Journal of Pharmacognosy and Phytotherapy Vol. 3(1), pp. 1-7, January 2011
Available online at http://www.academicjournals.org/jpp
ISSN 2141-2502 ©2011 Academic Journals

Full Length Research Paper

Antidiarrhoeal activity of aqueous leaf extract of *Momordica charantia* in rats

Bakare R. I.*, Magbagbeola O. A., Akinwande A. I., Okunowo O. W. and Green M.

Department of Biochemistry, College of Medicine, University of Lagos, Idi-Araba, Lagos State, Nigeria.

Accepted 9 December, 2010

Momordica charantia **Linn (Cucurbitaceae) is a medicinal herb, whose common name bitter melon, has been reported to possess antidiabetic property. However, its antidiarrhoeal potential is still unknown. The antidiarrhoeal activity of aqueous leaf extract of *M. charantia* (MC) was evaluated on castor oil-induced diarrhoea, gastrointestinal transit, intestinal fluid accumulation and gastric emptying in rats. The aqueous extract of the plant showed inhibitory activity against castor oil induced diarrhoea. A significant reduction ($p< 0.05$) in the gastrointestinal motility in charcoal meal test in rats was observed. The extract decreased volume of intestinal secretion induced by castor oil with a significant effect ($p< 0.05$) on the gastric emptying of the test animals compared to control rats. Inhibition of the gastrointestinal propulsion and fluid secretion by the extract suggest the extract might exert its antidiarrhoeal activity by antisecretory mechanism.**

Key words: Anti-diarrhoeal, bitter melon, castor oil, fluid accumulation, gastrointestinal transit, *Momordica charantia*.

INTRODUCTION

Momordica charantia (MC), balsam pear (bitter melon) is a creeping plant and is widely distributed in West Africa, Indian and Japan (Oliver, 1986). The plant belongs to the Cucurbitaceae family and has been used over the years in the preparation of various remedies for numerous therapeutic purposes. *M. charantia* is principally used in West Africa as a taenifuge as well as in the treatment of fever (Burkil, 1985). Medicinally, the plant is widely used for therapeutic purposes. A tea prepared from the leaf is used for diabetes, to expel intestinal gas, to promote menstruation, and as an antiviral agent against measles, hepatitis, and feverish conditions (Sofowora, 2006; Taylor, 2005). It is used tropically for sores, wounds, and infections and internally and externally for worms and parasites and to treat colic (Sofowora, 2006; Taylor, 2005). In Nigeria, Ghana and India peninsula, the root of the plant is used as an abortifacient together with the fruit, as well as an ingredient in aphrodisiac preparations (Sofowora, 2006). The young fruits and shoots are reported to serve as supplementary or emergency food in some parts of West Africa, and as an effective emenagogue to facilitate child birth in Ivory Coast (Burkil, 1985). The leaves and fruits are used in the Western world to make teas and beer and to season soups (Duke, 1985). In India and Japan, the whole plant is used on cutaneous infections along with other plants as an ointment for psoriasis, scabies and other diseases (Burkil, 1985). Other medicinal uses of the plant include treatment of heart diseases, measles, rheumatism, small pox, chicken pox, gastrointestinal disorder, gonorrhea as well as malignant ulcers (Burkil, 1985; Sofowora, 2006), for periodical pains and as an insecticide (Burkil, 1985).

Diarrhoea is one of the main causes of high mortality rate in developing countries where over five million children under the age of five die annually from severe diarrhoeal diseases (WHO, 1996). According to the World

*Corresponding author. E-mail: rasheedatbakare1@yahoo.com.

Health Organization (WHO), 3-5 billion cases occur annually, and approximately 5 million deaths are accountable to diarrhoea (Heinrich et al., 2005). Diarrhoea is mostly common in crowdy living conditions couple with poor hygiene. It is a major contributor to malnutrition, and also causes rapid dehydration in infant and elderly people, which could lead to death if treatment is not given (WHO, 1995; Yadzi and Chang, 1993).

Although Oral Rehydration Therapy (ORT) has been very helpful in the treatment of diarrhoeal diseases, the oral rehydration solution (ORS) formulae supplemented with cooked rice powder was more effective than ORS treatment (Gore et al., 1992).

Numerous plants have been widely used in the treatment of variety of disorders and diseases but the use of traditional medicinal plants in improving the efficiency of ORT has not been much applauded by scientists (Bhan et al., 1992; Mahalanabis, 1996). However, report of study by Martinez et al. (1998) showed that herbal remedies are still relevant in the treatment of diarrhoea by mothers in Mexico.

There are well documented reports on the hypoglycaemic property of *M. charantia* with no scientific evidence on its antidiarrhoeal potential. Previous study carried out on the plant showed that it contains appreciable amount of nutrients and its purported numerous medicinal actions may be as a result of the phytochemicals present in the plant (Bakare et al., 2010). In another study, the aqueous leaf extract was reported to enhance the absorptive roles of hydrolytic enzymes in the small intestine of diarrhoeagenic mice (Bakare et al., 2010). In view of this, the study therefore aimed to exploit the antidiarrhoeal activity of *M. charantia* in castor oil induced diarrhoeal model.

MATERIALS AND METHODS

Fresh leaves of *M. chara*ntia were harvested between June and August, 2006, from a home garden at Amuwo-Odofin LGA of Lagos State, Nigeria. The plant was identified and authenticated by Prof. J.D. Olowokudejo of the Department of Botany and Microbiology, University of Lagos, Nigeria. A voucher specimen was deposited in the herbarium. The plant material was sorted out to eliminate all extraneous materials. The leaves were dried in a hot air oven (SD 93114624, Gallenkamp, United Kingdom) for 5 days at 40°C and were further processed (wrapped in water proof bags) and kept until required (Odetola and Akojenu, 2000).

Preparation of extract

The dried leaf sample (1100 g) of *M. charantia* was extracted in 5500 ml boiling distilled water for 30 min and filtered using Whatman no 1 filter paper and also through a funnel plunged with glass wool. The residue was re-extracted in boiling distilled water and filtered. The resultant filtrates were pooled together and concentrated in a lyophilizer. The dried powder was kept in an air tight container and stored at 4°C until needed (Akueshi et al., 2002; Oben et al., 2006). The yield of the dried extract obtained was 5.85 ± 0.53%. A stock solution of the dried powder was reconstituted in distilled water at a concentration of 800 mg/ml and different doses 100, 200 and 400 mg/kg were prepared from the stock solution and administered orally to the animals.

Experimental animals

Swiss albino mice and Sprague Dawley rats of either sex, purchased from the animal house of the College of Medicine, University of Lagos, Nigeria were used. The animals were maintained under standard laboratory condition with food and water *ad libitum*. The animals were allowed to acclimatize for 2 weeks before being subjected to experimental protocol. The animals were treated in line with the guide and care of laboratory animals as approved by the Experimentation Ethics Committee on Animal use of the College of Medicine, University of Lagos, Nigeria.

Drugs

Morphine (Evans Medical Ltd. Liverpool/UK), castor oil (finest cold drawn commercial castor oil), methyl cellulose (Koch-light laboratories Ltd. England).

Oral toxicity tests

Forty-five Swiss albino mice (20 - 22 g) were randomly divided into nine groups of five animals each. The mice were fed on mice pellets and water *ad libitum*. The animals were starved for 12 h prior to testing. Eight doses of the extract (0.5-20 g/kg body weights) were administered by oral intubation to 8 groups of the animals respectively. The volume of the extract administered to each animal in the test group was calculated based on the body weight. The animals in the control group received 0.2 ml distilled water. All animals were observed for 24 h and general symptoms of toxicity and mortality were recorded (Lorke, 1983; Amida et al., 2007).

Intraperitoneal toxicity tests

Another group of 35 Swiss albino mice (20 - 22 g) were divided randomly into seven groups of five mice each. The animals were subjected to the same condition as done for the oral administration. The extract was suspended in distilled water and administered intraperitoneally in six doses ranging from 0.5 - 5 g/kg body weight for the six groups, while the animals in the control (vehicle) group received 0.2 ml distilled water. General symptoms of toxicity such as stomach gait, reactivity to light, environment and mortality were recorded for 24 h. Animals that survived in the different test groups were observed further for one week for any delayed toxic effects. The LD_{50} (the median lethal dose of the extract that will kill 50% of a given population) was estimated from the graph of percentage mortality against log-dose of the extract (Adzu et al., 2003).

Tests for antidiarrhoeal activity

Castor oil-induced diarrhoea in rats

Rats of either sex (180 - 220 g) fasted for 18 h were randomly allocated to five groups of six animals each. Group I received 10 ml/kg of distilled water, group II, III and IV received 100, 200 and 400 mg/kg of body weight of the aqueous *M. charantia* leaf extract orally while, group V was given 10 g/kg body weight morphine subcutaneously. After 1 h of treatment with extract, distilled water or standard drug, diarrhoea was induced by administration of 1 ml of castor oil orally to each rat and observed for 4 h. The characteristic

diarrhoeal droppings were noted in the absorbent paper placed beneath the individual rat perforated cages (Izzo et al., 1992; Mukherjee et al., 1995).

Normal gastrointestinal transit

Normal gastrointestinal transit (motility) was investigated in rats according to the method of Aye-Than et al. (1989) as described by Odetola and Akojenu, (2000). Adult rats of both sexes weighing 180 - 220 g were divided into five groups of six animals each to determine the effect of the aqueous extract of *M. charantia* on normal intestinal transit of a marker meal. Group I received 10 ml/kg of distilled water, while animals in groups II - IV were treated orally with the graded doses of the aqueous extract (100, 200 and 400 mg/kg respectively) and those in group V received 10 mg/kg of morphine subcutaneously. One hour after the administration of distilled water, extract or morphine, each animal was given 1 ml standard charcoal meal (10% activated charcoal suspension in 5% gum acacia). The rats were sacrificed 1 h after the administration of the charcoal meal, the abdomen were opened and the small intestine was immediately isolated. The length of the intestine from pylorus to the caecum (LSI) and the distance traveled by the charcoal (LM) were measured. The peristaltic index (PI) for each mouse was calculated, expressed as percentage of the distance traveled by the charcoal meal relative to the total length of the small intestine. The percentage inhibition relative to the control was also calculated as:

PI = LM/LSI x 100%

Where: PI = Peristaltic Index
LM = Length of Charcoal Meal; LSI = Length of Small Intestine

% Inhibition = (Control – Test)/Control X 100

Castor oil induced gastrointestinal transit

Rats fasted for 18 h was divided into groups of five animals each. Group I received 2 ml distilled water, groups II,III, and IV received 100, 200 and 400 mg/kg body weight of the extract by oral intubation, and group V received 10 mg/kg of morphine subcutaneously, 1 h before oral administration of castor oil. 1 ml of a marker (10% charcoal suspension in 5% gum acacia) was administered orally 1 h after castor oil administration. One hour later each animal was sacrificed and the distance traveled by the charcoal meal from the pylorus was measured and expressed as a percentage of the total length of the intestine from the pylorus to the caecum of each animal (Mascolo et al., 1994; Mukherjee et al., 1995; Rani et al.,1999).

Castor oil induced intestinal fluid accumulation and electrolyte secretion

Rats were divided into three groups of five animals each; they were pretreated with distilled water (10 ml/kg), and extract (100 and 200 mg/kg) by oral intubation. One hour after, the rats received 2 ml of castor oil, and the animals sacrificed 1 h after castor oil administration. The small intestine was removed, tied with thread at the pyloric end and the ileocaecal junction and weighed. The intestinal content was milked into a graduated tube and their volume measured. The intestine was reweighed and the difference between full and empty intestines was calculated. The Na^+ and K^+ concentrations in the supernatant after centrifuging the intraluminal fluid were measured by flame photometry (Di-carlo et al., 1994; Azdu et al., 2003; Boominathan et al., 2005).

Gastric emptying test in rats

Following the method of Droppleman et al. (1980) as described by Adeyemi and Akindele (2008). Rats fasted for 24 h prior to the experiment were divided into three groups of six animals each. Group I received distilled water (10 ml/kg) while groups II and III received 100 and 200 mg/kg body weight of the extract. One hour after, 3 ml of a semi solid test meal (based on methyl cellulose) was administered to the animals. The animals were sacrificed and laparatomized 1 h after the treatment and the stomach removed. The full stomach was weighed, opened and rinsed, excess moisture was mopped and the empty stomach weighed. The difference was subtracted from the weight of 3 ml of the test meal, and was taken as the quantity emptied from the stomach during the test period.

Statistical analysis

All experiments were repeated at least six times and the results expressed as mean ± S.E.M. The statistical analysis of data was done using one-way ANOVA (Analysis of Variance) with level of statistical significance taken as $p< 0.05$ with Duncan's Multiple Range test. The statistical package used was Statistical Package for Social Science (SPSS 11).

RESULTS

Acute toxicity studies

Oral administration of the aqueous leaf extract of *M. charantia* produced no visible signs of toxicity in the animals except for an initial huddling observed at the highest dose of 20 g/kg body weight. No mortalities were recorded in all the doses. In addition, no toxic symptoms were observed and neither food nor water intake was found to be reduced during the period.

Intraperitoneal Administration (i.p.) of the aqueous leaf extract of *M. charantia* showed visible signs of toxicity in the animals, although no toxic symptom or deaths were recorded at the lowest doses of the extract (0.5 - 2.0 g/kg body weight) via this route of administration. Animals on higher doses (3 - 5 g/kg body weight) were more agitated than those on the lower doses (Table 1). The LD_{50} obtained via the i.p. route was 2790 mg/kg.

Castor oil induced diarrhoea

The aqueous leaf extract of *M. charantia* at different doses significantly ($P< 0.05$) inhibit the frequency of defaecation when compared to the untreated rats (control) (Table 2).

Normal gastrointestinal transit in rats treated with *M. charantia* aqueous leaf extract

As shown in Table 3, the extract decreases intestinal propulsion of the charcoal meal when compared with the control group. In control animal, the charcoal meal traveled 61.33 ± 7.55 of the total length of the small

Table 1. Behavioral observations on intraperitoneal acute toxicity study.

Dose (g/kg)	Control	0.50	1.00	2.00	3.00	4.00	5.00
Sniffing and Grooming	-	-	-	-	-	-	-
Abdominal Writhes	-	-	-	+	+	+	+
Piloerection	-	-	-	-	-	-	-
Respiration	Normal	Normal	Normal	Normal	Normal	High Rate	High Rate
Tremors	-	-	-	-	-	-	-
Convulsion	-	-	-	-	-	-	-
Abdominal Gait	-	-	-	-	+	+	+
Reactivity to Light	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Reactivity to Environment	Normal	Normal	Normal	Normal	Increased	Increased	Increased

Table 2. Effects of leaf extract of MC on castor oil-induced diarrhoea in rats.

Group	Treatment	Dose (mg/kg)	Mean wt. of faeces after 4 h	% Inhibition of defaecation
I	Control	-	2.28 ± 0.09^{d}	-
II	MC	100	1.17 ± 0.11^{c}	48.69
III	MC	200	0.66 ± 0.19^{b}	71.05
IV	MC	400	0.47 ± 0.06^{ab}	79.39
V	Morphine	10	0.25 ± 0.11^{a}	89.04

[1]n = 6, values are means ± SEM; mean values with different superscript down the column are significantly different at p< 0.05. [2]Superscripts a, b, c, d represents level of significant difference by Duncan's multiple range tests.

Table 3. Normal gastrointestinal transit in rats treated with MC aqueous leaf extract.

Group	Treatment	Dose (mg/kg) body weight	Peristaltic Index (PI) (%)	Inhibition (%)
I	Control	-	61.33 ± 7.55^{d}	-
II	MC	100	54.89 ± 3.56^{cd}	10.50
III	MC	200	47.50 ± 4.17^{b}	22.55
IV	MC	400	49.28 ± 6.06^{bc}	19.65
V	Morphine	10	16.48 ± 1.84^{a}	73.13

[1]n = 6, values are means ± SEM; mean values with different letters down the column are significantly different at p< 0.05.
[2]Superscripts a, b, c, d represents level of significant difference by Duncan's multiple range tests.

intestine. The aqueous leaf extract of *M. charantia* (200 - 400 mg/kg) produce significant ($p < 0.05$) reduction in normal intestinal transit. This effect was lower to that produced by morphine 16.48 ± 1.84 (73.13% inhibition).

Castor oil induced gastrointestinal transit in rats

The charcoal meal moved farther in the castor oil induced intestinal transit compared to the normal intestinal transit. In the castor oil-induced intestinal transit, the standard antidiarrhoeal agent, morphine reduced the motility of the intestine to a greater extent. The antimotility effect of the extract at the dose of 200 mg/kg was significantly ($p< 0.05$) higher than the other concentrations. This effect was significantly ($p< 0.05$) lower than that produced by morphine (Table 4).

Intestinal fluid accumulation and electrolyte secretion in rats

The leaf extract (100 and 200 mg/kg body weight) significantly ($p < 0.05$) inhibited castor oil-induced intestinal fluid accumulation in the rats. The treatment of rats with *M. charantia* extract significantly ($p < 0.05$) reduced the Na^{+} concentration in the intestinal fluid at both doses, and also significantly ($p < 0.05$) reduced the K^{+} concentration at 100 mg/kg body weight (Table 5).

Table 4. Castor oil induced gastrointestinal transit in rats.

Group	Treatment	Dose (mg/kg) body weight	Peristaltic Index (PI) (%)	Inhibition (%)
I	Control	-	32.55 ± 2.22[c]	-
II	MC	100	25.85 ± 2.00[bc]	20.58
III	MC	200	20.89 ± 0.81[ab]	35.82
IV	MC	400	24.36 ± 1.42[b]	25.16
V	Morphine	10	16.36 ± 1.51[a]	49.74

[1]n = 6, values are means ± SEM; mean values with different letters down the column are significantly different at p< 0.05.
[2]Superscripts a, b, c represents level of significant difference by Duncan's multiple range tests.

Table 5. Intestinal fluid accumulation in rats.

Group	Treatment	Dose (mg/kg) body weight	Wt. of Intestinal content (g)	Vol. of Intestinal content (ml)	Conc. of Na^+ (meq/l)	Conc. of K^+ (meq/l)
I	Control	-	2.59 ± 0.34[b]	2.00 ± 0.18[b]	29.03± 0.29[c]	9.39± 0.05[b]
II	MC	100	1.96± 0.62[ab]	1.42± 0.26[ab]	12.90 ±0.12[a]	7.74± 0.31[a]
III	MC	200	1.56 ± 0.16[a]	1.30 ± 0.23[a]	22.87± 1.14[b]	9.35 ± 0.01[b]

[1]n = 6, values are means ± SEM; mean values with different letters down the column are significantly different at p< 0.05.
[2]Superscripts a, b, c represents level of significant difference by Duncan's multiple range tests.

Table 6. Effect of aqueous leaf extract of MC on gastric emptying in rats.

Group	Treatment	Dose (mg/kg) body weight	Diff. between weight of full and empty stomach (g)	Quantity emptied (g)
I	Control	-	0.57 ± 0.08[a]	2.29 ± 0.06[b]
II	MC	100	0.95 ± 0.22[ab]	1.95 ± 0.18[ab]
III	MC	200	1.19 ± 0.15[b]	1.71 ± 0.15[a]

[1]n = 6, values are means ± SEM; mean values with different letters down the column are significantly different at p< 0.05.
[2]Superscripts a, b represents level of significant difference by Duncan's multiple range tests.

Gastric emptying test in rats

The result in Table 6 showed that there was a significant ($p < 0.05$) reduction in the quantity of test meal emptied in the control group and the test group in 1 h.

DISCUSSION

The extract was well tolerated by the animals when administered orally, no sign of acute toxicity like restlessness or seizures were observed over the period of observation. There were no deaths recorded after the oral administration of the aqueous leaf extract of *M. charantia*. However, when the extract was administered via the intraperitoneal route, the animals were hyperactive, particularly those on higher doses. Deaths were recorded after the intraperitoneal administration of 2000, 3000, 4000 and 5000 mg/kg of the aqueous leaf extract of *M. charantia*.

Castor oil was used in this study to induced diarrhoea. It is well documented that castor oil produces diarrhoea due to its most active metabolite, ricinoleic acid by hypersecretory response, which stimulates peristaltic activity in the small intestine, leading to changes in the electrolyte permeability of the intestinal mucosa (Zavala et al., 1988; Hardman and Limbird, 2001). Its action also stimulates the release of endogenous prostaglandins E and F which cause stomach cramp and diarrhoea due to the effect on the smooth muscle and secretion (Galvez et al., 1993; Saito et al., 2002). Among the several mechanisms proposed to explain the diarrhoeal effect of castor oil are activation of adenylate cyclase or mucosal CAMP mediated active secretion (Capasso et al., 1994), stimulation of prostaglandin formation (Capasso et al., 1992) and nitric oxide (Mascolo et al., 1996; Uchida et al., 2000).

In this study, there was a statistically significant reduction in the incidence and severity of diarrhoeal stool produced in the experimental animals. The extract tested at 200 and 400 mg/kg like the standard drug, morphine significantly inhibited the frequency of defecation droppings compared to untreated control rats. This result is in support of previous claims in respect of antidiarrhoeal herbs. Antidiarrhoeal plants are known to reduced number of wet stools as reported for *Eremomastax speciosa* and *Xylocarpus granatum* (Oben et al., 2006; Rouf et al., 2007).

The aqueous leaf extract of *M. charantia* inhibited gastrointestinal propulsion in the castor oil induced transit than in normal transit. This makes it beneficial as a preventive agent. Antidiarrhoeal treatment in patient is achieved through the objective of the therapy which includes increasing resistance to flow (segmental contraction and decrease propulsion) and increased mucosal absorption or decreasing secretion (Burks, 1991). This is indicative of the ability of the plant to alter normal peristaltic movement and hence decrease the movement of materials in the intestinal tract allowing greater time for absorption.

In the fluid accumulation test, the extract significantly reduced both the weight and volume of intestinal content. This may promote reabsorption of materials in the intestine due to decrease propulsion of material in the intestinal tract, and the extract might have exerted its antidiarrhoeal action by antisecretory mechanism. The plant extract also inhibited normal gastric emptying; this effect may be linked to the reduction in gastrointestinal propulsion observed in the animals. Decrease in intestinal transit time by morphine and atropine is linked to delay in gastric emptying (Izzo et al., 1999; Uchida et al., 2009). This suggests that the plant may have morphine-like action in exerting its antidiarrhoeal activity.

Conclusion

The result of the present study suggests that the aqueous leaf extract of *M. charantia* possess significant antidiarrhoeal activity due to its effect on reduction of number of diarrhoea stool, delayed in gastrointestinal propulsion and inhibition of fluid accumulation in the intestinal tract of rats. Further studies are ongoing to determine the exact compound(s) responsible for its antidiarrhoeal action.

REFERENCES

Adeyemi OO, Akindele AJ (2008). Antidiarrhoeal activity of the ethylacetate extract of *Baphia nitida* (Papilionaceae). J. Ethnopharmacol., 116: 407-412.

Adzu BS, Amos S, Amizan MB, Gamaniel KS (2003). Evaluation of the antidiarrhoeal effects of Z. Spina-christi Sterm bark in rats. Acta Trop., 6(1): 1-5.

Akueshi CO, Kadiri CO, Akueshi EU, Agina SE, Ngurukwem C (2002). Anti-microbial potential of *Hyptis suaveolens poit* (Lamiaceae). Nig. J. Bot., 15: 37- 41.

Amida MB, Yemitan OK, Adeyemi OO (2007). Toxicological Assessment of the Aqueous Root Extract of Sanseviera liberica Gerome and Labroy (Agavaceae). J. Ethnopharmacol., 113: 171-175.

Aye-Than HJ, Kukarni W, Tha SJ (1989). Antidiarrhoeal Efficacy of Some Burmese Indigenous Drugs Formations in Experimental Diarrhoeal Test Models. J.Crude Drug Res., 27(4): 195-200.

Bakare RI, Magbagbeola OA, Akinwande AI, Ebuehi OAT (2010). Effect of aqueous leaf extract of *Momordica charantia* on intestinal enzymes activities in diarrhoeagenic mice. Nig. Quart. J. Hosp. Med., 20(1): 24- 28.

Bakare RI, Magbagbeola OA, Akinwande AI, Okunowo OW (2010). Nutritional and chemical evaluation of *Momordica charantia*. JMPR (in press).

Bhan MK, Mahalanabis D, Fontaine O, Pierce NF (1992). Clinical trials of improved oral rehydration salt formulation: A review. Bull. WHO, 72: 945-955.

Boominathan R, Devi BP, Dewanjee S, Manda SC (2005). Studies on antidiarrhoeal activity of Ionodium suffruticosam ging, (violaceae) extract in rats. Recent Progress in Medicinal Plants (Phytotherapeutics), 10: 375-380.

Burkil HM (1985). Useful plants of West Tropical Africa. 2nd edn. Kew Royal Botanical Garden, pp. 597-599.

Burks TF (1991). Gastrointestinal drugs In. Kist, K. (edn). Human pharmacology: molecular to clinical. Wolfe Publ. Itc London, pp. 789-800.

Capasso F, Tavares IA, Bennet A (1992). PAF formation by human gastrointestinal mucosa/submucosa in vitro: release by ricinoleic acid, and inhibition by 5-aminosalicylic acid. J. Pharm. Pharmacol., 44: 771- 772.

Capasso F, Mascolo N, 1zzo AA, Gaginella TS (1994). Dissociation of castor oil-induced diarrhea and intestinal mucosal injury in rat: Effect of NG nitro-L-arginine methylester. Br. J. Pharmacol. 113: 1127-1130.

Di-carlo GD, Mascolo N, Izzo AA, Capasso F (1994). Effect of quercetin on the gastrointestinal tract in rats and mice. Phytother Res. 8: 42-45.

Droppleman DA, Gregory R, Alphin RS (1980). A simplified method for assessing drug effects on gastric emptying in rats. J. Pharmacol. Methods. 4: 227-230.

Duke JA (1985). CRC Handbook of Medicinal Herbs. Boca Raton,Fl: CRC Press. pp 315-316.

Galvez J, Zavzuelo A, Crespo ME, Lorente MD, Ocete MA, Jimenez J (1993). Anti-diarrhoeic activity of *Euphorbia hirta* extract and isolation of an active flavonoids constituent. Planta Med., 59:333-336.

Gore SM, Fontaine O, Pierce NF (1992). Impact of rice based ORS on stool output and duration of diarrhea, analysis of clinical trials. Br. J. Med. 304: 387-291.

Hardman JG, Limbird LE (2001). Drugs affecting gastrointestinal function. In The pharmacological basis of therapeutics. 10th edn. Goodman and Gilman's edn. New York.Macgraw Hill, pp. 1023-1024.

Heinrich M, Heneka B, Ankli A, Rimpler H, Sticher O, Kostiza T(2005). Spasmolytic and antidiarrhoeal properties of the Yucatec mayan medicinal plant *Casimiroa tetrameria*. J. Pharm. pharmacol., 57: 1081-1085.

Izzo AA, Nicoletti M, Giannattasio B, Capasso F (1992).Antidiarrhoeal activity of *Terminalia sericea* Burch ex. DC extract. In: Capasso, F., Mascolo, N. (Eds), Natural Drugs and the Digestive Tract. EMSI, Rome, pp. 223-230.

Izzo AA, Mascolo N, Capasso R, Germano MP, De pasuele R, Capasso F (1999). Inhibitory effect of cannabinoid agonists on gastric emptying in rat. Arch. Pharmacol., 360: 221-223.

Lorke D, (1983) A new approach to practical acute testing. Arch. Toxicol., 54: 275-287.

Mahalanabis D (1996). Current status of the oral rehydration as a strategy for control of diarrhoeal diseases. Indian J. Med. Res., 104: 115-124.

Martinez H, Ryan GW, Guiscafre H, Gutierrez G (1998). An International comparison of home case management of acute diarrhea in Mexico: Implications of program planners. Arch. Med. Res. (Mexico, D.F), 29: 351-360.

Mascolo N, Izzo AA, Antore G, Barbato F, Capasso F (1994). Nitric oxide and castor oil induced diarrhea. J. Pharmacol. Exp. Ther., 268: 291-293.

Mascolo N, Izzo AA, Gagnella TS, Capasso F (1996). Relationship between nitric oxide and platelet activating factor in castor oil-induced mucosal injury in the rat duodenum. Naunyn Schmiedebergs Arch. Pharmacol., 353: 680-684.

Mukherjee PK, Das J, Balasubramanian R, Saha K, Pal M, Saha BP (1995). Antidiarrhoeal evaluation of Nelumbo nucifera rhizome extract. Indian J. Pharmacol., 27: 262-264.

Oben JE, Assi SE, Agbor GB, Musoro DF (2006). Effect of *Eremomastax speciosa* on experimental diarrhoea. Afr. J. Tradit. Complement. Altern. Med., 3(1): 95- 100.

Odetola AA, Akojenu SM (2000). Antidiarrhoeal and gastrointestinal potentials of the aqueous extract of *Phylluanthus amarus* (Euphorbiaceae). Afr. J. Med. Sci., 29: 119- 122.

Oliver B (1986). Medicinal plants in Tropical West Africa. Cambridge University Press. Cambridge, pp. 247.

Rani S, Ahamed N, Rajaram S, Saluja R (1999). Antidiarrhoeal evaluation of *Clerodendrum phlomidis* Linn leaf extract in rats. J. Ethnopharmacol., 68: 315 - 319.

Rouf R, Uddin SJ, Alamgir M (2007). Assessment of antidiarrhoeal activity of the methanol extract of *Xylocarpus granatum* bark in mice model. J. Ethnopharmacol., 109: 539 - 542.

Saito T, Mizutani F, Iwanaga Y, Morikawa K, Kato H (2002). Laxative and anti-diarrheal activity of polycarbophil in mice and rats. Jpn. J. Pharmacol. 89:133 -141.

Sofowora A (2006). Medicinal Plants and Traditional Medicine in Africa. 2nd Edn., Spectrum Books Ltd., Ibadan, Nigeria, pp. 151-153, 209-214.

Taylor L (2005). Bitter melon: Herbal properties and actions. In: The Healing Power of Rainforest Herbs. Raintree Nutrition Inc. Square one Publishers Inc. NY.11040, pp. 1-5.

Uchida M, Kato Y, Matsuede K, Shode R, Muraoka A, Yemato S (2000). Involvement of NO from nerves in diarrhea induced by castor oil in rats. Jpn. J. Pharmacol., 82: 168-170.

Uchida M, Yoshida K,Shimizu K (2009). Effect of atropine sulfate on gastric emptying and gastrocecal transit time evaluated by using the [1_^{13}C] acetic acid and lactose [^{13}C] ureide breath test in conscious rats. J. Breath Res., 3(4):7003.

World Health Organisation, WHO (1995). Manual for treatment of diarrhoeal diseases. WHO/CDR: Geneva, 3.

World Health Organisation, WHO (1996). Scientific working Group. Resistance to antimicrobial agents. Bull. World Health Organisation; 71: 335-336.

Yadzi AJ, Chang EB (1993). The pharmacological basis of treatment of diarrhoea. Practical Gastroenterol., 17: 29- 37.

Zavala I, Barrera E, Nava A(1988). Ceftriaxone in the treatment of bacterial meningitis in adults. Chemotherapy. 34: 47-52.