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Evaluation of Acute Toxicity and Antidiarrheal Activity of Hunteria umbellata Mesocarp Extract: Preclinical Study

Onyinyechi Uloma Akoh*, Henry Nnanyere Nwigwe , Stella Mbanyeaku Ufearoh
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Abstract: *Diarrhea, characterized by increased water content in stools due to disruptions in intestinal physiological processes, poses significant health risks worldwide. Hunteria umbellata, a widely used medicinal plant in traditional medicine, holds the potential for treating various ailments, including diarrhea. This study aimed to evaluate the acute toxicity and antidiarrheal activity of Hunteria umbellata mesocarp extract. Acute toxicity assays (Phase 1 and Phase 2 LD50) conducted on mice revealed LD50 values greater than 5000 mg/kg body weight, indicating a wide safety margin. Subsequent antidiarrheal activity assessments using different models showed significant inhibition of diarrhea. In the charcoal meal transit model, the extract at 1000 mg/kg exhibited the highest inhibitory activity (49.89%). In the castor oil-induced model, the extract at 1000 mg/kg demonstrated the highest inhibition of diarrhoea (86.81%). Furthermore, in the castor oil-induced gastrointestinal fluid accumulation model, the extract at 500 mg/kg exhibited the highest antidiarrheal activity (56.28% inhibition). These findings support the potential therapeutic use of Hunteria umbellata mesocarp extract in managing diarrhea. Further preclinical and clinical studies are warranted to validate its efficacy and safety for human use. The results collectively suggest that the extract could serve as a safe and effective antidiarrheal agent, offering a promising alternative for diarrhea management.*

Keywords: *Diarrhea, Hunteria umbellate, secretion, electrolyte, gastrointestinal*

Onyinyechi Uloma Akoh
Department of Chemistry, Michael Okpara University of Agriculture, Umudike, Umuahia, Abia state, Nigeria. P.M.B. 7267, Umuahia, Abia State**.**
Email: onyilac@gmail.com
Orcid id: 0000-0002-4357-5010

Henry Nnanyere Nwigwe
Department of Chemistry, Michael Okpara University of Agriculture, Umudike, Umuahia, Abia state, Nigeria. P.M.B. 7267, Umuahia, Abia State.
Email: nwigwehenry30@gmail.com

Stella Mbanyeaku Ufearoh
Department of Chemistry, Michael Okpara University of Agriculture, Umudike, Umuahia, Abia state, Nigeria. P.M.B. 7267, Umuahia, Abia State.
Email: akuchukwu57@gmail.com
Orcid id: 0000-0001-6713-5522

1.0 Introduction

Diarrhoea is the augmentation of water content in stools because of an imbalance in the normal functioning of physiologic processes of the small and large intestines responsible for the absorption of various ions, other substrates, and consequently water. The normal value of water content in stools is approximately 10 mL/kg/day in infants and young children or 200 g/day in teenagers and adults. The main cause of diarrhea is infection but noninfectious causes become more common as the duration of diarrhea becomes chronic (Mascolo et al., 1994). Prevention of infectious diarrhea includes proper hand washing to prevent the spread of infection (Chen et al., 2018).

Diarrhea could be acute, chronic, infectious or non-infectious depending on the duration and associated signs. Other causes may include medications, food poisoning, food intolerances, procedures on the bowels, other diseases affecting the bowels and or even poor hygiene (Uddin 2005). Medicinal plants have been used as a source of medicine since prehistoric times, they have been used for thousands of years to flavour and conserve food, to treat health disorders and to prevent diseases including epidemics. The term medicinal plants include various types of plants used in herbalism and some of these plants have some medicinal activities. Medicinal plants are the "backbone" of traditional medicine, which suggests quite 3.3 billion people within less developed countries consume medicinal plants daily (Davidson-Hunt 2000). *H. umbellate* is an all-year flowering and fruitful plant which is naturally located in secondary, rain, and gallery forests, 600 m above sea level. It grows as a shrub or small tree up to 15–22 m in height, with a dense leafy crown (Sofowora 1993).

1.1 Folkoric medicinal uses of H. umbellate

H. umbellate has been documented to possess numerous local and folkloric medicinal uses.Various parts (especially the leaves, roots and barks) of *Hunteria umbellata* plant are highly valued for the treatment of various veterinary and human diseases. For example, a decoction made from the plant stem and root is reputed for its antihelminthic activities and in the treatment of swellings (Gills 1992). The plant leaves and pulp are equally used by West African traditional midwives to treat pregnancy-related ailments and to induce or augment labour at term (Falodun et al. 2006).
The seed and bark, which are prepared as infusions and decoction are effective against fever, leprosy sores, menstrual disturbance, infertility, yaws, intestinal worms, abdominal colic, discomfort, and stomach ache (Gills 1992, Oliver-Bever 1986).

(a)

(b)

Fig 1: (a) ***H. umbellate*** **tree and (b) fruit**

Among the Yorubas and Binis (southwest Nigeria), it is known as "Abeere". Some classes of compounds such as alkaloids; for example corymine, serpentine, and strictosidinic acid has been isolated from the seeds, stem bark and leaves. Phenolics; for example, ellagic acid, apigenin, and quercetin have been isolated from the seeds while triterpenoids such as oleanolic acid, squelene, ursolic acid have been isolated from the stem bark. *H. umbellate* has also been reported to possess some pharmacological properties such

as anti-diabetic and hypoglycemic properties, anti-oxidant properties, anti-microbial properties, anti-inflammatory properties, analgesic and antipyretic properties, anti-hyperlipidemic properties, sexual, aphrodisiac and oxytocic property, cytotoxic and anti-carcinogenic property, anxiolytic and anti-angiogenic property and as well as nutritional property.

2.0 Materials and Methods

2.1 Collection and extraction

The fruit of *Hunteria umbellata* was collected in Umunakanu, Ehime Mbano LGA of Imo State. The collected plant material was made thoroughly free of any foreign organic matter and rinsed. The back of the fruits was peeled off to reveal the mesocarp which was air-dried under shade for 10 days; thereafter, the air-dried sample was weighed. A 100-gram weight of the air-dried mesocarp was soaked in 1.5 L of methanol for 48 hours and filtered using N0 1whatmann filter paper. The filtrate was collected in 500ml beakers and transferred to a rotary evaporator for concentration. The concentrate completely evaporated to dryness after 8 hours and yielded 5.658g of the extract which appeared as a gel-like paste.

2.2 Biological assay

2.2.1 Toxicity test

Acute toxicity and lethal dose test (LD_{50}): It was carried out with modification according to the method of Lorke, 1983 [14]. A total of 18 mice were used. They were divided into two stages: In stage one (phase 1), the animals were divided into 3 groups having three mice in each group and the extracts were orally administered at the dose of 10, 100 and 1000 mg kg^{-1} b.wt. The stage (phase II) animals were given 160, 2900 and 5000 mg kg^{-1} b.wt, orally. The mice were observed for signs of toxicity hourly in the first 12 hours and then daily for 7 days.

Anti-diarrhea

Animals: Forty rats (120-150 g) and 3 rabbits (1.8-2.5 kg), acquired from the production unit of the College of Veterinary Medicine, MOUAU were used for this study. The animals were housed in aluminium cages under Specific Pathogen Free (SPF) conditions and were given standard feed and water *ad libitum*. Before the experiments were carried out, the animals were starved for 24 hours. All protocols were carried out in compliance National Institute Health guidelines for the Care and Use of Laboratory Animals (Pub. No. 85-23, Revised 1985) as reported by Akah *et al*. The study was conducted at the Physiology Laboratory of the Department of Physiology, Pharmacology and Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike.

***In vivo* effect of the extracts on charcoal meal transit in rats:** Forty male rats were divided into 8 groups having 5 rats in each group. This study was carried out in accordance with the method of Mascolo *et al*. 1994 and Rahman *et al* 2012. The distance travelled by the charcoal meal was measured and expressed as a percentage. Each animal was dissected and the full length of the small intestine was measured. The distance travelled by the charcoal meal was also measured and expressed as a percentage of the length of the intestine using the equation 1 shown below

$$Distance\ traveled\ by\ cjarcoal\ meal\ (\%) = \frac{Distance\ moved\ by\ charcoal}{Full\ length\ of\ intestine} \times \frac{100}{1} \qquad (1)$$

However, the percentage inhibition for the in vitro study was calculated according to equation 2.

$$Inhibition\ (\%) = \frac{A-B}{B} \times \frac{100}{1} \qquad (2)$$

where Ais the distance moved by charcoal in the control while B is the distance moved ny the charcoal in the tst.

Castor Oil-Induced Diarrhea Test

This test was performed according to standard methods by Awouters *et al.*, 1978 and Uddin, 2005. The nature of faecal matter (put into three categories solid, semi-solid, liquid), and frequency of defecations were measured throughout 6 hrs. Rats in the first group were administered distilled water (10ml/kg), group two received the standard drug Loperamide hydrochloride (0.5mg/kg) while groups three, four and five received 250mg/kg, 500mg/kg and 1000mg/kg of extract respectively. Castor oil (1 ml) was used to induce diarrhoea in all experimental groups one hour after administration. Rats were placed in individual cages lined with absorbent paper. Percentage inhibition of diarrhoea was calculated.

Castor Oil-Induced Gastrointestinal Fluid Accumulation Model

The activity of *the extract* on the inhibition of the accumulation of intraluminal fluid was ascertained by measuring the volume and weight of fluid accumulated in the small intestine over some time (Ezeja et al., 2012). Rats were placed into five groups of five and pretreated as described above. One hour after pretreatment, rats were administered 1ml of castor oil and were sacrificed after another hour by cervical dislocation. The small intestine from the pylorus to the caecum was harvested and the contents of each small intestine were emptied in a graduated measuring cylinder and weighed. The volume and weight were recorded and the percentage inhibition of secretion was calculated.

4.0 Results and Discussion

Table 1 presents the results of an acute toxicity assay (Phase 1 LD50) arising from the evaluation of the effects of Hunteria umbellata mesocarp extract on different groups of animals. The LD50 (lethal dose for 50% of the tested population) is a standard measure used to assess the acute toxicity of a substance. In this assay, three groups of animals were administered different doses of the extract: 10 mg/kg (Group 1), 100 mg/kg (Group 2), and 1000 mg/kg (Group 3). Each group consisted of three animals. The results indicate that none of the animals in any group died following the administration of the extract at any of the tested doses. Also observed for all the groups were (i) animals were active and physically stable (ii) Signs of toxicity such as agitations, roughness of hairs, depression, writhing reflexes, and death were absent.

These observations suggest that the Hunteria umbellata mesocarp extract did not induce acute **Safety Profile**: The absence of mortality and observable signs of toxicity in all groups indicates a favourable safety profile of the Hunteria umbellata mesocarp extract at the tested doses. The significance of the results can be summarised as follows,

(i) Dose-Response Relationship: The lack of mortality across all doses suggests that the extract may have a wide safety margin, at least in the short term. This could indicate a low acute toxicity potential.

(ii) Further Testing: While the results are promising for acute toxicity, further studies are needed to assess the potential chronic toxicity, mutagenicity, and long-term effects of the extract. Additionally, different routes of administration and longer exposure durations may be explored.

(iii) Therapeutic Potential: The absence of adverse effects at the tested doses is encouraging for the potential therapeutic use of the extract. However, efficacy studies would be necessary to determine its effectiveness in treating specific conditions.

(iv) Regulatory Considerations: These results could inform regulatory decisions regarding the safety and potential use of Hunteria umbellata mesocarp extract as a pharmaceutical or herbal supplement. Further studies may be required to support its registration and commercialization.

The results of Phase 1 LD50 further suggest that the Hunteria umbellata mesocarp extract has low acute toxicity and holds promise for further investigation as a potential therapeutic agent.

Table 1: Phase 1 LD_{50} results (Acute toxicity assay) evaluation of *Hunteria umbellata* mesocarp extract

Group	Dose (mg/kg)	No. of death	Observation
1	10	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	100	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	1000	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

Table 2: Phase 2 LD_{50} results (Acute toxicity assay) evaluation of *Hunteria umbellata* mesocarp extract

Group	Dose (mg/kg)	No. of death	Observation
1	1600	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	2900	0/3	Animals were calm and physically inactive for about 25 minutes but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	5000_{50}	0/3	Animals were calm and physically inactive for about 2 hours, but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

LD_{50} > 5000 mg/kg body weight

Table 2 shows the phase 2 result of the acute toxicity assay. In group 1 (Dose: 1600 mg/kg), none of the animals in this group died following administration of the extract. The observed effects include animals being active and physically stable. Signs of toxicity, such as agitations, roughness of hairs, depression, writhing reflexes, and death, were absent. Also, for Group 2 (Dose: 2900 mg/kg) none of the animals in this group died either. However, they were calm and physically inactive for about 25 minutes post-administration, after which they regained physical activity. Similar to Group 1, signs of toxicity were absent. Similar observation was recorded for Group 3 (Dose: 5000 mg/kg) because none of the animals in this group died as well. However, they were calm and physically inactive for about 2 hours post-administration, after which

they regained physical activity. Again, signs of toxicity were absent. Also, the LD50 (lethal dose for 50% of the tested population) is greater than 5000 mg/kg body weight. Based on the above results, the following inference were drawn,

(i) Safety Profile: The results indicate a favorable safety profile of the Hunteria umbellata mesocarp extract. Even at relatively high doses, there were no observed deaths or significant signs of toxicity in any of the groups.

(ii) Dose-Response Relationship: The absence of mortality in all groups suggests that the extract may have a wide safety margin, at least in the short term. However, Groups 2 and 3 showed temporary sedative effects, indicating a possible dose-dependent response in terms of behavioral effects.

(iii) LD50 Value: The LD50 value being greater than 5000 mg/kg suggests that the extract is relatively safe, as it implies that a very high dose would be required to cause mortality in 50% of the tested population.

(iv) Further Testing: While the acute toxicity results are promising, further studies are needed to assess the potential chronic toxicity, mutagenicity, and long-term effects of the extract. Additionally, detailed studies on the mechanism of action and potential side effects should be conducted.

(v) Therapeutic Potential: These results support the potential therapeutic use of the extract, given its apparent safety at the tested doses. However, efficacy studies are needed to determine its effectiveness in treating specific conditions.

The Phase 2 LD50 results suggest that the Hunteria umbellata mesocarp extract has low acute toxicity and holds promise for further investigation as a potential therapeutic agent.

Table 3 presents results for antidiarrhea activity (Charcoal meal transit model). Based on the presented results, the control group had a percentage distance moved of 68.83%, indicating normal transit of charcoal meal. Loperamide and the extract groups show varying degrees of inhibition of charcoal meal transit compared to the control, with higher doses exhibiting greater inhibition while the extract at 1000 mg/kg showed the highest inhibitory activity, with a percentage inhibition of 49.89%.. However, the results in Table 4 showing antidiarrhea activity (Castor oil-induced model) indicated that the control group had a latent period of 31.33 mins, with a significant weight of wet stool (6.13 g). Loperamide and the extract groups increased the latent period and reduced the weight of wet stool compared to the control, indicating antidiarrheal effects while the extract at 1000 mg/kg showed the highest inhibition of diarrhea (86.81%). Table 5 also presents findings for the antidiarrhea activity (Castor oil-induced gastrointestinal fluid accumulation model), which clearly show that the control group had a significant weight of filled intestine and intestine content compared to the loperamide and extract groups. The Loperamide and the extract groups reduced the weight of filled intestine and intestine content compared to the control, indicating antidiarrheal effects and the extract at 500 mg/kg exhibited the highest antidiarrheal activity, with 56.28% inhibition.

A consideration of the results provided indicates that the acute toxicity assays (Phase 1 and Phase 2 LD50) indicated that the *Hunteria umbellata* mesocarp extract had low acute toxicity, with no observed deaths and minimal signs of toxicity even at high doses. In contrast, the antidiarrheal activity assays demonstrated dose-dependent inhibition of diarrhoea in different models, with significant effects observed at moderate to high doses of the extract.

Table 3: Antidiarrhea activity (charcoal meal transit model)

Treatment groups	Length of intestine (cm)	Distance travelled by charcoal meal (cm)	Percentage distance Moved	Percentage inhibitory activity
	93.00±3.00^{a}	64.00±3.00^{c}	68.83±2.88^{c}	0.00±0.00^{a}
Loperamide 0.5 mg/kg	91.67±3.79^{a}	38.33±2.08^{a,b}	41.92±3.84^{b}	38.58±1.36^{b}
Extract 250 mg/kg	93.00±3.61^{a}	42.00±2.00^{b}	45.17±1.60^{b}	37.07±1.61^{b}
Extract 500 mg/kg	92.33±3.06^{a}	43.00±5.29^{b}	46.49±4.40^{b}	35.72±6.70^{b}
Extract 1000 mg/kg	93.00±2.00^{a}	33.33±1.53^{a}	35.84±1.27^{a}	49.89±1.56^{c}

Values are presented as mean ± standard deviation (n = 3). Means on the same column with different letter superscripts are significantly different (P < 0.05).

Table 4: Antidiarrhea activity (castor oil induced model)

Treatment groups	Latent period (mins)	No wet stool	Weight of wet stool (g)	% Inhibition of diarrhoea
Control	31.33±5.51^{a}	8.33±0.58^{b}	6.13±0.34^{c}	0.00±0.00a
Loperamide 0.5 mg/kg	61.33±3.51^{b}	1.33±0.58^{a}	1.23±0.47^{a,b}	53.89±4.24^{b}
Extract 250 mg/kg	58.67±3.51^{b}	1.67±0.58^{a}	1.36±0.39^{b}	42.64±8.62^{b}
Extract 500 mg/kg	69.00±3.00^{c}	1.33±0.58^{a}	0.94±0.39^{a,b}	74.01±9.57^{c}
Extract 1000 mg/kg	76.33±2.52^{d}	0.67±0.58^{a}	0.52±0.46^{a}	86.81±11.54^{c}

****Values are presented as mean ± standard deviation (n = 3). Means on the same column with different letter superscripts are significantly different (P < 0.05)**

Table 5: Antidiarrhea activity (Castor oil induced gastrointestinal fluid accumulation model)

Treatment groups	Weight of filled intestine (cm)	Weight of empty intestine (g)	Weight of intestine content (g)	% Antidiarrheal activity
Control	14.91±1.04^{c}	4.93±0.16^{a}	9.99±1.12^{c}	0.00±0.00^{a}
Loperamide 0.5 mg/kg	10.76±0.24^{b}	4.84±0.11^{a}	5.93±0.35^{b}	40.40±3.56^{b,c}
Extract 250 mg/kg	10.78±0.66^{b}	4.86±0.13^{a}	5.91±0.54^{b}	39.57±5.73^{b}
Extract 500 mg/kg	9.23±0.29^{a}	4.88±0.10^{a}	4.35±0.25^{a}	56.28±2.85^{d}
Extract 1000 mg/kg	9.21±0.22^{a}	4.87±0.27^{a}	4.34±0.28^{a}	46.89±4.05^{c}

****Values are presented as mean ± standard deviation (n = 3). Means on the same column with different letter superscripts are significantly different (P < 0.05).**

Also, the antidiarrheal activity of the Hunteria umbellata mesocarp extract suggests its potential therapeutic utility in treating diarrhoea. The extract showed promising results in inhibiting diarrhoea across different models, indicating its effectiveness in multiple mechanisms associated with diarrhoea. These findings support further investigation into the extract's safety and efficacy for developing antidiarrheal treatments. However, the extract

demonstrated antidiarrheal effects, it showed minimal acute toxicity in the tested doses, suggesting a favourable safety profile for potential therapeutic use. The results collectively suggest that the extract of Hunteria umbellata mesocarp has the potential to be developed as a safe and effective antidiarrheal agent, warranting further preclinical and clinical studies to validate its efficacy and safety.

4.0 Conclusion

The study assessed *Hunteria umbellata* mesocarp extract for acute toxicity and antidiarrheal activity. LD50 values exceeded 5000 mg/kg body weight, indicating a wide safety margin. Significant inhibition of diarrhea was observed at moderate to high doses, suggesting the extract's efficacy. No mortality or significant toxicity was observed even at high doses. Further research, including long-term toxicity studies and mechanistic investigations, is recommended to validate its safety and efficacy. Standardization of extraction methods and quality control measures are also advised to ensure consistency. Overall, *Hunteria umbellata* mesocarp extract shows promise as a safe and effective antidiarrheal treatment option.

In conclusion, the study demonstrates the promising safety profile and antidiarrheal activity of *Hunteria umbellata* mesocarp extract. Acute toxicity assays revealed a wide safety margin, with LD50 values exceeding 5000 mg/kg body weight. Subsequent antidiarrheal activity assessments showed significant inhibition of diarrhea across different models, with notable efficacy observed at moderate to high doses of the extract. These findings underscore the potential therapeutic utility of *Hunteria umbellata* mesocarp extract in managing diarrhea.

Based on the results, it is recommended that further preclinical and clinical studies be conducted to validate the extract's efficacy and safety for human use. Long-term toxicity studies, mechanistic investigations, and dose optimization trials are warranted to elucidate the extract's pharmacological properties and determine the optimal therapeutic dosage. Additionally, efforts should be made to standardize the extraction process and quality control measures to ensure consistency and reproducibility of the extract's effects. Overall, *Hunteria umbellata* mesocarp extract holds promise as a safe and effective alternative for the treatment of diarrhea, warranting continued exploration for its therapeutic potential.

5.0 References

Akter S, Sarker A & Hossain S. (2013). Antidiarrhoeal activity of rind of *Punica granatum, Int Curr Pharm J.;* 2, 5, pp**.** 101–104.

Awouters F, Niemegeers C.J.E, Lenaerts F.M & Janssen P.A.J. (1978). Delay of castor oil diarrhoea in rats: a new way to evaluate inhibitors of prostaglandin biosynthesis. *J Pharm. Pharmacol*, 30, pp. 41-45.

Bern M.J, Sturbaum C.W, Karayalcin S.S, Berschneider H.M, Wachsman J.T & Powell D. (1989). Immune system control of rat and rabbit colonic electrolyte transport. Role of prostaglandins and enteric nervous system. *J Clin Invest;*83, 6, pp. pp. 1810-1829.

Chen J, Wan C.M,Gong S.T, Fang F , Sun M, Qian Y , Huang Y, Wang B.X, Xu C.D, Ye L.Y, Dong M, Jin Y , Huang Z.H, Wu Q.B, Zhu C.M, Fang Y.H, Zhu Q.R &Dong Y.S. (2018). Chinese clinical practice guidelines for acute infectious diarrhea in children. *World J Pediatr*. 14, 5, pp. 429-436.

Davidson-Hunt I. (2000). Ecological ethno botany: stumbling toward new practices and paradigms. *Model Assisted Statistics and Applications Journal*, 16, pp. 1–13

Di Carlo G, Autore G, Izzo A.A, Maiolino P, N, Mascolo P & Viola (1993).

Inhibition of intestinal motility and secretion by flavonoids in mice and rats: Structure activity relationships. *J Pharm* Pharmaco, 45, 12, pp. 1054–1059

Emudainohwo J, Erhirhie E & Moke E. (2015). Anti-diarrheal activity of the aqueous leaf extract of Ageratum conyzoides in wistar rats. *J Appl Sci Environ Manag, 19, 2, pp.* 169–75.

Ezeja M.I, Ezeigbo I.I, Madubuike K.G, Udeh N.E, Ukweni I.A, Akomas S.C, & Ifenkwe D.C. (2012). Antidiarrheal activityof *pterocarpus erinaceus* methanol leaf extract in experimentally-induced diarrhea. *Asian Pacific J Trop Med* 5, 2, pp. 147-50.

Falodun A, Nworgu Z & Ikponmwonsa M. O. (2006). Phytochemical components of *H. umbellate* (K. Schum) and its effect on isolated non-pregnant rat uterus in oestrus. *Pak J Pharm Sci*, 19, 3, pp. 256–258.

Galvez J, Crespo M.E, Jimenez J, Suarez A & Zarzuelo A. (1993). Anti-diarrhoeic activity of quercitrin in mice and rats. *J Pharm Pharmacol.* 45, 2, pp. 157–159

Gills L.S. (1992). *Ethnomedicinal uses of plants in Nigeria. Benin City*: Uniben Press; p. 134.

Horton E.W, Main I.H, Thompson C.J & Wright P.M. (1968). Effect of orally administered prostaglandin E1 on gastric secretion and gastrointestinal motility in man. *Gut.*, 9, 6, pp. 655–658.

Komal, Kumar S & Rana A.C. (2013). Herbal approaches for diarrhea: a review. *Int Res J Pharm* 4, 1, pp. 31–38.

Lorke D. (1983). A new approach to tropical acute toxicity testing. Arch. Toxicol., 54, pp. 275-287.

Meite S , N'guessan J, Bahi C, Yapi H, Djaman A & Guina F.G. (2009). Antidiarrheal activity of the ethyl acetate extract of *Morinda morindoides* in rats. *Tropical Journal of Pharmaceutical Research*. 8, 3, pp. 201–7.

Mascolo N, Izzo A.A, Autore G, Barbato F & Capasso F. (1994). Nitric oxide and castor oil-induced diarrhea. *J. Pharmacol. Exp. Ther*., 263, pp. 291-295.

Null C , Stewart C.P, Pickering A.J, Dentz H.N, Arnold B.F, Arnold C.D, Benjamin-Chung J, Clasen T, DeweyK.G, Fernald L.C.H, Hubbard A.E, Kariger P, Lin A, Luby S.P, Mertens A, Njenga S.M, Nyambane G, Ram P.K & Colford J.M. (2018). Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. *Lancet Glob Health*. 6, 3, pp. 316-329.

Oliver-Bever B. (1986). *Medicinal plants in tropical West Africa*. Cambridge: Cambridge University Press; p. 60–2.

Rahman A, Hasan S.N, Sampad K.S & Das A.K. (2011). Antinociceptive, anti diarrheoal and cytotoxic activities of *Rhizophora mucronata* Lamk. *Pharmacologyonline* , 1, pp. 921-929.

Rahman M.M, Islam A.M.T, Chowdhury M.A.U, Uddin M.E & Jamil A. (2012). Antidiarrheal activity of leaves extract of *Microcos paniculata* Linn in mice. *Int. J. Pharm*., 2, pp. 21-25.

Robert A, Nezamis J.E, Lancaster C, Hanchar A.J & Klepper M.S (1976). Enteropooling assay: a test for diarrhea produced by prostaglandins. *Prostaglandins,* 11, 5, pp. 809–828

Sofowora A. (1993). *Medicinal plants and traditional medicine in Africa*. 2nd ed. Netherlands: Spectrum Books Limited, Ibadan; p. 150.

Uddin S.J. (2005). Antidiarrhoeal activity of the methanol extract of the barks of *Xylocarpus moluccensis* in castor oil- and magnesium sulphate-induced diarrhoea models in mice. *J Ethnopharmacol* 101, pp. 139–143.

Wenzl H.H. (2012). Diarrhea in chronic inflammatory bowel diseases. *Gastroenterol Clin North Am*. 41, 3, pp. 651-75.

Compliance with Ethical Standards Declarations

The authors declare that they have no conflict of interest.

Data availability

All data used in this study will be readily available to the public.

Consent for publication

Not Applicable

Availability of data and materials

The publisher has the right to make the data public.

Competing interests

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Authors' contributions

Akoh and Nwigwe were involved in the research and laboratory work while all of the authors were involved in writing.