and leucocyanidin in *Musa sapientum* is likely to contribute to its grastrointestinal effects (Kongkachuichai *et al.*, 2010). Also, some plants show antidiarrheal properties by their antimicrobial activities (Ilyas *et al.*, 1995). MSPL was shown to exhibit good antibacterial activity when tested against *Escherichia coli, Shigella dysenteriae* and *Staphylococcus aureus* and also supported to the previous study (Ferdinand *et al.*, 2009). Phytoconstituents such as saponin, phenolic compounds, flavonoids and glycosides have been reported to inhibit bacterial growth and to be protective to plants against bacterial and fungal infections. In the present study, this possibility is supported by the estimation of total polyphenols and flavonoids (Kongkachuichai *et al.*, 2010) which was found to be present in high concentration and was found to be 84.23±0.81 mg equivalent of gallic acid/g plant extract and 21.34±0.39 mg equivalent of quercetin/g plant extract, respectively. Moreover (Mokbel and Hashinaga, 2005), isolated various antibacterial compound viz. β-sitosterol, malic acid, succinic acid, palmatic acid, 12-hydroxystrearic acid, glycoside, the d-malic and 12- hydroxystrearic acid. So, the antibacterial activity showed by the extract may be due to the presence of those compounds.

CONCLUSION

The results obtained in the present study suggest that *M. sapientum* peel and pulp extracts have beneficial effect in controlling the diarrhea in experimental animals. The antidiarrheal property of *M. sapientum* is mediated through inhibition of hypersecretion, gastrointestinal motility and increase of gastric transit time. The *Musa sapientum* could be used in the treatment of diarrhea.

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