ANTIMOTILITY EFFECT OF A SOUTHEAST NIGERIAN POLYHERBAL COMBINATION (*AJUMBISE*): AN *IN-VITRO* AND *IN-VIVO* EVALUATION

[1]IJIOMA, Solomon, [2]OSIM, Eme, [3]NWANKWO, Azubike, [4]KANU, Kingsley, [5]ORIEKE, Daniel and [6]EZIKE, Johnson

[1]Department of Zoology and Environmental Biology, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

[2]Department of Physiology, University of Calabar, Calabar, Cross River State, Nigeria.

[3]Department of Physiology, Abia State University, Uturu, Abia State, Nigeria.

[4]Department of Environmental Management and Toxicology, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

[5]Department of Biochemistry, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

[6]Department of Animal Breeding and Physiology, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

Corresponding Author: Kanu, K. Department of Environmental Management and Toxicology, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. **Email:** kanu.kingsley@mouau.edu.ng **Phone:** +234 8035238277

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ABSTRACT

The antimotility effect of Ajumbise polyherbal extract (APE) and its composite plants were evaluated in-vitro and in-vivo. In the in-vitro study, about 2 – 3 cm of a rabbit jejunum mounted in a 30 ml organ bath containing tyrode solution and bubbled with air was set up before the applications of graded doses of acetylcholine and extracts. In the in-vivo study, 16 groups of 5 rats each were pretreated with the extracts and atropine followed by charcoal meal after 30 minutes before being sacrificed 30 minutes later and opened up to assess gastrointestinal transit of the administered charcoal meal. Application of acetylcholine caused a dose dependent increase in the amplitude of contraction when compared with basal value (p<0.05), while APE on the same isolated tissue was inhibitory with each dose significantly lowering basal amplitudes of contraction (p<0.05). Extracts of the various plants constituents of Ajumbise also produced varying degrees of inhibitory activities (p<0.05) with Ceiba pentandra, Napoleona vogelii, Spondias mombin and Euphorbia convolvuloides producing high but short lived inhibitory activities while Uvaria chamae and Barteria fistulosa produced low effects. Results of the in-vivo study agreed completely with that of the in-vitro evaluation, as APE and extracts from the different plants constituents in the polyherbal significantly inhibited gastrointestinal motility and transit time in all treated rats when compared with control (p<0.05) but lower than that of atropine. Ajumbise polyherbal and its components inhibit normal peristaltic movement of the gastrointestinal tract and as such may be potential anti- diarrheal agents.

Keywords: Acetylcholine, Ajumbise, Polyherbal extract, Gastrointestinal tract, Rabbit jejunum

INTRODUCTION

Diarrhoea is currently one of the diseases whose prevalence has attained staggering level. A recent report by the World Health Organization (WHO) puts its global incidence for children under 5 years at 1.7 billion cases yearly with 525000 deaths (Ijioma *et al.,* 2014a). This

makes diarrhoea the second leading cause of death amongst children less than 5 years globally and is taught to account for a whopping 3.6% of global disease burden (Thiam *et al.,* 2017). A major physiologic change accompanying the onset of diarrhea is the increase in gastrointestinal smooth muscle contractions and uncontrolled peristalsis in the gastrointestinal tract, accounting for excessive body fluid and electrolyte loss coupled with dehydration. Increased gastrointestinal motility also reduces transit time and may affect the absorption of food materials, posing the risk of malnutrition. This may be why in addition to body fluid and electrolyte replacement, control of intestinal smooth muscle contraction is a major strategy in the management of diarrhea (Ijioma *et al.,* 2014b). The relationship between GIT motility and smooth muscle contractions is well established. Smooth muscles in the body are found not only in the uterus but also in the walls of hollow visceral organs such as the intestines, stomach, urinary bladder, respiratory passages and blood vessels (Osim, 2002). The rabbit jejunum and uterine smooth muscle preparations are known for their intrinsic spontaneous contractile waves via mechanisms associated with membrane depolarization due to Ca^{2+} influx across the plasma membrane and neurotransmitter activities (Berridge, 2008).

Although several over the counter orthodox medicines abound for the management of diarrhea, alternative medicine of which herbal medicine is part, has gained wide acceptance in the treatment of the disease for reasons of cost, availability, accessibility, acclaimed efficacy and increasing cases of drug resistance often associated with the use of orthodox medicines (Ijioma, 2015; Thiam *et al.,* 2017). Pains in the stomach and intestinal cramps may be caused by increased gastric acid secretion (gastrointestinal acidosis) and increased motility due to above normal contractions of the gastro intestinal smooth muscles (Curatolo, 2011).

Ajumbise is a combination of the leaves, stem, bark and roots of different plants. In its original form as purchased in the market, Ajumbise was found to contain by percentage dry weight 34.97 % *Barteria fistulosa,* 23.72 % *Napoleona vogelii,* 3.72 % *Euphorbia convolvuloides,* 11.45 % *Spondias mombin,* 10.09 % *Uvaria chamae* and 16.60 % *Ceiba pentandra.* Preliminary investigation of the phytochemical composition of APE showed the presence of high amounts of alkaloids, flavonoids, and saponins, moderate amounts of tannins and terpenoids, and low amounts of steroids, phenols and cardiac glycosides (Ijioma *et al*., 2017a). Ajumbise is commonly found in southeast Nigeria and used for the treatment of stomach pain and cramps in addition to other uses. At the moment, there is no scientific data or report to validate the claims on *Ajumbise* and as such, the current study represents the first scientific attempt to investigate and perhaps validate the indigenous claims on *Ajumbise* as it is commonly package and sold at Onu-imo in Obowo Local Government Area, Imo State, Nigeria. Few plant species that make up the combination have previously been investigated for their anti-motility/anti-diarrhea and gastro protective activities including *Spondias mombin L.* (Akubue *et al.,* 1983), *Napoleona vogelii* Hook and Planch (Akah *et al*., 2007) and *Uvaria chamae*, are traditionally used for the treatment of diarrhea (Okwu and Iroabuchi, 2009).

The fact that the antidiarrhoeal effects of plants have continued to be investigated via *in-vitro* and *in-vivo* gastrointestinal smooth muscle studies (Ehlert *et al*., 1999; Eno and Azah, 2004; Akomas and Ijioma, 2015) makes the current study paramount. The evaluation of an agent for antimotility effects on the GIT may explain possible antidiarrhoeal effect of the agent. In this study, attempt was made to evaluate the antimotility effects of *Ajumbise* as a whole and that of its six components separately in *in-vitro* and *in-vivo* animal studies.

MATERIALS AND METHODS

Collection and Identification of Plant Material: *Ajumbise* was collected from Onu-imo in Obowo Local Government Area of Imo State, Nigeria and was separated into its component plants having been previously segregated and identified by taxonomists at the Department of Forestry and Environmental Management, Michael Okpara University of

Agriculture, Umudike as *Barteria fistulosa* Mast. (34.97 %, MOUAU/VPP/16/001), *Napoleona vogelii* Hook. and Planch. (23.72 %, MOUAU /VPP/16/002), *Euphorbia convolvuloides* Hochst. exBenth (3.72 %, MOUAU/VPP/16/003), *Spondias mombin* Linn. (11.45%, MOUAU/VPP/16/006), *Uvaria chamae* P.Beauv. (10.09 %, MOUAU/VPP/16/004) and *Ceiba pentandra* (L.) Gaertn. (16.60 %, MOUAU/VPP/16/005) as documented in Ijioma *et al.* (2017a).

Preparation of Plant Extracts: Extracts were prepared from the polyherbal as whole and also from each individual plant component (Table 1). Fifty (50) grams of powdered *Ajumbise* was introduced into the extraction chamber of the soxhlet extractor for extraction with ethanol as solvent over a period of 48 hours. At the end of the period, the extract in solution was evaporated to dryness at low temperature to obtain a crude extract which weighed 8.69 grams and represented a yield of 17.38 % *Ajumbise* ethanolic extract. The same procedure was repeated on the separate powdered materials of the six ajumbise plants component. For the components, percentage yields obtained were *B. fistulosa* (32.40 %), *N. vogelii* (31.60 %), *E. convolvuloides* (15.00 %), *S. mombin* (29.00 %), *U. chamae* (10.20 %) and *C. pentandra* (7.72 %). The extracts were preserved in the refrigerator until needed. For the purpose of this study, the polyherbal extract is hereafter referred to as ajumbise polyherbal extract (APE) while those from the separate components were referred to by their individual names.

Table 1: Name of plants and parts used in *Ajumbise* polyherbal extract production

S/N	Botanical name	Local (Igbo) name	English name	Plant part used
1	*Barteria fistulosa* Mast.	*Oje*	-	Leaves
2	*Napoleona vogelii* Hook. and Planch.	*Nkpodanwaoba*	African nut tree	Leaves
3	*Euphorbia convolvuloides* Hochst. exBenth.	*Egele*	-	Whole plant
4	*Spondias mombin* Linn	*Ichikara*	Hog plum	Leaves
5	*Uvaria chamae* P.Beauv.	*Mmimiohia*	-	Stem
6	*Ceiba pentandra* (L.) Gaertn.	*Akpuogwu*	Cotton tree	Stem bark

Experimental Animals: Five rabbits (1.8 – 2.5 kg) and 101 rats (120 – 160 g) obtained from the Animal Production Unit of the College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike were used. They animals were housed under specific pathogen free conditions and were provided standard feed (Vital Feed, Nigeria) and water *ad libitum*, but starved for 12 hours before the commencement of experiments.

Ethical Approval: The study was carried out in the Physiology Laboratory of the Department of Physiology and Pharmacology, College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike, Nigeria in accordance with the standard protocols for use of laboratory animals (NIH Publications Number 80-23) (NIH, 2002), Ethical approval was obtained from the Ethics Committee of the host Department with reference number EC/VPP/016/005.

Acute Toxicity (LD_{50}) Evaluation of *Ajumbise* Polyherbal Extract: For the acute toxicity evaluation, a modified method of Lorke (1983) was adopted as was used by Chinedu *et al.* (2013). Three phases of tests were carried out on 21 rats. In the first phase, three groups of 3 rats each were administered 1000, 2000, and 3000 mg/kg BW of APE as treatments for groups 1, 2 and 3 respectively. With zero mortality observed in the first phase, the test proceeded to the second phase in which another 3 groups of 3 rats each were administered 4000, 5000, and 6000 mg/kg bw. With zero mortality still recorded the test proceeded to the final and confirmatory stage on a group of three rats which were administered the highest dose used (6000 mg/kg BW). Treatments in all cases were oral and mortalities were checked after 24 hours of treatment and a further seven days. The LD_{50}

was calculated using Lorke's formular thus: $LD_{50} = \sqrt{(D_0 \times D_{100})}$, where: LD_{50} = Lethal Median Dose, D_0 = Highest dose that gave no mortality and D_{100} = Lowest dose that produced 100% mortality

Effect of *Ajumbise* Polyherbal Extract and that of its Composite Plant Extracts on an Isolated Rabbit Jejunum: The method used by Uchendu (1999) was adopted. The abdomen of each of the five euthanized rabbit was cut open and the jejunum was isolated and transferred into a beaker of tyrode solution continuously bubbled with air and maintained at 37^0C. Tyrode solution per liter of distilled water was constituted by the dissolution of NaCl (8.0 g), KCl (0.2 g), $CaCl_2$ (0.2 g), $NaHCO_3$ (1.0 g), NaH_2PO_4 (1.0 g), $MgCl_2$ (0.1 g) and glucose (2.0 g). Three (3) cm of the jejunum was suspended vertically in a 30 ml organ bath by means of ligatures attached at one end to a tissue holder and at the other end to an isometric force displacement transducer connected to a digital physiograph and computer screen for displaying isometric contractions. Slack in the tissue was removed by readjusting the resting tension in the muscle strip. The mounted tissue was allowed to equilibrate within 30 minutes before regular rhythmic contractions were recorded to serve as basal values. Dose-response relationships were then established for acetylcholine, APE and the different extracts prepared from the individual components. The activity of acetylcholine was also challenged separately with atropine and APE to evaluate possible mechanism of action of the extract on the piece of tissue. A minimum time of 30 seconds was allowed for each administration for the recording of individual tissue responses before washing of the tissue three times with tyrode solution. Concentration of doses administered was presented as final bath concentrations (FBC). Percentage activity for each contractile response was calculated using the expression: Percentage activity = test amplitude – basal amplitude ÷ basal amplitude x 100. While for inhibitory response, it was: Percentage activity = basal amplitude – test amplitude ÷ basal amplitude x 100. FBC value for each dose applied was calculated using the relationship: FBC = C_IV_1/V_2. Where C_1 = Initial drug concentration, V_1 = Volume of drug added to tissue chamber, V_2 = Volume of the tissue chamber (30 ml in this case) and FBC values were expressed in micrograms per ml.

Effect of *Ajumbise* Polyherbal Extract and its Component Plant Extracts on Gastrointestinal Transit in Rats (*in-vivo*): Eighty rats were divided into 16 groups of 5 rats each and were treated orally except group 2 which was administered intraperitoneally. The rats were treated with 400 and 800 mg/kg corresponding to $1/15^{th}$ and $1/7.5^{th}$ respectively of the highest dose of 6000 mg/kg bw tested during the acute toxicity test.

Group 1 animals received 0.2 ml normal saline orally and served as the control group. Group 2 animals received 0.1 mg/kg Atropine and served as standard control. Group 3 animals received 400 mg/kg APE, Group 4 animals received 800 mg/kg APE, Group 5 animals received 400 mg/kg *B. fistulosa,* Group 6 animals received 800 mg/kg *B. fistulosa,* Group 7 animals received 400 mg/kg *N. vogelii,* Group 8 animals received 800 mg/kg *N. vogelii,* Group 9 animals received 400 mg/kg *E. convolvuloides,* Group 10 animals received 800 mg/kg *E. convolvuloides,* Group 11 animals received 400 mg/kg *S. mombin,* Group 12 animals received 800 mg/kg *S. mombin,* Group 13 animals received 400 mg/kg *U. chamae,* Group 14 animals received 800 mg/kg *U. chamae,* Group 15 animals received 400 mg/kg *C. pentandra* and Group 16 animals received 800 mg/kg *C. pentandra.*

Thirty minutes after treatment, 5 ml/kg body weight of activated charcoal meal was also administered orally to all the rats. In a further 30 minutes the animals were sacrificed by cervical dislocation and opened to isolate the full length of the small intestine which was measured and the length recorded. The distance travelled by the charcoal meal for each animal was also measured in centimeters and expressed as a percentage of the full length of the small intestine by the application of the formula: Percentage distance moved by charcoal meal = distance moved by charcoal meal ÷ full length of small intestine x 100.

Statistical Analysis: Data collected were subjected to statistical analysis using one way analysis of variance (ANOVA), while Turkey's post hoc test was used to obtain the specific significant differences among the treatment group means at $p<0.05$. Results were expressed as mean ± standard error of mean (SEM). All analysis was performed with IBM SPSS version 21.

RESULTS

Acute Toxicity Values of *Ajumbise* Polyherbal Extract: The result of acute toxicity study of APE showed no mortality at all doses administered. The animals instead had normal dispositions and retained their physical activities, except for the groups treated with 6000 mg/kg BW which were inactive immediately after administration but recovered before the end of 24 hours. The acute toxicity value of APE was therefore > 6000 mg/kg BW (Table 2).

Table 2: Acute toxicity evaluation of *Ajumbise* polyherbal extract

Phase	Group	Dose (mg/kg)	Number of deaths
1	1	1000	0/3
	2	2000	0/3
	3	3000	0/3
2	1	4000	0/3
	2	5000	0/3
	3	6000	0/3
3	1	6000	0/3

LD_{50} value is >6000 mg/kg bw

Effect of Acetylcholine, *Ajumbise* Polyherbal Extract and Component Plants on Gastrointestinal Smooth Muscle (*In-vitro*)

Effect of acetylcholine on the rhythmic activity of the rabbit jejunum: Each concentration of acetylcholine on application to the isolated induced significant increase ($p<0.05$) in the amplitude of contraction of the isolated rabbit jejunum when compared with basal value and occurred in a dose dependent manner (Figure 1).

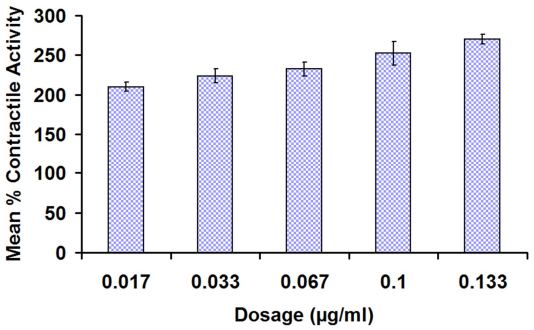

Figure 1: Effect of graded doses of acetylcholine on an isolated rabbit jejunum

Effect of *Ajumbise* polyherbal extract and the components on the rhythmic activity of the rabbit jejunum: The effect of APE on the same piece of isolated tissue was inhibitory in nature as each dose applied significantly lowered the amplitude of contractions when compared with basal amplitudes. Figure 2 is a comparison of the inhibitory effect of graded doses of APE and its components on the isolated rabbit jejunum. Extracts prepared from the various plant part components of *Ajumbise* when tested on the piece of isolated jejunum all produced varying degrees of inhibitory activities ($p<0.05$) when compared with basal contractions. However, *C. pentandra, N. vogelii, S. mombin* and *E. convolvuloides* had high inhibitory activities, while *U. chamae* and *B. fistulosa* had low inhibitory effects.

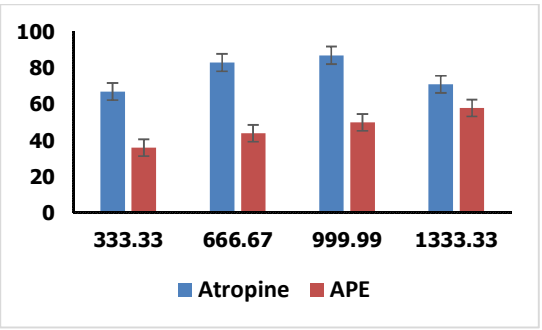

Figure 2: Comparison of the inhibitory effect of graded doses of *Ajumbise* polyherbal extract and its components on a isolated rabbit jejunum

The order of the inhibitory effects at 333.3 µg/ml was APE > *N. vogelii* > *C. pentandra* > *E. convolvuloides* > *S. mombin* > *B. fistulosa* > *U.*

chamae; at 666.67 µg/ml it was APE > *C. pentandra* > *S. mombin* > *N. vogelii* > *E. convolvuloides* > *B. fistulosa* > *U. chamae;* at 1333.33 µg/ml it was *C. pentandra* > *E. convolvuloides* > *S. mombin* > *N. vogelii* > APE > *B. fistulosa* > *U. chamae.*

Effect of atropine and *Ajumbise* polyherbal extract on acetylcholine induced contractions (*in-vitro*): The contractile effect of acetylcholine on the piece of isolated tissue in the presence of atropine was significantly lower ($p<0.05$) than that produced by acetylcholine when applied alone. APE also significantly inhibited ($p<0.05$) acetylcholine induced contractions. The blocking effect of atropine on acetylcholine contractions was however significantly higher ($p<0.05$) when compared with that produced by APE (Figure 3).

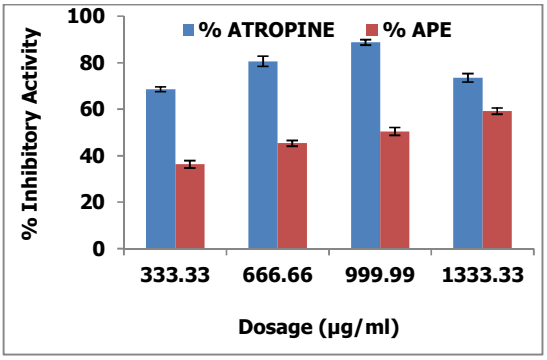

Figure 3: Comparing the effects of atropine and *Ajumbise* polyherbal extract on acetylcholine induced contraction

Effect of *Ajumbise* polyherbal extract and its component plants on gastrointestinal transit (*in-vivo*): Results of the *in-vivo* study showed that when compared with control, APE significantly inhibited ($p<0.05$) gastrointestinal motility and transit time in all treated rats. Extracts from the different plants constituents in the polyherbal also produced varying degrees of inhibitory effects with *S. mombin* and *C. pentandra* producing higher effects and *U. chamae* and *B. fistulosa* producing the least. The inhibitory effects of APE and that of its constituent plants were however lower than that of atropine, the standard drug used (Table 3).

DISCUSSION

In this study, the LD_{50} value for APE was found to be greater than 6000 mg/kg body weight, which translates into high margin of safety. Results of similar studies have shown that non-observance of mortality at doses up to 5000 mg/kg bw indicate a good measure of safety for any plant. This may be why Ajumbise has over the years being used as a medicinal agent in South-east Nigeria without any reported case of toxicity extract (Ijioma *et al.*, 2017b). In pursuit of the objectives of the current study, the results obtained showed that APE and extracts prepared from the various plants constituents in the polyherbal drug contain agents which can lower acetylcholine induced contractions of the gastrointestinal smooth muscle. Saponins, alkaloids and tannins have been reported to exhibit inhibitory effects by inhibition of the contractile mechanism (Gamaniel and Akah, 1996; Adeyemi *et al.,* 2009). The rabbit jejunum is indeed one of the smooth muscle preparations which on their own display spontaneous rhythmic myogenic activities under the control of the autonomic nervous system (Ijioma *et al.*, 2014b). Results obtained also suggest that the extracts may have achieved the observed gastrointestinal muscle relaxation activity via the anticholinergic pathway arising from possible interaction with muscarinic receptors in the gastrointestinal tract to lower acetylcholine activity. The smooth muscle of the gastrointestinal tract is host to numerous muscarinic receptors of both M_2 and M_3 subtypes. Either secreted *in-vivo* or administered *in-vitro*, acetylcholine molecules bind to this receptors to elicit contractile responses as a fall out of its effects on the circular and longitudinal muscles of the smooth muscle tissue (Osim, 2002). While the M_3 receptors does so by triggering phosphoinositide hydrolysis, Ca^{2+} mobilization and direct contractile response, M_2 subtype does same by inhibiting adenylcyclase and Ca^{2+} activated K^+ channels and potentiating Ca^{2+} dependent, non-selective conductance (Ehlert *et al.*, 1999; Eglen, 2001; Ehlert, 2003). The contraction of the jejunum like other smooth muscle tissues is brought about by an increase in cytosolic free

Table 3: Effect of *Ajumbise* polyherbal extract and its constituent plants on gastrointestinal motility (*in-vivo*)

Group	Treatment	Length of small intestine (cm)	Distance travelled by charcoal meal (cm)	Percentage movement of charcoal meal
1	Control	87.60 ± 1.86	80.40 ± 2.25	91.74 ± 5.77
2	Atropine (0.1 mg/kg)	84.80 ± 200	41.60 ± 3.59	49.07 ± 3.63
3	APE(400 mg/kg)	86.20 ± 3.14	70.40 ± 3.83	81.60 ± 2.61
4	APE(800 mg/kg)	89.20 ± 3.80	65.00 ± 6.66	72.60 ± 5.88
5	*Barteria fistulosa* (400 mg/kg)	83.10 ± 3.30	72.67 ± 3.21	87.44 ± 3.23
6	*Barteria fistulosa* (800 mg/kg)	91.30 ± 3.63	77.80 ± 2.11	85.21 ± 4.80
7	*Napoleonaea vogelii* (400 mg/kg)	89.70 ± 2.80	63.07 ± 4.01	70.31 ± 2.90
8	*Napoleonaea vogelii* (800 mg/kg)	89.20 ± 3.88	51.55 ± 3.91	57.79 ± 3.77
9	*Euphorbia convolvuloides* (400 mg/kg)	85.70 ± 4.80	56.20 ± 3.31	65.58 ± 3.09
10	*Euphorbia convolvuloides* (800 mg/kg)	82.33 ± 3.70	52.19 ± 2.81	63.39 ± 2.19
11	*Spondias mombin* (400 mg/kg)	88.20 ± 3.26	44.79 ± 2.68	50.78 ± 4.34
12	*Spondias mombin* (800 mg/kg)	90.71 ± 4.17	42.12 ± 2.09	46.43 ± 1.22
13	*Uvaria chamae* (400 mg/kg)	87.55 ± 2.98	78.97 ± 4.22	90.20 ± 2.75
14	*Uvaria chamae* (800 mg/kg)	86.43 ± 3.75	75.06 ± 3.33	86.84 ± 3.39
15	*Ceiba pentandra* (400 mg/kg)	88.20 ± 4.44	50.22 ± 2.13	56.94 ± 2.01
16	*Ceiba pentandra* (800 mg/kg)	93.78 ± 5.80	40.74 ± 2.81	43.44 ± 2.41

calcium levels and entry of same via voltage dependent Ca^{2+} which is one of the major mechanisms of calcium influx for the initiation of contraction in jejunum (Uchendu, 1999; Chokri *et al*., 2010). Therefore any process which antagonizes this acetylcholine effect ultimately brings about relaxation as was observed following the application of atropine and also reported by Rang *et al*. (2007). Blockage of calcium channels is another mechanism that produces smooth muscle relaxation (Chokri *et al*., 2010) which the extracts may have exploited. The relaxation produced by APE and its constituent plant extracts in the *in-vitro* experiment and corroborated by the *in-vivo* results suggest that the extract may contain principles with anticholinergic activities. Plants phytocomponents including terpenoids, steroids, flavonoids, tannins, saponins and glycosides have all been implicated in gastrointestinal smooth muscles relaxation (Zorofchian *et al*., 2013). These phytochemicals have been reported in APE (Ijioma *et al*., 2017a). Although all plant components in APE exhibited significant inhibitory activity on the gastrointestinal smooth muscle, *C. pentandra* appeared to have the highest mean activity particularly at higher doses suggesting that the implicated phytochemical agents may have being more in *C. pentandra.* Although there is paucity of information on the effects of the identified plants components in the polyherbal on smooth muscles, the report of this study is in agreement with the report that *S. mombin* leaves are traditionally used to treat diarrhea (Ayoka *et al*., 2008).

In a study carried out to determine the effect of *U. chamae* extract application on gastrointestinal smooth muscles showed that the extract produced significant smooth muscle relaxant and antispasmodic effects and as such was indicative of possible antidiarrheal and antiulcer potentials (Langason *et al*., 1994).The anti-ulcer and antidiarrhoeal activity of *C. pentandra* extract has also been reported (Anosike *et al*., 2014). No reports were found on previous gastrointestinal study carried out on *B. fistulosa, N. vogelii* and *E. convolvuloides,* except for Akomas and Ijioma (2014) had earlier reported on sympathetic effect of *Euphorbia hirta* on the gastrointestinal tract of rabbits.

Conclusion: Results of this study have shown that extract from *Ajumbise* polyherbal and those prepared from four of its constituent plants (*C. pentandra, N. vogelii, S. mombin* and *E. convolvuloides*) have shown significant

antimotility effect on the gastrointestinal tract smooth muscles and may therefore be of value in the management of diseases associated with excessive gastrointestinal contractions and over secretion of acetylcholine to the GIT due to above normal innervations of the tract by the parasympathetic arm of the autonomic nervous system.

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