International Journal of Advanced Research and Publications
ISSN: 2456-9992

Laxative Potential Of Aqueous Extract Of The Aerial Parts Of Euphorbia Heterophylla In Loperamide-Induced Constipated Wistar Albino Rats

Wellington, E.O, Peters, D.E, Onyeike, E.N

Department of Biochemistry, Faculty of Science,
University of Port-Harcourt.

Initial: Wellington, E.O Department of Biochemistry, Faculty of Science,
University of Port-Harcourt Choba, Rivers State, Nigeria. +234(0)9074578612
ewellington41@yahoo.com

Abstract: Background and Objectives: Euphorbia heterophylla is a medicinal plant that is known to elicit several medicinal properties such anti-malaria, anti-anaemic, treatment of asthma and many other health problems. This study investigated the laxative potential of aqueous extract of the aerial parts of E heterophylla in constipated wistar rats. Materials and Methods: Constipation was induced by oral administration of 1ml of 3mg/kg body weight of loperamide for three days and the passage of dry and reduced number of faecal pellet was indicative of the episode of constipation in the rats. Results: The faecal properties such as number of faecal pellet, faecal, faecal water content and gastrointestinal motility were determine following the "Cho'' method of determination faecal properties in condition of constipation. Plasma electrolytes (Na^+, K^+, Cl^-, Ca^{2+} and Mg^+) and urea concentrations were determined using colorimetric method. Significant increases ($p \leq 0.05$) were observed in the number of faecal pellet (171.29± 30.13), weight of faecal pellet (38.69± 2.92g) and faecal water content (2.01±0.12ml) in 1500mg/kg b.w treated group when compared to their respective control values. Gastrointestinal motility significantly increased ($p \leq 0.05$) for 1500mgkg b.w treated group (94.23%) in comparison to the constipated control (73.45%). Significant increase ($p \leq 0.05$) in concentrations of plasma sodium (Na^+), potassium (K^+), chloride (Cl^-), magnesium (Mg^{2+}), calcium (Ca^{2+}) and urea (147.20 ± 1.48, 4.35± 0.09, 133.20 ± 2.05, 2.19 ± 0.01, 2.71 ± 0.01, and 9.25 ± 0.03 respectively) were observed for 1500mg/kg b.w treatment in comparison to the control values. Conclusion: The significant increases in the number of faecal pellet, weight of faecal pellet, faecal water content, gastrointestinal motility and the plasma electrolyte concentrations is indicative that aqueous extract of the aerial parts of Euphorbia heterophylla elicited laxative potential against constipation induction.

Keywords: Euphorbia heterophylla, loperamide, constipation, laxatives, faecal properties, electrolytes, wistar rats, gastrointestinal motility, intestinal fluid, biochemical assays

1.2 Introduction

Constipation is a common gastrointestinal health problem with a tendency to cause discomfort and affect patient quality of life [1]. Constipation is a highly prevalent functional gastrointestinal disorder affects 3–15 % of the general population [1]. Constipation also cause abdominal pain, vomiting, restlessness, gut obstruction and perforation, and may even be associated with aspiration or fatal pulmonary embolism [2]. Presently, constipation disproportionately affects older adults, with prevalences of 50% among the community-dwelling elderly and 74% in nursing-home residents [3]. Loperamide-induced delay in colonic transit is accepted as spastic constipation due to the inhibition of stool frequency and increased colonic contractions and peristalsis in humans [4]. The drug inhibits intestinal water secretion and electrolytes [5] and colonic peristalsis [6], which extends to delay in the fecal evacuation time and decreased intestinal luminal transit [4]. Thus, loperamide-induced constipation is considered to be a model of spastic constipation [2]. Euphorbia heterophylla is commonly known as desert milk weed and it grows up 2.5-6 cm [7]. Alternative names of this weed include Euphorbia geniculate, Euphorbia pronifolia, Poinsettia geniculata and Poinsettia heterophylla [7]. Euphorbia heterophylla has been shown to elicit purgative and diuretic effect and is used in traditional medicine for the treatment of constipation [8]. E. heterophylla is reported to possess and elicit diuretic and purgative effects and to it is use in the treatment of proximal bronchial relaxation [9]. Extract of E. heterophylla is used to treat ear pain, induce milk flow and improve sperm quality and quantity [8]. The plant is used by traditional healers for the treatment of bacterial, plasmodial, gonorrheal and inflammatory diseases [9]. In the present study, number of faecal pellet, weigh of faecal pellet, faecal water content, gastrointestinal transit ratio plasma electrolytes were observed in rats with loperamide-induced constipation in order to analyze the laxative effects of Euphorbia heterophylla.

2.1 Material and methods

2.1.1 Drugs and Chemicals

Loperamide-hydrochloride was purchased from Riverland Chemists LTD Hospital Road, Port Harcourt (Manufactured by Janssen-Cilag 2013, marketing company). Senokote was purchased from Alpha Pharmacy LTD Ikotun, Lagos State (Manufactured by Reckitt Benkiser Healthcare UK.

2.1.2 Quantitative phytochemical screening using high performance liquid chromatography

The leaves of Euphorbia heterophylla subjected to phytochemical screening which was carried out at Multi Environmental Management Consultants Limited. Memac building, Olujunwo Avenue, Laara-igbe, Ikorodu, Lagos.

2.1.3 Plant extraction

The fresh aerial parts of E. heterophylla were harvested, washed with clean water and air-dried under shade for five weeks . The dried aerial parts were pulverized into coarse powder. Two hundred and fifty grams (250 g) of the powdered sample was macerated in 500ml of distilled water at room temperature for 72 hours. The mixture was filtered using a Whatzman filter paper grade 1 (542 mm) and the filtrate condensed and evaporated to dryness using a rotary evaporator and water bath at 50˚C. The extract which weighed 85g was stored in air-tight containers in a refrigerator until when required for analysis.

2.1.4 Experimental Animals

Animal studies were carried out following the Korean Food and Drug Administration Guidelines for Good Laboratory Practice (notification no: 2000-116, 2009). A total number of thirty (30) wistar albino rats were used for this studies (four months old) weighing between 140-170g were used for this experiment after acclimatization for a period of fourteen days. The experimental rats were housed, with five rats per polycarbonated cage, at a temperature of 24^0C and humidity- (45-50%) controlled room and were given free access to rat feed and water in the University of Port Harcourt Animal House, Choba. Constipation was induced in the wistar albino rats after oral administration of 3 mg/kg loperamide hydrochloride (Sigma-Aldrich, St. Louis, MO, USA) daily for six days at 1 h prior to test extract, as described previously (Bustos et al.,[10] while the control rats were administered saline. Aqueous extract of the aerial parts of Euphorbia heterophylla (500, 1000 and 1500mgkg) were dissolved in 10ml of distilled water and administered orally one hour after oral administration of loperamide, daily four three days. Senokot (15mg/kg weight) was dissolved in distilled water and were orally administered as reference drug (Méité et al., [11]. In the vehicle and constipation groups, the control rats were given access to distilled water only. The wistar albino rats were selected based on body weight and were separated into six groups (five rats/group) at the first day before administration of the extract. The rats were arranged in order of weight and the heavier rats were randomly assigned to each of the six groups. This order of arrangement was carried out until the thirty rats were assigned to each of six groups. The vehicle (normal) control group received distilled water, the constipation control group received loperamide treatment and distilled water administration. The Senokot group received loperamide treatment and Senokot administration. Three graded dose of the extract at 500, 1000 and 1500mg/kg to three groups of the rats, serving as the tested groups. This was approved by the Ethics Committee of University of Port Harcourt, Choba, Nigeria.

2.1.5 Fecal parameter measurements

The faecal pellet of the individual rate were collected over 24 hours on day 6 of oral administration. The total number of faecal pellet, wet weight of faecal matter and faecal water content were determined following the Pazhani et al., [27]. The faecal water content was calculated using the formula: Faecal water content (%)=[(faecal wet weight-faecal dry weight) faecal wet weight) x 100

2.1.6 Measurement of intestinal charcoal transit ratio

Evaluation of the gastrointestinal motility of a charcoal meal was determined according to the method proposed by Sagar et al., [12] with minor modifications. The rats were fasted for 22 h prior to the experiment, but were given access to feed. At 15 min after the last drug (extract/Senokot/distilled water) administration, the animals were fed 1 ml charcoal meal (3% suspension of activated charcoal in 0.5% aqueous methylcellulose; Sigma-Aldrich). At 30 min after the charcoal meal administration, the animals were sacrificed by cervical dislocation and the total intestine length (pyloric sphincter to cecum) and charcoal meal transit distance were measured. The intestinal charcoal transit ratio was calculated as follows: Charcoal transit ratio (%) = [(total small intestine length - transited distance covered by charcoal meal)/total small intestine length] × 100.

1.2.7 Biochemical Assays

Urea, creatinine, sodium ion (Na^+), potassium ion (K^+), chloride ion (Cl^-), total protein, albumin, total bilirubin, alkaline phosphatase (ALP), alanine amino transfeerase (ALT), aspartate transaminase (AST) and gamma glutamyl transferase (GGT), total cholesterol, triglyceride, HDL, LDL were measured by using Randox kits.

1.2.8 Statistical analysis

All Data are represented as means ± standard deviation (M±S) were analyzed using Statistical Package foe Social Sciences (SPSS) for window version 16 USA. Descriptive statistics was done by one way analysis of variance (ANOVA) and multiple comparison was done using Turkey Post hoc at ($p \leq 0.05$) confidence interval.

3.1 Results

3.2 Phytochemical screening and quantification of the aerial parts Euphorbia heterophylla

Qualitative and quantitative phytochemical screening of the aerial parts of E. heterophylla showed the presence alkaloid (719.18 mg/100g), flavonoid (376.20 mg/100g, saponin (139.80 mg/100g), sterol (33.16 mg/100g), glycoside (80.60 mg/100g), phenolic acid (25.32 mg/100g), of isoflavan (19.22 mg/100g), anthrocyanin (8.68 mg/100g), terpenoid (1.92 mg/100g), lignans (1.72^{-1} mg/100g) and anthraquinone (1.13 mg/100g). Alkaloids, tannins, phlabotannins, saponins, and Anthraquinones extracted from Vernonia amygdalina were reported to act on the muscarinic receptors (M3) and cause purgative effects [13].

3.3 Effect of the Extract on faecal water content, number of faecal pellet and weight faecal pellet

The mean ± standard deviation of the total number of faecal pellet of the untreated constipated rats were significantly decreased at $p \leq 0.05$ when compared to the normal control values. The mean ± standard deviation of the total number of faecal pellet of the treated groups were also significantly increased at $p \leq 0.05$ when compared to the untreated constipated and normal control values which also competed with group 6 treated with the reference drug as shown in Table 1. The mean ± standard deviation of the weight of faecal pellet of the untreated constipated

rats were significantly decreased at $p \leq 0.05$ when compared to the normal control values. The mean ± standard deviation of number of faecal pellet of the treated groups (at 500, 1000 and 1500 mg/kg.b.wt) were also significantly increased at $p \leq 0.05$ when compared to the untreated constipated and normal control values which also competed with group 6 treated with the reference drug as shown in Table 1. The mean ± standard deviation of faecal water content of the untreated constipated rats were significantly decreased at $p \leq 0.05$ when compared to the normal control values. The mean ± standard deviation of the faecal water content of the treated groups (at 500, 1000 and 1500mg/kg b.wt) were also significantly increased at $p \leq 0.05$ when compared with the untreated constipated and normal control values which also competed with group 6 treated with the reference drug as shown in Table 1.

Table 1 *Effect of aqueous extract of the aerial parts of Euphorbia heterophylla on faecal properties of loperamide-induced constipated wistar rats*

Groups	Faecal Water Content (ml)	Number of Faecal Pellet	Weight of Faecal Pellet (g)
N/ control	2.35 ± 0.52^{a}	177.00± 6.09	33.97±4.67^{a}
C/ control	1.88 ± 011^{b}	148.71± 14.61^{b}	29.74 ± 2.92^{b}
E.H 500mg/kg + Lop.	2.01 ± 0.13^{bc}	189.14± 9.33^{abc}	37.63± 3.27^{abc}
E.H 1000mg/kg + Lop.	1.94 ± 0.13^{bc}	169.14± 30.09^{abc}	38.34± 3.10^{abc}
E.H1500mg/kg + Lop.	2.01 ± 0.12^{bc}	171.29± 30.13^{abc}	38.69± 2.92^{abc}
SN 15mg/kg + Lop.	2.35 ± 0.15^{bc}	174.71± 32.13^{abc}	39.79± 2'.40^{abc}

Data are reported as mean ± standard Deviation (M ± SD), n =5 .Values bearing similar Superscript"$^{(a,bc)}$" down the column indicates a statistical significant difference ($p \leq 0.05$) when compared to the control groups. superscript "^{bc}" is not significantly different from normal but different from the constipated control

3.4 Effect on the total intestinal length and gastrointestinal motility

The mean and standard deviation of the total intestinal length and gastrointestinal motility of the normal control (group 1) was 95.30± 2.02cm and 87.43% respectively. Oral administration of 1ml of 3mg/kg b.wt of loperamide for three days resulted in a significantly decreased at $p \leq 0.05$ the mean values of the total intestinal length and gastrointestinal motility of 77.86± 6.81 cm total intestinal length and 73.45 % gastrointestinal motility (GIT) in comparison to the normal control values as shown in Table 2. Treatment with the extract at 500, 1000 and 1500 mg/kg b.wt caused a significantly increased at ($p \leq 0.05$) mean values of the total intestinal length and gastrointestinal motility of groups 3-5 rats when compared to the control values as shown in Table 2.

Table 2 *Effect of aqueous extract of the aerial parts of Euphorbia heterophylla on total intestinal length and gastrointestinal motility in loperamide-induced constipated rats*

Group	Total intestinal length (cm)	Distance covered by charcoal meal (cm)	(%) GIT
Normal control	114.12±1.23	95.30± 2.02^{a}	87.43^{a}
Constipated control	112.56±1.08	77.86± 6.81^{b}	73.45^{b}
E.H 500mg/kg + Lop	114.02±1.11	93.72± 3.15^{bc}	84.43^{bc}
E.H 1000mg/kg + Lop	114.22±1.00	101.60± 4.51^{bc}	92.77^{bc}
E.H1500mg/kg + Lop.	114.78±1.09	111.00± 1.22^{abc}	94.23^{abc}
SN 15mg/kg + Lop.	114.41±1.02	113.80± 1.09^{abc}	97.93^{abc}

E.H: Euphorbia heterophylla, SN: Senokot, GIT: gastrointestinal tract, Lop: loperamide. Data are reported as mean ± standard Deviation (M ± SD), n =5 .Values bearing similar Superscript"$^{(a,bc)}$" down the column indicates a statistical significant difference ($p \leq 0.05$) when compared to the control groups. superscript "^{bc}" is not significantly different from normal but different from the constipated control. The significant increased observed on the number of faecal pellet, weight of faecal pellet and on the gastrointestinal motility (GIT) is reflective of the laxative potential of aqueous extract of the aerial parts of Euphorbia heterophylla at 500, 1000 and 1500 mg/kg b.wt in loperamide-induced constipated rats. These effects are in line with the report of Sabiu et al., [14] on the toxicological implication and laxative potential of ethanol leaf extract of Morella sereta in loperamide-induced wistar rats.

3.5 Effect on plasma electrolyte concentrations

The mean values of plasma electrolytes (Na^{+}, K^{+}, Cl^{-}, Mg^{2+}) and urea of the normal control (group 2) following oral administration of 1ml of 3 mg/kg b.wt of loperamide for three days were significantly decreased at $p \leq 0.05$ in comparison the normal control values as shown in Table 3. Oral administration of 500, 1000 and 1500 mg/kg b.wt of aqueous extract of aerial parts of Euphorbia heterophylla significantly increased the plasma electrolytes of the loperamide-induced constipated rats when compared to the normal and constipated control values which also competed with those treated with the reference drug as presented in Table 3. The significant decrease in the plasma urea and electrolyte concentrations observed in untreated constipated rats (i.e group 2) is suggestive that induction of constipation following oral administration of 1ml of 3mg/kg b.w of loperamide caused a decrease in the metabolism of urea and secretion and release of intestinal fluid and electrolytes as shown in Table 3. Consequently, the concentration-dependent restoration to normal of the plasma electrolyte and urea concentrations following treatment with the extract particularly at 1000 and 1500mg/kg body weigh in the

constipated rats when compared to the normal and constipated controls is indicative of the ability of the extract in the enhancement of urea metabolism and the release of intestinal fluid and electrolyte. This result agrees with the report of Ashafa et al., [15] on the laxative potential of ethanolic leaf extract of Aloe vera (L.) in Wistar rats with loperamide-induced constipation.

Table 3 *Effect of aqueous extract of the aerial parts of E. heterophylla on kidney biomarkers of loperamide-induced constipated albino wistar rats*

Group	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/l)	Mg^{2+} (mmol/l)	Urea (mmol/l)
N/control	143.20±2.77^{a}	4.26± 0.02^{a}	98.60 ± 2.19^{a}	0.72±0^{a}	6.66 ± 0.04^{a}
C/ control	135.40 ±1.67^{b}	1.62 ± 0.06^{b}	50.75 ± 0.07^{b}	0.08±0^{b}	3.45 ± 0.03^{b}
E.H500mg/kg +L	135.40 ±1.67^{d}	3.90 ±0.04^{abc}	106.40±3.05^{abc}	1.30±0.02^{abc}	8.40 ±0.36^{abc}
E.H1000mg/kg+L	145.40±1.67^{abc}	4.25 ± 0.02^{d}	124.20±5.72^{abc}	1.89±0.05^{abc}	8.77 ±0.17^{abc}
E.H1500mg/kg+L	147.20±1.48^{abc}	4.35 ±0.09^{abc}	133.20±2.05^{abc}	2.19 ± 0.01^{abc}	9.25 ±0.03^{abc}
SN 15mg/kg + L	151.20±1.48^{abc}	4.76 ±0.02^{abc}	137.80±0.84^{abc}	2.46 ± 0.02^{abc}	9.53 ±0.03^{abc}

Data are reported as mean ± standard Deviation (M ± SD), n =5. Data are reported as mean and standard Deviation (M ± SD), n =5 .Values with the Superscript "$^{(abc)}$" down the group are significantly (p≤0.05) different from normal and constipated control. Superscript "^{d}" Not significantly different from constipated control but significantly (p≤0.05) different from the normal control. Effect on the Plasma Liver Biomarkers

Table 8 showed the effect of aqueous extract of the aerial parts of E. heterophylla on the liver biomarkers of loperamide-induced toxicity in rats. The plasma concentrations of total bilirubin (TBIL), total protein (TP) and albumin (ALB) concentrations of the negative control were significantly different from the normal control following oral administration of 3mg/kg of loperamide hydrochloride as shown in Table 8. Treatment with 500, 1000 and 1500mg/kg significantly decreased the plasma concentrations which also competed with those treated with Senokot reference drug). The plasma gamma glutamyl transferase (GGT), aspartate transaminase (AST), alanine amino transferase (ALT) and alkaline phosphatase (ALP) activities observed in the negative control is reflective of hepatocellular toxicity facilitated by loperamide exposure. However, treatment with aqueous extract of the aerial parts of Euphorbia heterophylla significantly caused reduction on the plasma GGT, AST, ALT and ALP activities when compared to the normal and constipated control values as shown in Table 8. The significant decreased on the plasma TP, ALB and BIL concentrations and the elevated ALP, These effects are in conformity with the report of Schiller et al., (1984) on the mechanism of antidiarrheal effect of loperamide in rats. The significantly decreased plasma liver enzyme activities following oral administration of the extract is reflective of the ameliorative effect of the extract against loperamide-induced constipation. These results agrees with report of Sabiu et al., [14] on the toxicological implication of ethanol leaf extract of Morella sereta in loperamide-induced constipated rats.

Table 4 *Effect of aqueous extract of the aerial parts of E. heterophylla on liver biomarkers of loperamide-induced constipated albino wistar rats*

Group	TBIL (g/l)	TP (µmol/L)	ALB (mmol/l)	GGT (U/L)	AST (U/L)	ALT (U/L)	ALP (U/L)
Control	11.03±0.12^{a}	71.11±1.00^{a}	48.21±1.03^{a}	3.00±0.02^{a}	187.00±0.10^{a}	53.27±2.02^{a}	53.27±2.0^{a}
C/control	24.11±0.0^{abc}	54.34±1.00	20.67±2.09	10.32±1.23	210.12±1.23	89.07±0.00	71.15±1.55
E.H500mg/kg	19.21±2.05^{b}	57.45±1.34^{b}	28.31±1.56^{b}	10.01±0.02^{b}	197.87±1.09^{b}	77.00±1.01^{b}	68.22±2.07^{b}
E.H1000mg/k	16.37±1.32^{bc}	52.67±1.09^{bc}	34.67±1.45^{bc}	8.78±1.06^{bc}	194.34±1.22^{bc}	69.67±1.00^{bc}	62.78±0.00^{bc}
E.H1500mg/kg	12.89±2.21^{bc}	67.11±1.00^{bc}	38.91±2.12^{bc}	4.27±0.00	184.01±1.04^{bc}	58.01±0.23^{bc}	58.91±0.35^{bc}
SN 15mg/kg	10.02±1.05^{bc}	74.32±0.02^{bc}	45.67±2.07^{bc}	2.95±0.20^{bc}	175.00±0.8^{bc}	48.22±0.11^{bc}	45.78±0.21^{bc}

TP: total protein, ALB: albumin, TBIL: total bilirubin, ALP: alkaline phosphatase, ALT: alanine amino transferase, AST: aspartate transaminase, GGT: gamma glutamyl transferase.
Data are reported as mean ± standard Deviation (M ± SD), n =5. Values with the Superscript"$^{(bc)}$" down the group are significantly (p≤0.05) different from normal and constipated control.

Discussion of findings

Medicinal plants are rich source of novel drugs that forms the ingredients in traditional systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceuticals intermediates bioactive principles and lead compounds in synthetic drugs [16]. Euphorbia plants are widespread in nature ranging from herbs and shrubs to trees in tropical and temperate regions all over the world [17]. E. heterophylla leaf is used in traditional medical practices as laxative, anti-gonorrhoeal, migraine and heart cures [14]. Alkaloids, tannins, phlabotannins, saponins, and Anthraquinones extracted from Vernonia amygdalina were reported to act on the muscarinic receptors (M3) and cause purgative effects [13]. The alkaloid, saponin and anthraquinone present in Euphorbia heterophylla may be responsible for the laxative potential elicited in this study which agrees with the report of Cazis et al., [26] on the phytochemical screening and purgative activity of ethanolic extracts of Vernonia amygdalina Leaf in rats. Loperamide-induced

constipation is a known and well-established model of spastic constipation [19]. It inhibits intestinal water secretion and colonic peristalsis which consequently delays faecal evacuation time and intestinal luminal transit [20]. The loperamide-mediated reduction in the number of faecal pellet, weight of faecal pellet and water content in Table 1 clearly indicated episodes of constipation in the animals as shown in Table 1. The concentration-dependent reversion in the faecal properties particularly at 1000 and 1500mg/kg body weight of the extract as shown in Table 1 is reflective of the laxative potential of aqueous extract of the aerial parts of Euphorbia heterophylla amelioration of constipation. Evaluation of colonic transit time is usually adopted in gastrointestinal-related disorders including constipation. It gives quantitative information about colonic transit, enables the identification and characterization of transit abnormalities and allows assessment of the severity of the ailment as well as the response to treatment [21]. In the present study, the significantly increased intestinal motility in the extract-treated rats may probably be due to the action of the extract in enhancing release of fluid thereby increasing intestinal secretion. The improvement in the intestinal motility which facilitated corresponding increase in intestinal transit rate and colonic movement by the extract shown in Table 2 is also informative of the laxative potential of the extract and its effectiveness in the amelioration of bowel obstruction. Capasso a et al., [22] offered similar assertions while evaluating some pharmacologically potent laxative agents. Induction of constipation by oral administration of loperamide hydrochloride (3mg/kg body weight) caused a significant decrease in the serum electrolytes and urea concentrations leads to a corresponding decrease or fall in the renal glomerula filtration rate [20]. Purging or passage excessive watery stool is usually accompanied with loss of serum urea and electrolytes due to increased secretion and release of intestinal fluid and electrolytes by the nephrons [23]. In this study, the significant decrease in the plasma urea and electrolyte concentrations observed in untreated constipated rats (i.e group 2) is suggestive that induction of constipation following oral administration of 1mll of 3mg/kg b.w of loperamide caused a decrease in the secretion and release of intestinal fluid and electrolytes as shown in Table 3. Consequently, the concentration-dependent restoration to normal of the plasma electrolyte and urea concentrations shown in Table 3 following treatment with the extract particularly at 1000 and 1500mg/kg body weigh in the constipated rats when compared to the normal and constipated controls is indicative of the ability of the extract in the enhancement of the secretion and release of intestinal fluid and electrolyte. Similar report was reported by Ajani et al. [24] when evaluating the acute and sub-acute toxicity effect of ethanol leaf extract of Lagenaria brevifolia on hepatic and renal function of rats. Analysis of serum enzyme activity is an invaluable tool in clinical diagnosis. It gives information on the effect and nature of pathological damage to tissues. ALP is a marker enzyme often used to assess the integrity of plasma membrane and endoplasmic reticulum [25]. Injury to structural integrity of the liver is reflected by increase in the activity of ALP in the serum probably due to leakage from altered membrane permeability [23]. The observed increase in Table 4 in plasma activities of these enzymes observed in the untreated constipated rats in table 4 when compared with the normal control may be indicative of damage to the plasma membrane. AST and ALT are biomarkers that are used to predict physiological state of the liver and are significant in amino acid metabolism [26]. In this study, the increased plasma activities of these enzymes as observed in the untreated constipated rats in Table 4 is reflective of possible liver damage resulting from alteration in membrane permeability, which may consequently impact on the metabolism of amino acids in the liver. The alleviation in the plasma activities of all the assayed enzymes as shown in Table 4 in the rats following treatment with all doses under consideration is reflective of ameliorative effects of the extract on the liver of loperamide-induced constipated rats which could be due to the direct effects of flavonoids, terpenoids, isoflavan, glycoside which are known for their antioxidant properties associated with the aerial parts of the plant.

Conclusion

This study revealed that oral administration of aqueous extract of the aerial parts of Euphorbia heterophylla elicited laxative activity in the loperamide-induced constipation. This result is suggestive of the beneficial effects of herbs in the amelioration of bowel obstruction and improvement of gastrointestinal motility. Noteworthy is the fact that the extract at 1000 and 1500mg/kg.b.wt showed the best laxative action. These findings have lent scientific support to the use of Euphorbia heterophylla as a laxative agent in Nigerian folkloric medicine.

Acknowledgment

The authors wish to express their gratitude to the staffs of Multi environmental management and the department of Biochemistry, University of Port Harcourt Rivers state for creating an enabling environment facilities required to ensure the success of this study.

Conflict of interest

The authors declare that they do not have any conflict of interest

Significance Statement

This research provides understanding on the laxative potential of the aerial parts of Euphorbia heterophylla in wistar albino rats. Furthermore, the total phytochemical constituents of the aerial parts of the plant was quantified. Oral administration of aqueous extract of the aerial parts of Euphorbia heterophylla particularly at 1000 and 1500 mg/kg /body weight of the rats resulted in improvement on the faecal properties, gastrointestinal motility, secretion and released of intestinal fluid and electrolyte and on the plasma liver biomarkers of loperamide-induced constipation in rats. Extract of Euphorbia heterophylla elicited a non-toxic effect to the liver, kidney and intestinal tract of wistar albino rats and the findings lend scientific credence to the laxative potential of the plant against constipation induction, hence a potent herbal source of laxative agent.

References

[1] Talley, N. J., Stanghellini V., Heading, R. C., Koch, K. L., Malagelada, J. R., and G.N.

[2] JTutgat, 1999. Functional gastroduodenal disorders. Gasterology, 45:1137–1142.

[3] Drossman, D. A., Li, Z., Andruzzi, E., Temple, R. D., Talley, N. J., and W. G. Thompson, (1999). Biochemical and Biophysical Models of Constipation and Diarrhea Caused by Incorrect Dose or Uneven Intake of Edible Oils (Fats). Central Gastroenterology, 5(8):347-4723.

[4] Rout, S.P., Choudhury, K.A., Kar, D.M., Das, L., A. Jain, 2003. Plants in traditional medicinal system-future source of new drugs. Internl. J. Pharmacy Pharmaceurical. Sci, 1(1):1-23.

[5] Mostafa, S. M., Bhandari, S., Ritchie, G., Gratton, N and R. Wenstone, 2003. Constipation and its implications in the critically ill patient. Br J Anaesth, 91(6):815-9.

[6] Kakino, M., Tazawa, S., Maruyama, H., Tsuruma, K., Araki, Y., Shimazawa, M and H. Hara, 2010. Laxative effects of agarwood on low-fiber diet-induced constipation in rats. BMC Complement Alternative Medicine, 15; 10 ():68.

[7] Rao, S. S and J. T. Go, 2010. Update on the management of constipation in the elderly: new treatment options. Clin Interv Aging, 9; 5():163-71.

[8] Okeniyi, S.O, Adedoyin, B.J., and S. Garba, 2012. Phytochemical screening, cytotoxicity, antioxidant, and antimicrobial activities of stem and leave extracts of Euphorbia heterophylla. Bull Environmental Pharmacology of Life Science, 1(8): 87-91.

[9] Unekwe, P.C., Ughachukwu, P.O., and J. O. Ogamba, 2006. Some pharmacological studies of aqueous extract of leaves of Euphorbia heterophylla. Tropical Journal of Medical Research, 10(2): 1-5.

[10] Falodun, A., Agbakwuru, E. O., and G. C. Ukoh, 2003. Antibacterial activity of Euphorbia heterophylla Linn (Family-Euphorbiaceae). Pakistan Journal of Scientific and Industrial Research, 4(3):31-42.

[11] Bustos, D., Ogawa, K., Pons, S., Soriano, E., Banji, J. C., and F. L. Bustos, 1991. Effect of loperamide and bisacodyl on intestinal transit time, fecal weight and short chain fatty acid excretion in the rat. Acta Gastroenterol Latin America, 21:3–9.

[12] Méité, S., Bahi, C and D. Yéo, 2010. Laxative activities of Mareya micrantha (Benth.) Müll Arg (Euphorbiaceae) leaf aqueous extract in rats. BMC Complement Altern Med, 10:7.

[13] Sagar, L., Sehgal, R and S. Ojha, 2005. Evaluation of antimotility effect of Lantana camara L. var. acuelata constituents on neostigmine induced gastrointestinal transit in mice. BMC Complement Altern Med, 5:18.

[14] Cazis, C. H., Timothy, S. Y., Zakama, S. G and B. Habiba, 2013.Phytochemical screening and purgative activity of ethanolic extracts of Vernonia amygdalina del. Leaf. International Journal of Research in Avurveda and Pharmacy, 4(1):46-49.

[15] Sabiu S., Omotayo, T., and A. Anofi, 2016. Toxicological implications and laxativepotential of ethanolic root extract of Morella serrata in loperamide-induced constipated Wistar rats. Pharmaceutical Biology, 54(12): 2901-2908.

[16] Ashafa, A. O.T, Sunmonu, T.O, and A. A. Abbass, 2011. Laxative potential of the ethanol leaf extract of Aleo vera (L.) in wistar rats. Journal of National Pharmacology, 2:158–162.

[17] Praveen, N., Nayak, S., Kar, D. M and P. Das, 2010. Pharmacological evaluation of ethanolic extracts of the plant Alternantherasessilis against temperature regulation. J. Pharm. Res., 3(6):1381-1383.

[18] Ahmad, I., Mehmood, Z and F .Mohammad, 1989. Screening of some Indian medical plant for their antimicrobial properties. J. Ethnopharmacon, 62(2):183-193.

[19] Apiamu, A., Evuen, U. F and U I. Ajaja, 2013.Biochemical Assessment of the Effect of Aqueous Leaf Extract Of Euphorbia Heterophylla Linn on Hepatocytes of Rats . IOSR Journal Of Environmental Science, Toxicology And Food Technology (IOSR-JESTFT) e-ISSN: 2319-2402,p-ISSN: 2319-2399. Volume 3, Issue 5.

[20] Yamada, K and Y. Onoda, 1993. Comparison of the effects of T-1815, yohimbine and naloxone on mouse colonic propulsion. Journal of Smooth Muscle Research, 29(2):47-53.

[21] Schiller, L. R., Santa, A. C. A., Morawski, S. G., and J.S Fordtan, 1984. Mechanism of the antidiarrheal effect of loperamide. Gastroenterology, 86:1475–1480.

[22] L. Degan , 2007. Gastrointestinal motility, physiology and methods of measurement. Gasterology, 64:195–199.

[23] Capasso, F., Mascolo, N., Autore, G and V. J. Romano, 1986. Laxative and production of antacids by colon of rat.. Pharmacological therapy, 38(8):627-9.

[24] Sabiu S., Omotayo, T., and A. Anofi, 2016. Toxicological implications and laxativepotential of ethanolic root extract of Morella serrata in loperamide-induced constipated Wistar rats. Pharmaceutical Biology, 54(12): 2901-2908.

[25] Ajani, E., Sabiu, S., Bamisye, F. A and B. A. Salau, 2014. Acute and sub-acute Toxicity Effects of Ethanolic Leaves Extract of Lagenaria brevifolia (Bitter gourd) on Hepatic and Renal Function of Rats . Journal of National Pharmacology, 2:158–162.

[26] Shahjahan, M., Sabitha, K. E., Mallika, J., and C. S. Shyamala, 2004. Effect of Solanum trilobattum against Carbon Tetrachloride induced hepatic damage in albino rats. Indian Journal of medical Research, 4, 194-198.

[27] Xi, Y., Laura, K., Schnackenberg, Q. S., and F. L. William, 2001. Hepatic biomarkers. Experimental and Clinical Science, 15:317-828.

[28] Pazhani, G. P., Subramanian, N. N., Arunchalam, G.., Hemalatha, S., and V. Ravichandran, 2001. Antidiarrheal potential of Elephantopus scaber Linn leaf extract. Indian drugs, 38 (5): 269-271.