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THE ANTI-DIARRHOEA EFFECT OF *COMBRETUM PLATYPTERUM* (WELW) HUTCH & DALZIEL AND *COMBRETUM RACEMOSUM* P. BEAWV IN MICE AND RATS

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Abstract - Plant has always been a common source of medicine, either as active principles or traditional preparation. *Combretum platypterum* and *Combretum racemosum* belong to the family of Combretaceae. It is used to treat lower backache, fever, eye problems, malaria, swellings and mumps, conjunctivitis, coughs, sexually transmitted diseases, helminthiasis and diarrhoea. This study aimed at testing the anti-diarrhoea effect of aqueous leaf extract of *Combretum platypterum* and *Combretum racemosum.* Antidiarrhoea activity was carried out using Castor-Oil induced Diarrhea, Gastro-intestinal motility test and Castor oil Induced Enteropooling test. 8 groups of 4 rats per group. Group 1 Received distilled water (10ml/kg P. O), group2 Received Loperamide (1mg/kg I. P). Group 2 to 3 Received 100, 200 and 400mg/kg aqueous leaf extract of *Combretum platypterum,* O.P. Group 6 to 8 Received 100, 200 and 400mg/kg aqueous leaf extract of *Combretum platypterum,* O.P. In Castor-Oil induced diarrhea, the mean numbers of faceces were reduced at all dose level of aqueous leaf extract of *C. platypterum* and the leaf extract of *C. racemosum* reduced the number of diarrheal faeces at 200 mg/kg. *C. platypterum* in Gastro-intestinal motility test animal model, shows a significant intestinal motility inhibition at all dose level and *C. racemosum* at 400mg/kg of the leaf extract reduced the percentage travel by charcoal compared to control. In Castor oil induced enteropooling, *C. platypterum* has no effect on weight volume of intestinal content and *C. racemosum* at 100 mg/kg, 200 mg/kg, 400 mg/kg and loperamide (1mg/kg) were significant in reducing the weight of intestinal content. *Combretum platypterum* and *C. racemosum* posses' anti-diarrhoea activity.

keywords: Diarrhoea, *Combretum platypterum*, *Combretum racemosum*, Gastro-intestinal motility, Enteropooling, Castor oil

INTRODUCTION

Diarrhoea is defined by the World Health Organization as having three or more loose or liquid stools per day, or as having more stools than is normal for that person (Dupont, 2014). It is a major medical problem worldwide (Agunu *et al.*, 2005; Njoroge and Kibunga, 2007). It is gastrointestinal disorder and one of the common diseases. It is caused by both infectious and non-infectious agents (Palombo, 2006; Collise and Nomalungelo, 2012**).** It kills 2,195 children per day more than measles, AiDs and malaria **(**Liu et al., 2012). 88% of diarrhea deaths are because of dirty water, poor sanitation, and lack hygiene (Black *et al*., 2003; WHO, 2008). Diarrhoea is caused by bacteria and Parasites (WHO, 2008). The causative organism that causes diarrheal is adenovirus types 40 and 41, astroviruses, *Campylobacters* sp., *Salmonella* sp., *Shigella* sp. Some strains of *Escherichia Coli*, *Clostridium difficile* and *Entamoeba histolytical* (Uhnoo *et al*., 1990; Mitchell, 2002, viswanathan *et al*., 2009; Rupnik *et al*., 2009; Dans

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and Martinez, 2006). Mal-absorption such as enzyme deficiencies or mucosal abnormality, Pernicious anemia; inability to absorb Vitamin $B_{12,}$ Loss of pancreatic secretions because of cystic Fibrosis or Pancreatitis, Structural defects like short bowel Syndrome, radiation fibrosis and cancer treatment and drugs, like orlistat, which inhibits the suck up of fat. Inflammatory bowel disease such as ulcerative colitis, Corhn's disease and microscopic colitis. Treatment of diarrhoea include: fluid intake, eating**,** medication such as antibiotics, antiamoebic, anti- histamime, tetracycline (Kiser *et al.*, 2008).

Plant has always been a common source of medicine, either as active principles or traditional preparation (Akerele, 1993). Medicinal plants have a Unique and different characteristic to conventional drug; they have a wider range of therapeutic use and are suitable for chronic treatment. They are available and cheaper than Synthetic drugs (Calixto, 2000; Idu, 2010). Some plants used to treat diarrhea are *Aegele marmelos, Asparagus racemosus, Azadirachta indica, Centella asiatica, Holarrhena antidysenterica, Terminalia chebula* (Damiki and Siva, 2011).

Combretum platypterum and *Combretum racemosum* belong to family Combretaceae. *Combretum platypterum* occurs from guinea east to DR Congo and Southern Sudan and South to Northern Angola (Dalziel, 1973). *C. platypetrum* occur in rain forest, secondary forest and scrub Savanna, sometimes in swampy localities, from sea-level up to 450 m altitude. It is commonly called Akan asante in Ghana, Kissi Yekpomdeo- Chuaboa in Sirra leone, Mano Kpadah in Liberia and in Nigeria called in Igbo: mmanya nza; Igbo (Awka) achicha nza; Yoruba: Ogan, Ogan dudu; (Ife) Ogan ibule (Bredenkamp, 2000). *C. platypetrum* is used to treat lower backache, fever, eye problems, malaria, swellings and mumps, conjunctivitis, coughs, sexually transmitted diseases, helminthiasis and diarrhea. It is also used as a tonic, febrifuge and to stop post-partum bleeding (Liben, 1983; Bongers *et al.*, 2005). Despite its traditional uses, pharmacological analyses have not been carried out on this species.

Combretum racemosum belongs to family Combretaceae. A straggling shrub, scandent or liane to 15 m long, of mixed deciduous forest from Senegal to Southern Nigeria and Fernando Po, and widespread across Africa to Sudan, Kenya, Zaire and Angola. The plant bears a mass of crimson flowers, spectacular and worthy of cultivation. It flowers in December/January in Southern Nigeria, gaining the local English name of Christmas rose (Burkill, 1985). The common name is Christmas rose. In Ghana

it is called akan-akyem, akye betzo in Ivory Coast, manding-bambara kotri in Mali, balanta kinde in Senegal**,** limba bede in Sierra leone. In Nigeria it is called okoso in Edo, alagame in Igbo (Umuahia) and ogan pupa in Yoruba (Burkill, 1985). It is used to treat anti-helmintic, kill a roundworm, dysenteries, haemorrhoids, bleeding during pregnancy, haematuria, convulsive, circumcision wounds, toothache, coughing and tuberculosis (Burkill, 1985; Walker and Sillans, 1962; Dalziel, 1973; Oliver-Bever, 1986).

Okwuosa *et al.* (2006) tested the anti-Ulcer and antimicrobial of *Combretum racemosum* leaf extract and found that it possess anti-ulcer and antimicrobial activities. *Combretum racemosum* have protective effect on the Liver and bone marrow (Okwuosa *et al.,* 2012). Phytochemical present are alkaloids Saponins, Flavonoids, terpenoids, glycosides, resins, carbohydrate and steroid (Okwuosa *et al.,* 2012). Schepetkin *et al.* (2013) report the immunomodulatory and hemag glutinating activities of an aqueous extract of *Combretum racemosum*. The methanol extract have antioxidant activity (Francine *et al.,* 2012*).* The phytochemical screening is for hexane, ethyl acetate and methanol extract. Steroids cardiac glycoside are presenting in hexane extract. Alkaloids, steroids, saponins and reducing sugar are present in ethyacetale and alkaloids, anthraquinonies, tannins, saponins and reducing sugar are present in a methanol extract (Okwuosa *et al.,* 2012). Okwuosa *et al.* (2012) reported that the LD50 > 5500 mg/kg. However, there is no animal study on it anti-diarrhea. This study aimed at testing the anti-diarrhoea activity of aqueous leaf extract of *Combretum platypterum* and *Combretum racemosum.*

MATERIALS AND METHODS

Collection of Plant Material

Fresh leaves of *Combretum platypterum* and *Combretum racemosum* were collected in Sakponba Forest. The plants were identified and authenticated by Dr. H Akinnibosun at the Department of Plant and Biotechnology Faculty of life Sciences, University of Benin City, Edo State, Nigeria.

Preparation of Plant Material

The leaves were washed and air dried in Pharmacognocy Department, University of Benin, Benin City. For one week. Leaves were further subjected to another 24 hours of drying in an oven maintained at

40^{O}C. Leaves were pulverized into a smooth powder using impact mill. Pulverized material (200g) was mixed with distilled water (5.0 litres) and left for 72 hours. Mixture was stirred regularly. At the end of the 72 hours the extracts were filtered, and the filtrate were concentrated over a water bath and yield 60g. The concentrated extracts were stored in Universal bottles labeled and refrigerated at 4^{O}C before use.

Experimental Animals

Albino rat weighing 100-220g and mice weighing 20–35g were acquired at commercial farm in Benin City and housed in Biochemistry animal house, University of Benin, Benin City. The animals were acclimatization for 2 weeks and kept under standard Laboratory conditions of light/dark at 12/12 hours Cycle. They were fed with standard rodent pellet diet and water ad libitum. Litter in the cages was renewed thrice a week to make sure hygienicity and greatest comfort for animals. Animals were handed according to standard protocols for Laboratory animals (National Institute of Health USA: Public Health Service policy on humane care and use of Laboratory Animals 2002).

Experimental designed

Antidiarrhoea Activity

Castor-Oil induced Diarrhea:
Castor-oil induced diarrhoea method as described by Awouters *et al*. (1978) and modified by Ezenwali *et al*. (2010).

Group 1: Received distilled water (10ml/kg P. O)
Group 2: Received Loperamide (1mg/kg I. P).
Group 3: Received aqueous extract of *Combretum platypterum* (100mg/kg, P. O)
Group 4: Received aqueous extract of *Combretum platypterum* (200mg/kg, P. O).
Group 5: Received aqueous extract of *Combretum platypterum* (400mg/kg, P. O).
Group 6: Received aqueous extract of *Combretum racemosum* (100mg/kg, P. O)
Group 7: Received aqueous extract of *Combretum racemosum* (200mg/kg, P. O).
Group 8: Received aqueous extract of *Combretum racemosum* (400mg/kg, P. O).

The animals in each were fasted overnight before the experiment 30 minute after administration, 0.3ml of castor oil was administered to each mouse in across the groups. The number of watery stool and dry store counted and recorded

Gastro-intestinal motility test:
Gastro-intestinal motility was assed using castor oil-induced intestinal motility in mice by Mascolo *et al* (1994). Modified by Ezenwali *et al* (2010).

Group 1: Received distilled water (10 ml/kg P. O)
Group 2: Received Loperamide (1mg/kg I. P).
Group 3: Received aqueous extract of *Combretum platypterum* (100 mg/kg, P. O).
Group 4: Received aqueous extract of *Combretum platypterum* (200 mg/kg, P. O).
Group 5: Received aqueous extract of *Combretum platypterum* (400mg/kg, P. O).

Group 6: Received aqueous extract of *Combretum racemosum* (100 mg/kg, P. O).
Group 7: Received aqueous extract of *Combretum racemosum* (200 mg/kg, P. O).
Group 8: Received aqueous extract of *Combretum racemosum* (400mg/kg, P. O).

The animals were fasted overnight. 0.3ml of castor oil was administered orally to all the mice one hour before extract, loperamide, distilled water administration. One hour after extract administration, 0.2ml of 10% Charcoal meal in 10% gum Acacia orally. 20 minutes after administration, the animals were sacrificed; the total length and the distance travel by charcoal were measured.

Castor oil Induced Enteropooling test:

Castor oil-induced enteropooling method by Robert *et al* (1976) was used. Five group of 4 rats each was fasted overnight. Castor oil (1ml) was orally administered to all the animals in the groups. One hour later, group 1 received distilled water (2ml/kg P.O), group 2 received loperamide (1mg/kg I. P), Group 3 to 5 receive aqueous extract of *Combretum platyperum* (100, 200 and 400 mg/kg, P. O). Group 6 to 8 receive aqueous extract of *Combretum racemosum* (100, 200 and 400 mg/kg, P. O). Two hours after treatment the animals were scarified using Chloroform as anaesthesia. The small intestine removed after tying at both ends with Ligature and weighed. Intestinal contents were collected by milking into a graduated 10ml measuring cylinder and their volumes were measured. The intestine was re-weighed and the difference between full and empty intestines calculated.

Statistical Analysis

Data were expressed as mean ± standard error of mean (SEM) and n is the number of rats or mice per group. One-way analysis of Variance (ANOVA) was performed and multiple comparisons were made using Newman keul multiple range test. All data were analyzed using GraphPad prism software. $P<0.05$ shows a significant difference.

RESULTS AND DISCUSSION

Castor Oil induced diarrhea:

The mean numbers of faeces were reduced at all dose level of aqueous leaf extract of *C. platypterum* including the standard Loperamide (**P < 0.01, *P < 0.05) Table 1.

The leaf extract of *Combretum racemosum* reduced the number of diarrheal faeces at 200 mg/kg. The reduction was significant compared to control ($P < 0.05$). 100 and 400 mg/kg were not significant compared to control ($P > 0.05$). loperamide were significant ($P < 0.05$) Table 2

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Small intestinal transit:

Table 3 shows the inhibitory effect of the aqueous leaf extract of *Combratum platypterum* and loperamide. It shows a significant inhibition at all dose level ($P < 0.05$).

Table 4 show a reduction in percentage travel by charcoal at all dose level (100, 200 and 400 mg/kg) and loperamide. The reduction was significant at 400mg/kg and loperimide the standard antidiarrhoea drug compared to control (**$P < 0.01$, *$P < 0.05$).

Castor oil induced enteropooling:

C. platypterum aqueous leaf extract at all dose level (100, 200, and 400 mg/kg) in figure 1a, 1b, and 2a, 2b were not significant in weight and volume of intestinal content compared to control ($P >0.05$). The standard show significant difference compared to control ($P < 0.05$).

In fig 3a and 3b, 4a and 4b extract of *C. racemosum* show a reduction on weight and volume of intestinal content at all dose levels (100, 200 and 400 mg/kg) and loperamide standard drug. At 100 mg/kg, 200 mg/kg, 400 mg/kg and loperamide (1mg/kg) were significant in reducing the weight of intestinal content ($P <0.05$). The reduction of the volume of intestinal content was not significant at all dose levels including the standard ($P > 0.05$).

Table 1: Anti-diarrhoea activity of the aqueous leaf extract of C. *platypterum* and loperamide on castor Oil induced diarrhea in mice.

Treatment (mg/kg)	Fecal Dropping	
	Number	Inhibition of defecation (%)
Control	9.00±1.47	-
100	4.25±0.47	52.78
200	3.50±0.87*	61.11
400	2.50±1.44**	72.22
Loperamide (1)	1.25±1.25**	86.11

** $P < 0.01$, * $P < 0.05$ Compare to control, (n = 4 animal per group).
Values are represented as mean ± S.E.M.

Table 2: Anti-diarrhoea activity of *C. racemosum* and loperamide on castor oil induced diarrhoeal in mice.

Treatment (mg/kg)	Fecal Dropping	
	Number	Inhibition of defecation (%)
Control	9.00±1047	-
100	5.25±1.11	41.67
200	3.75±1.11*	58.33
400	5.75±1.18	36.11
Loperamide (1)	1.25±1.25**	86.11

***** $P < 0.05$, ** $P <0.01$ Compared to control (n = 4 animals per group).
Values are presented as Mean ± SEM.

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Table 3: The inhibitory effect of an aqueous extract of *C. platypterum* transit in mice.

Treatment (mg/kg)	Percentage distance travelled by the charcoal	% inhibition pan
Control	82.47±8.47	
100	40.50±8.87**	50.89
200	53.53±8.63*	35.09
400	59.49±4.18*	27.86
Loperamide (1)	26.58±5.45***	67.77

*** P < 0.001, ** P < 0.01, * P < 0.05 Compare to Control, (n = 4 per group).

Table 4: The inhibitory effect of aqueous leaf extract of C. *racemosum* and loperamide on transit in mice.

Treatment (mg/kg)	Percentage distance travelled by Charcoal	Percentage inhabitation
Control	82.47±8.47	-
100	67.31±17.25	18.38
200	54.29±4.45	34.17
400	34.72±5.35*	57.90
loperamide (1)	26.58±5.45**	67.77

* P < 0.01, * P <0.05, Compared to control, n = 4 animals per group.

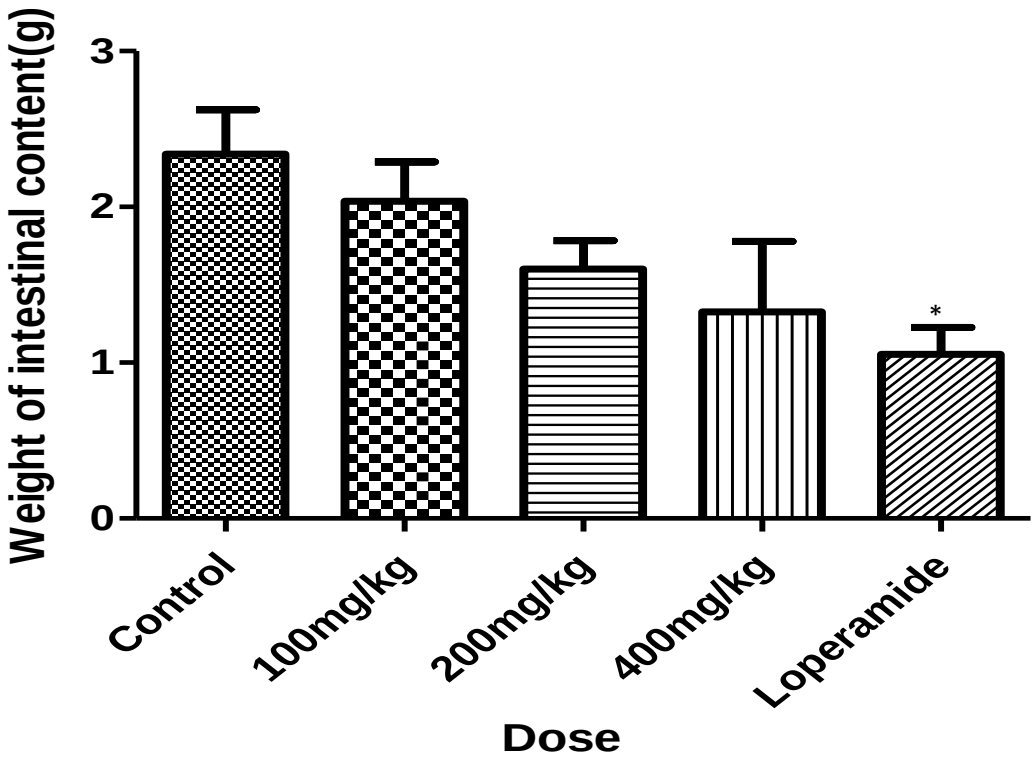

Figure 1a: Graph representing the effect of aqueous leaf extract of *Combretum platypterum* and loperamide on castor oil induced enteropooling. Values are present as mean ± S.E. M.

There were observable dose dependent reduction of diarrhoeal, weight of intestine content however, the reduction compare to control at all dose levels were not statistically significant (P>0.05) the standard loperamide show significant reduction (P. <0.05), n=4 animals per group

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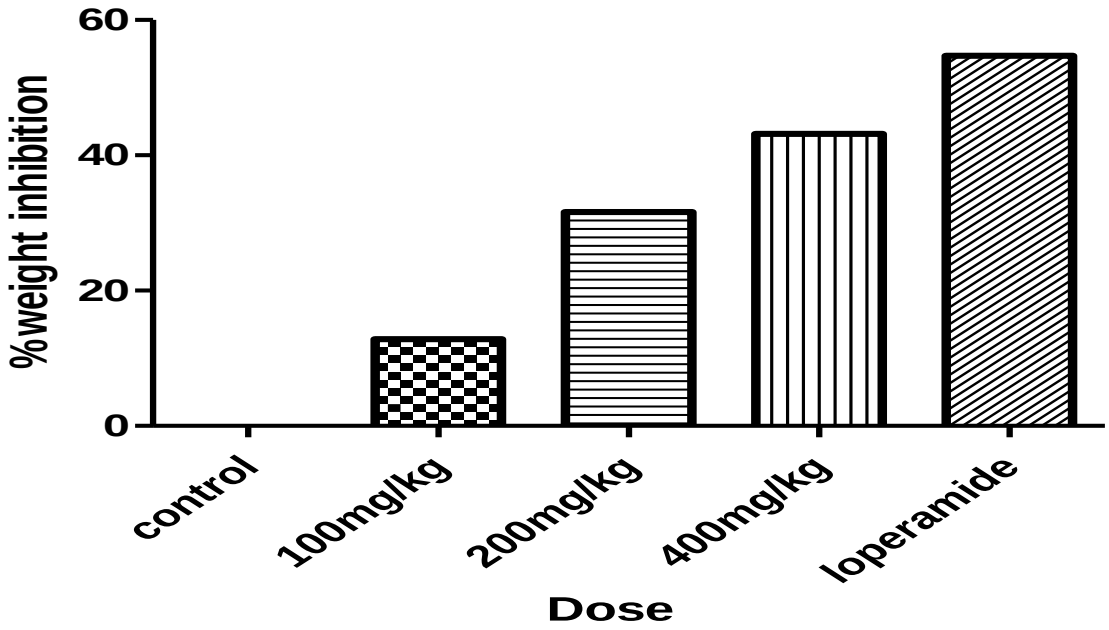

Figure 1b: The percentage inhibition *C. platypterum* on weight content on castor-oil induced enteropooling. There is dose dependent of the leaf extract of *C. platypterum* on Weight of intestine content in castor oil induced enteropooling.

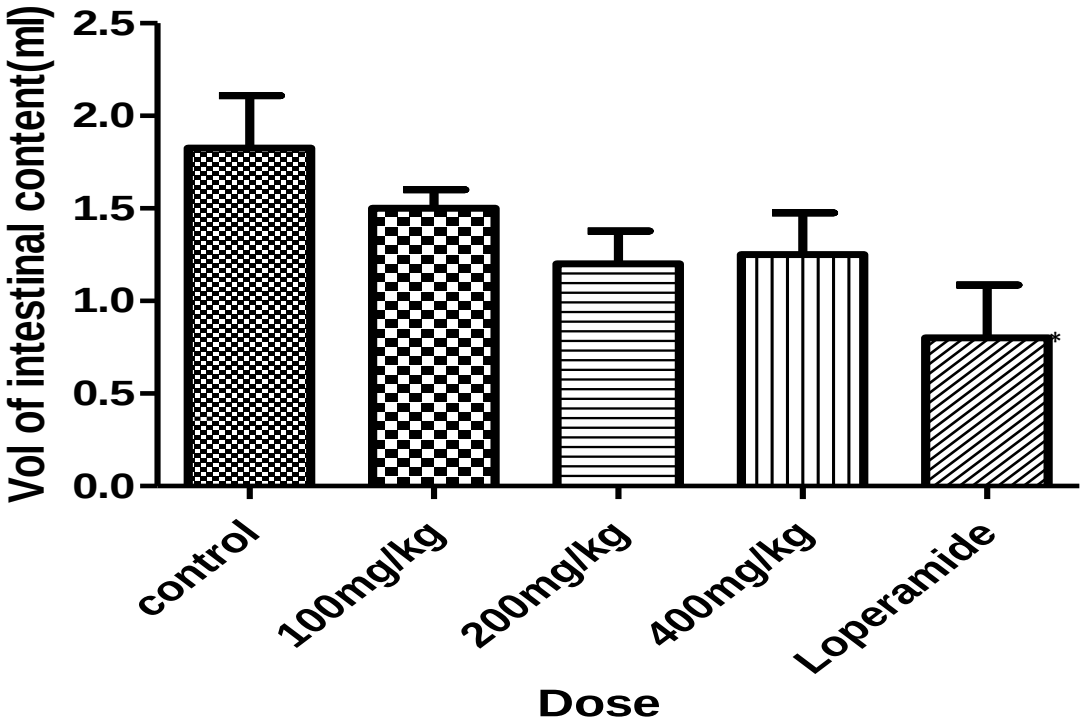

Figure 2a: The effect of aqueous *C. platypterum* and Loperamide on volumn of intestinal content. Values are presented as meant S.E.M. Loperamide standard drug show a significant difference compare to control ($P < 0.05$). The extract at all dose level show observable reduction of intestinal content, however, the reduction was significant compare to control ($P > 0.05$), n=4 animals per group.

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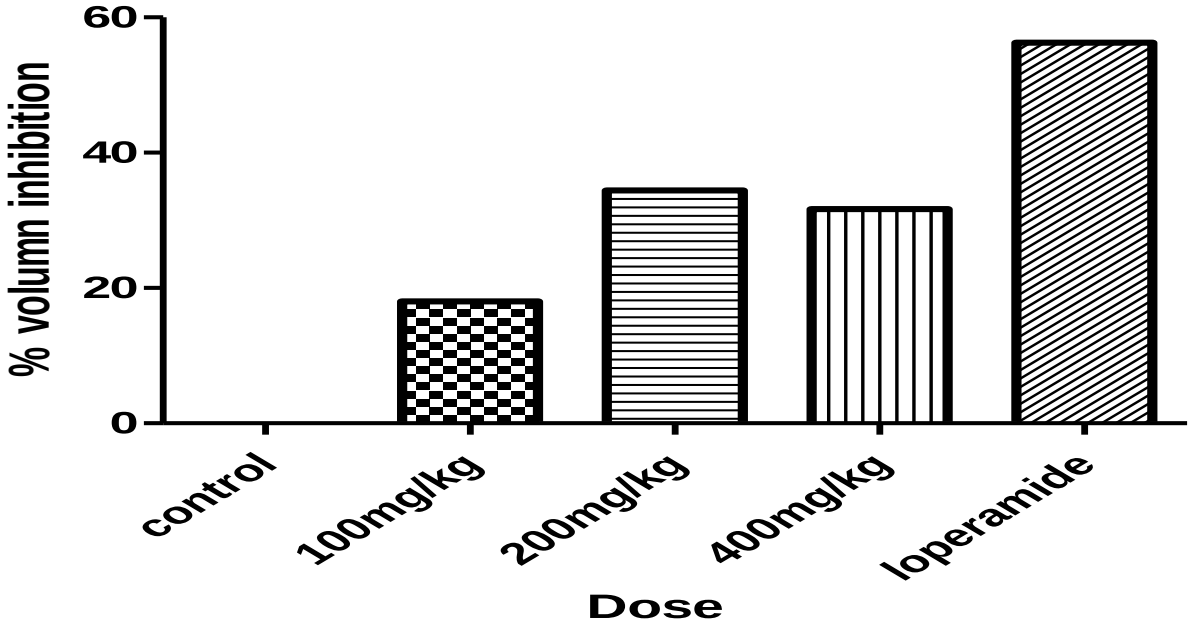

Figure 2b: Graph representing the percentage inhibition of C. *platypterum* on volume of intestinal extent on castor-oil induce enteropooling. *C. platypterum* aqueous leaf extract show slight inhabitation of volume of intestinal content however, the inhibition were not significant statistically compared to control ($P > 0.05$) Loperamide show significant inhibition ($P < 0.05$), n = 4

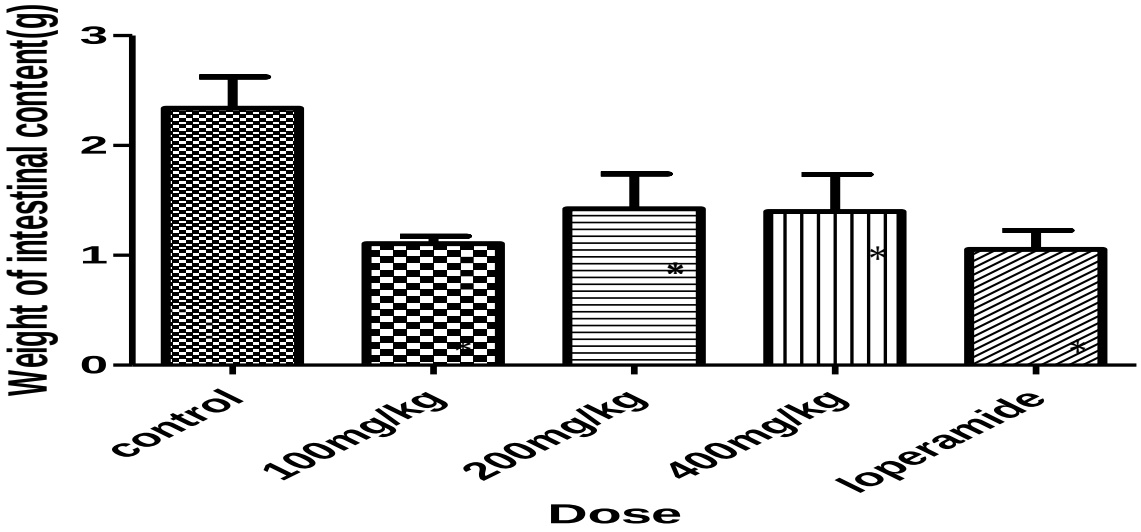

Figure 3a: Graph representing the effect of aqueous leaf extract of *C. racemosum* and loperamide on weight of intestinal content on castor oil induced enteropooling. Values are present as mean $\pm$ S.E. M. They were a significant reduction of weight of intestinal content compared to control ($P < 0.05$), n=4 animals per group.

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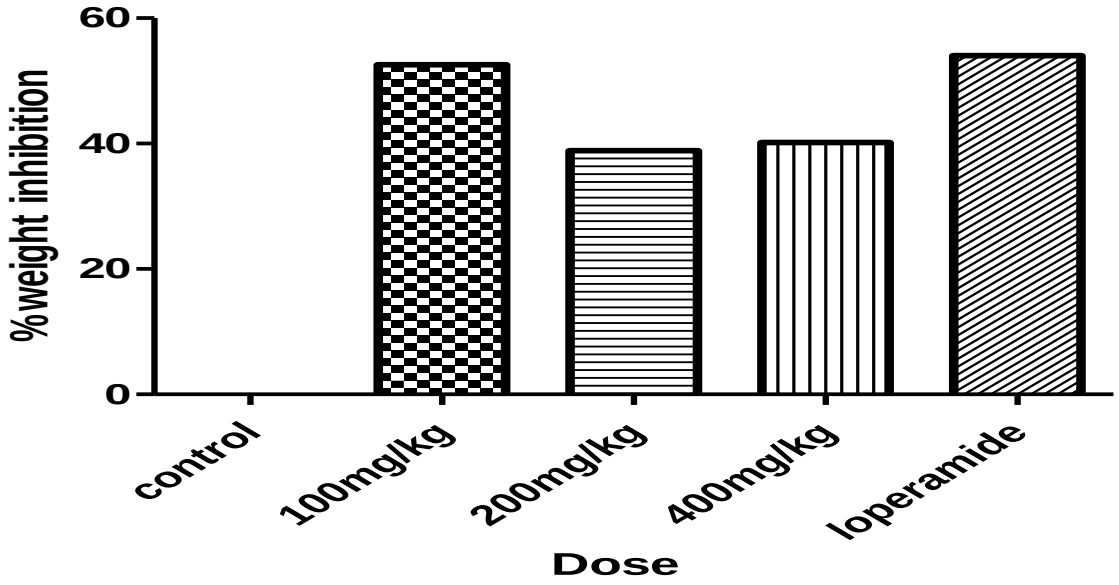

Figure 3b: Graph of percentage inhibition of aqueous leaf extract of *C. racemosum* on weight of intestinal content on castor oil induced enteropolling. There was significant inhibition of the weight content ($P < 0.05$). n = 4 per group.

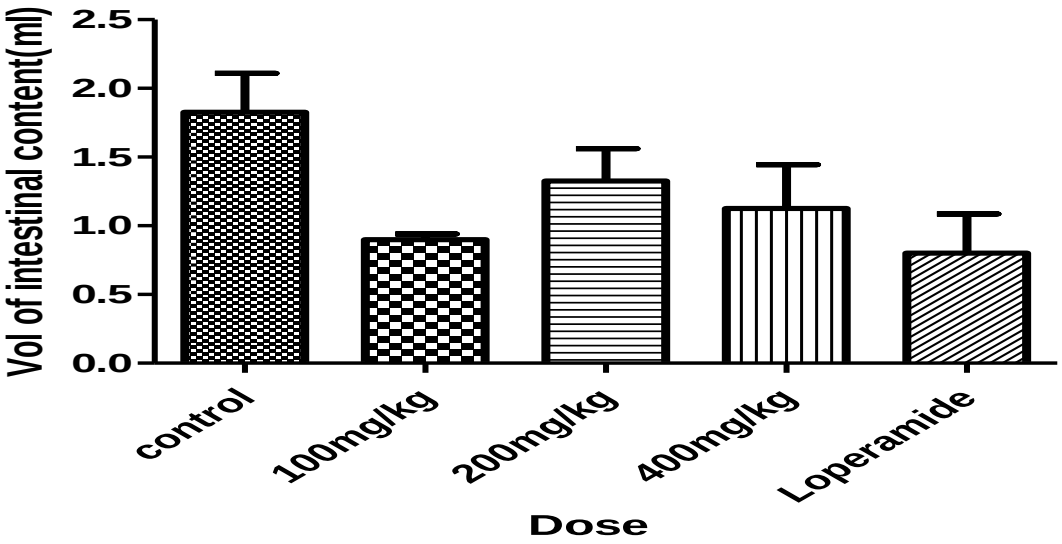

Figure 4a: Effect of aqueous leaf extract of C. *racemosum* and loperamide on volume of intestinal content on castor-oil induced enteropooling. Values are presented as mean $\pm$ S.E.M. There were no significant different in the reduction when compared to control ($P > 0.05$). n = 4 animals per group.

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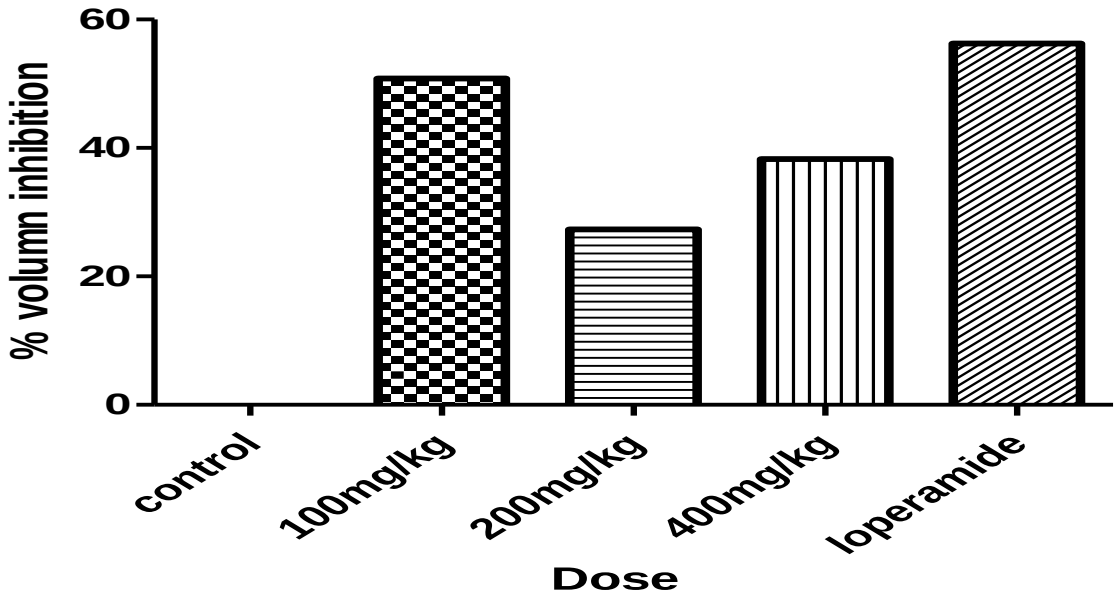

Figure 4b: Graph of Percentage inhibition volume of aqueous leaf extract of C. *racemosum* on intestinal content on castor oil induced enteropooling. There was observable inhibition at 100 mg/kg and loperamide (1mg/kg) and inhibition at 200mg/kg and 400 mg/kg of the extract.

The effect of an aqueous extract of *C. platypterum* leaf on diarrhea induced by castor oil in mice in table 1, showed a significant reduction in the frequency of defecation, a number of diarrhea stools and wetness of the fecal dropping. Result in Table 1, shows that in castor oil induced diarrheal, the aqueous leaf extract of *Combretum platypterum* effect, is comparable to loperamide. Pharmacological effect of loperamide is because of its antimitility and antisecretory properties (Couper, 1985; Sule *et al.*, 2009). The liberation of ricinoliele acid from castor oil results in irritation and inflammation of the intestinal mucosa leading to release of prostaglandins, which stimulate motility and secretion (Ammon *et al*., 1974; Sule *et al.*, 2009). The mechanism of action is not known, the reduction in fecal wetness suggest it may inhibit gastrointestinal hyper-secretion. Result of intestinal transit in mice in Table 3, the pre-treatment with the extract suppressed the propulsive movement through the gastrointestinal tract. This shows that the aqueous leaf extract of *Combretum platypterum* may be capable of reducing the frequency of stooling in diarrheal condition. The delay of gastric motility enhances absorption of water from feces and may reduce its watery texture. The study on enteropooling shows that aqueous leaf extract *Combretum platypterum* has no effect on the weight and volume of in intestinal content in fig.

1a, 1b, 2a, and 2b. Reduce frequency of defecation, a number of diarrheal stool and wetness of fecal dropping and the reduction of propulsive movement through gastrointestinal track in transit in mice by an aqueous extract of C. *platypterum* support it usage in traditional medicine as antidiarrheal.

Combretum recemosum in Table 2, Show a significant reduction in frequency of defecation, a number of diarrheal stool and Wetness of fecal dropping at the dose of 200mg/kg while 100mg/kg and 400 mg/kg show no effect in their reduction. In transit in mice in table 4, show significance in propulsive movement of the gastrointestnal track at dose 400mg/kg. The study of enteropooling shown that *Combretum racemosum* has a significant reduction in weight of the intestinal content. but, the Volume was not affected in Fig 3a, 3b, 4a and 4b. Antidiarrhoea effects of medicinal plants were found to be due to alkaloids, Saponins, Flavonoids and reducing sugar (Sule *et al*., 2009). The anti-diarrheal effect of C. *platypterum* and *C. recemosum* support their usage in traditional medicine as antidiarrhoea.

CONCLUSION

This study shows that aqueous leaf extract of C. *platypterum* and *C. recemosum* possesses anti-diarrheal activities. The anti-diarrheal effect of C. *platypterum* and *C. recemosum* support their usage in traditional medicine as antidiarrheal.

REFERENCES

Agunu, A., Yusuf, S., Andrew, G .O., Zezi, A .U. and Abdurahman, E .M. (2005). Evaluation of five medicinal plants used in diarrhoea treatment in Nigeria. *J Ethnopharmacol,* 101: 27–30

Akerele, O. (1993). Summary of WHO guideline for the assessment of herbal medicin. *Herbal gram,* 28: 13–17.

Ammon, H. V., Thomas, P. J. and Phillips, S. (1974). Effect of oleic andricinoleic acid on net jejuna water and electrolyte movement. *Journal of Clinical Investigation,* 53: 374–379.

Awouters, F., Niemegeers, C. J. E., Lenaerts, F. M. and Janssen, A. J. P. (1978). Delay of castor oil diarrhea in rats; a new way to evaluate inhibitors of prostaglandin biosynthesis. *Journal of. Pharmacology*, 30: 41–45.

Black, R.E., Morris, S. and Bryce, J. (2003). Where and why are 10 million children dying every year? Lancet, 361(9376): 2226–2234.

Bongers, F., Parren, M. P. E. and Traoré, D. (2005). Forest Climbing Plants of West Africa: Diversity, Ecology and Management. CABI, Wallingford, United Kingdom. 273 p.

Bredenkamp, C. L. (2000). Combretaceae: In: O. A Leistnered, Seed plants of southern Africa: Families and Genera *Strelitzia.* National Botanical Institute. *Pretoria*, 10: 228–229.

Burkill, H. M. (1985). The useful plants of West Tropical Africa. 2nd Edition. Volume 1, Families A–D. Royal Botanic Gardens, Kew, Richmond, United Kingdom. 960p

Calixto, J. B. (2000). Efficacy, Safety, quality control, marketing and regulatory guidelines for herbal medicines (Phytotherapeutic agents). *Braziliam Journal of Medical and Biological Research*, 332: 179–189.

Collise Njume and Nomalungelo I. Goduka. (2012). Treatment of diarrhoea in rural african communities: an overview of measures to maximise the medicinal potentials of indigenous plants.*Int J Environ Res Public Health*. 9(11): 3911–3933.

Couper, I. M. (1985). Inhibition of intestinal motility and the secretion by flavonoids in mice and in rats: structural activity relationship. *Journal of Pharmacy and Pharmacology,* 45:1054–1059.

Dalziel, J. M. (1973). The Useful Plants of West Tropical Africa. Crown Agents Ed. Royal Botanic Gardens. Kew Richmond, United Kingdom. pp166–179.

Damiki Laloo and Siva Hemalatha. (2011). Ethnomedicinal plants used for diarrhea by tribals of meghalaya, northeast india. Pharmacogn Rev, 5(10): 147–154

Dans, L. and Martinez, E. (2006). "Amoebic dysentery".*Clinical Evidence* (15): 1007 – 1013.

DuPont, H. L. (2014). Acute infections diarrhea in immune competent adults. *The New England Journal of Medicine,* 370 (6): 1532–1540.

Ezenwali, M. O.,. Njoku, O. U. and Okdi, C. O. (2010). Studies on the anti-diarrheal properties of seed extracts of monodoratenuifolia. *International Journal of Applied Research in Natural products,* 2(4): 20–26.

Francine, N. M., Charaf, E. I. K., Jeanine, F., Guy, B., Pierre, D., Jose, L. N. and Stephanie, P. (2012). Vascular effects and antioxidant activity of two *Combretum* species from Democratic Republic of Congo. *Journal of Ethnopharmacology*, 42: 194–200.

Idu, M. (2010). Phytomedicine in Nigeria – Past, Present and Future. 7th Professor James Ogonor Memorial Lecture. Woman's Health and Action Research centre, Benin City. Pp 10 – 31.

Kiser, J. D., Paulson, C. P., Brown, C. (2008). Clinical inquiries, What's the most effective treatment for giardiasis. *The Journal of Family Practice,* 57 (4): 270 – 272.

Liben, L., (1983). Combretaceae. Flore du Cameroun. Volume 25. Muséum National d'Histoire Naturelle, Paris, France. 97 p.

Liu, L., Johnson, H.L., Cousens, S., Perin, J., Scott, S., Lawn, J .E., Rudan, I., Campbell, H., Cibulskis, R., Li, M., Mathers, C. and Black, R .E.(2012). Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet.* 379(9832): 2151 – 2161.

Mascolo,N., Izzo, A.A., Autore, G., Barbato, F. and Capasso, F.(1994). Nitric oxide and castor oil induced diarrhea. *American Society* for *Pharmacology and Experimental* Therapeutics,

Njoroge, G .N. and Kibunga, J. W.(2007). Herbal medicine acceptance, sources and utilization for diarrhoea management in a cosmopolitan urban area (Thika, Kenya). *African Jounal of Ecology,* 45: 65–70.

Okwuosa, C. N., Achukwu, P. U. O., Azubikend, V. and. Abah, N. C. X. (2012). Protective effect of the leaf *Combretum racemosum* Beauv (Combretaceae) on cyclophospahamide induced pancytopaenia and liver injury. *Journal of Pharmacology*, 6: 30–34.

Okwuosa, C., Nwobode, E. and Chilaka. K. (2006). The anti-ulcer activities of leaf extracts of *Combretum racemosum* (family: Combracaceae). *Journal of Biomedical Mestigation,* 4(1): 9–14.

Oliver-Bever, B. (1986). Medicinal Plants in Tropical Africa. University Press Cambridge. p117–168.

p - ISSN: 2536 – 6866
e - ISSN: 2659 - 1529

Palombo, E.A.(2006). Phytochemicals from traditional medicinal plants used in the treatment of diarrhoea: Modes of action and effects on intestinal function. Phytother. Res, 20:717–724

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

Rupnik, M., Wilcox, M. H. and Gerding, D. N. (2009). Clostridium difficile infection: new developments in epidemiology and pathogenesis. *Nature Reviews Microbiology 7* (7): 526 – 536.

Schepetkin, I. A., Kouakou, K., Yapi, A., Kirpotina, L. N., Jutila, M. A. and Quinn, M. T. (2013). Immunomodulatory and hemagglutinating activities of acidic polysaccharides isolated from *combretum racemosum*. *International Immunopharmacology*, 15(3): 628–637.

Sule, M. I., Njinga, N. S., Musa, A., Magaji, M. G. and Abdullali, A. (2009). Phytochemical and anti-diarrhoeal studies of the stem back of Ceibapentandra (Bombacaceac). *Nigeria Journal of Pharmaceutical Sciences*, 8(1):143–148. Walker, A. R. and Sillans, R. (1961). *Les plantes utiles du Gabon.*, Paul Lechevalier, Paris. pp.

Uhnoo, I., Svensson, L. and Wadells G. (1990). *Enteric adenoviruses.Baillieres Clinical Gastroenterology*, 4 (3): 627-642.

Viswanathan, V.K., Hodges, K. and Hecht, G. (2009). "Enteric infection meets intestinal function: how bacterial pathogens cause diarrhea". *Nature Reviews Microbiology,* 7(2): 110 – 119.

World Health Organisation (2008).Weekly epidemiological record. 83(47):421– 428.