**Abstract**

**Background:** The stem-bark extract of *Carpolobia lutea* (Polygalaceae), used in ethno-medicine as anti-diarrhea was pharmacologically evaluated. This was the first report of assessment of the ethanolic stem extract (ESE), of *C. lutea* as anti-diarrhoeal agent in rats. The anti-diarrhoeal effects, acute toxicity and ionic profile are investigated and reported.

**Materials and Methods:** The acute toxicity was established using Lock’s method. The anti-diarrhoeal effects were demonstrated using castor oil-induced diarrheal and fluid accumulation and its effect on normal intestinal transit. The mechanism elucidated using yohimbine, isosorbide dinitrate, and diphenoxylate. The elemental and ionic profile of ESE was established using inductively coupled argon-plasma emission spectrometer and potentiometric titration respectively. The finger print of ESE was revealed by Jasco (Tokyo, Japan), HPLC and active compounds by phytochemical screening using standard procedure.

**Results:** The LD₃₀ obtained is 866.025 mg/kg (i.p.). The doses of 43.3, 86.6, and 173.2 mg/kg of ESE showed inhibition of castor oil–induced diarrheal (p<0.05 - 0.001). The most abundant cations in the extract are potassium and phosphorus (1.00 ±0.01 and 0.80 ± 0.030 mg/g respectively); while the most abundant anions are phosphate and sulphate (33.50±7.09 and 7.19±3.29 mg/g respectively). The HPLC fingerprint of ESE revealed UV spectra of biomolecules. Phytochemical screening revealed presence of saponins, polyphenols and glycosides.

**Conclusion:** These investigations indicate presence of bioactive and elemental substances which could play major role in diarrheal management. This investigation justifies the use of stem-bark of *C. lutea* in illicit gin (akpatashi), among the Effiks in Nigeria as anti-diarrheal.

**Key words:** *Carpolobia lutea*, stem-bark extract, antidiarrheal, elemental and ionic profile.

**Introduction**

Diarrhea remains a major health challenge to the populations of most poor tropical countries and is the leading cause of morbidity and mortality in all age groups, with as much as four million cases occurring each year (Farthing, 2002). Heinrich et al. (2005) reported that WHO estimates that 3-5 billion diarrheal cases occur yearly (1 billion in children less than 5 years of age), and that approximately 5 million deaths are due to diarrheal annually (2.5 million in children less than five years of age), Martinez et al. (1998) demonstrated that, the form of treatment that is administered primarily to children, mothers inclusive are herbal remedies. The use of herbal substances for the treatment of ailments among Africans is as old as antiquities. The accessibility of herbal medicine practitioners, their inexpensive products and the consideration of traditional practice as part of African heritage by the generality of the population have created a big market for herbal products in Africa. Plants play important role in drug discovery, and their search through logical strategy in the search for new drugs (Andreto et al., 2006).

*Carpolobia lutea* G. Don (Polygalaceae) is a small tree distributed in West and Central African tropics. It grows in rainforest and Guinea savannah of Sierra Leon to Cameroon. It occurred as a dense overgrowth or, as an evergreen shrub or small tree that is up to 5 m high. *C. lutea* stem-bark has been used for headaches, general pain and the prevention of sleep due to fatigue. The root is reported to have aphrodisiac activity (Etebong et al., 2012). It has analgesic, anti-inflammatory properties, and is reputed to cure rheumatism, fever and to combat sterility. Others include insanity, dermat infection, venereal diseases, and promotion of child birth; taeniafuge and vermifuge (Burkill 1985; Etukudo 2003; Muanya & Odukoya, 2008). Pharmacological reports of investigations on the activities of the leaf material include anti-inflammatory and anti-arthritis (Iwu & Ayanwu, 1982), anti-ulcerogenic and anti-diabetes (Nwafor and Bassey, 2007), anti-hemorrhoid property (Soladoye et al., 2011), gastroprotective (Nwidu and Nwafor, 2009); antinociceptive (Nwidu et al., 2011a); anti-diarrheal mechanism (Nwidu et al., 2011b), antimicrobial (Nwidu et al., 2012a); neuropharmacological effects (Nwidu et al., 2012b), the amino acids, antioxidants and ionic profile (Nwidu et al., 2012c), anti-ulcer effects (Nwidu et al., 2012d) and anti-inflammatory and anti-pyretic effects (Nwidu et al., 2012e). Two new cinnamoyl 1-deoxyglucosides and cinnamic acid have been isolated from the leaf by semi-preparative HPLC, and the structures established by NMR (Nwidu et al., 2012b). In this study, we evaluated the fingerprint of the ESE, preliminary phyto-chemical screening, elemental and anionic evaluation and anti-diarrheal profile of the stem-bark extract of the plant on castor oil-induced diarrheal and fluid accumulation in addition to its activity on normal intestinal transit in rats. The choice of ethanolic extract is predicated on soaking the stem-back in illicit gin (akpatashi) by local people who use the plant in Nigeria.

**Materials and Methods**

**Collection of plant materials**

Collection of the plant was done in January, 2009. The stem-bark was collected from Itak- Ikot Akap village in Ikono Local Government Area of Akwa Ibom State. The plant was collected by an Herbalist Mr. Okon Etefie attached to Pharmacognosy Department in the University of Uyo, and identified by a Botanist named Dr (Mrs.) Margret Bassey of Botany Department in the University of Uyo. A voucher specimen (UUH 998), was...
deposited at the University Herbarium. The stem-bark was air-dried and powdered. The pulverized plant material were stored at room temperature until used.

**Preparation and extraction of plant materials**

The stem-bark collected was air-dried and pulverized using harmer mill. The powder plant materials were weighed using weighing balance (BG 4000). Five hundred grams of the stem-bark was weighed and immersed in 3 x 500 ml of ethanol (99.8%) for 72hrs. The soaked extract was shaken twice daily. The supernatant were filtered using Whatman filter paper (pore sizes-20-25µ). The filtrate of ethanol solvent was reduced in volume nearly to dryness in a rotatory evaporator (BUCCHI USA), at 40 °C. The residue from filtration process were air-dried for 24hrs, and subjected to the same procedure for three successive time. After which the extract was dried under a flow of nitrogen until constant weight was obtained. The yield was 43.4%. The extract was stored in an air tight container in a refrigerator until used. Prior to pharmacological assay, a sample of extract was dissolved in distilled water and used for the animal experiments.

**Finger Print Analysis**

The chromatographic fingerprint of the C. lutea stem-bark extract was established using a Jasco (Tokyo, Japan), liquid chromatograph equipped with a PU-2089, quaternary solvent pump, a MD-2010 PAD, and an AS-2055, autosampler injector with a 20 μL sample loop. The analytical column was a Phenomenex Synergi Hydro RP18, (250 × 4.6 mm i.d.; 4 μm), equipped with a Phenomenex security guard column (4.0 × 2.0 mm i.d.). The mobile phase composition was: water (eluent A), and metanol (eluent B), both containing 0.05% of TFA. The gradient program was linear starting with 0% B to 100% B in 60 min. The flow rate was 1.0 mL/min. EZChrom Elite Data System software (Chromatec, Idstein, Germany) was used for both the operation of detector and for data processing. The stem-bark extract (2 mg), was dissolved in 2 mL methanol, filtered through a 0.45-µm membrane polytetrafluoroethylene (PTFE), filter (Milllex), resuspended in 3 mL of water and 20 μL was surrendered to HPLC analysis.

**Phytochemical Analysis**

The ESE of C. lutea was subjected to qualitative chemical screening using standard procedure to reveal glycosides, polyphenols and saponins (Trease and Evans, 2001).

**Elemental analysis of the plant stem-bark**

The elemental component of ESE stem-bark of C. lutea was elucidated using the method of Dahlquist & Knoll, (1978) as reported for the C. lutea leaf fractions (Nwidu et al., 2012d).

**Determination of ionic content of plant stem-bark**

This determination was carried out by potentiometric titration as previously reported for leaf fractions (Nwidu et al., 2012d).

**Animals**

Swiss albino mice weighing between 25-30 g, and adult albino rats (100-150 g), of both sexes were obtained from the Faculty of Pharmacy Animal House, University of Uyo, Uyo, Nigeria. All the animals were housed in standard cages under laboratory condition in Department of Toxicology/Pharmacology in Niger Delta University to acclimatized the animals. All animals used have free access to tap water under standard conditions of 12 h dark 12 h light and temperature (21±1%). The animals were fed with pellet feeds (Vita Feed, Ibadan). The experiment were carried out between June to August 2012, in conformity with standard protocol for use of laboratory animals for experiments (Zimmerman, 1983). The protocols were approved by the Niger Delta University, Faculty of Pharmacy Institutional Animal Care and Use Committee which follows the guidelines of Committee for the purpose of control and supervision of experimental animals (CPSCEA; NDUFPAEC No. 2012/004).

**Drugs and chemicals**

Castor oil (Finest cold drawn commercial castor oil), Morphine (Morph) (Evans Medical Ltd., Liverpool), solvents from Reidel-de Haen (Germany) of analytical grade were used and while the pure drugs used are: Yohimbine Sigma, Aldrich (St. Louis, USA), Diphenoxylate (diph) and Isosorbide dinitrate, Isordil® (Actavis) (IDN). The ESE of C. lutea was dissolved in water and used in the experiment.

**Acute toxicity test (LD₅₀)**

The LD₅₀ of the ESE of C. lutea was estimated by procedure described by Lorke 1983, with modification. Albino mice (25-30 g), of either sexes were used. This method involved an initial lethal dose finding procedure, in which the animals were divided into seven groups of three (3), animals per group. Doses of 10, 100, 1000, 2000, 3000, 4000 and 5000 mg /kg were administered intraperitoneally (i.p), for each group of three mice. The treated animals were monitored for 24hrs, for mortality and general behavioral characteristic indicative of animal toxicity. The LD₅₀ was then estimated by taking the square root of the least dose that killed all the animals, and the highest dose that do not kill any animal/s or the geometric mean
of the lowest dose causing death and the highest dose causing no death. That is, LD_{50} is equal to (highest dose causing no death multiply by lowest dose causing death)^{1/2}

Castor oil-induced diarrhea

Adult albino rats (100-150g), fasted for 24hrs, but with free access to water were used. Water was withdrawn 2 hrs to bioassay. The rats were weighed and randomly allocated to seven groups of six rats each. Group I received 10 ml/kg of distilled water orally (p.o), group II-IV received 43.3, 86.6 and 173.2 mg/kg of ESE p.o. Group V received 5 mg/kg of morphine i.p, group VI and VII received 0.5 mg/kg of diphenoxylate (Diph), and 1 mg/kg of yohimbine intra-peritoneally respectively 15min., after oral administration of extract; 30 minutes later diarrhea was induced with 2 ml of castor oil. The onset time of stooling, the total mass of solid, semi-solid and wet faeces and the total faeces were recorded in each group. Diarrheal was evaluated using the procedure of Awouteur et al., (1978).

The parameter observed are: onset time of diarrhea, number of wet feces, the total frequency of fecal output and the total number of diarrhea episodes were counted per group for 4hrs. A numerical score based on stool consistency was assigned- 1 (normal stool), 2 (semi-solid stool), and 3 (watery stool). The onset time is measured as the time interval in minutes between the administration of castor oil and the first appearance of diarrhea stool.

Castor oil-induced fluid accumulation

Intraluminal fluid accumulation was determined by the method of Robert et al., (1976). The rats were fasted for 24hrs, but allowed free access to water. The rats were randomized and allocated to five (5), groups of six (6), rats per group. Group I (negative control); Groups II-V, were subjected to same treatment as in castor oil induced diarrheal above. One hour after the last dose of castor oil the rats were killed by cervical dislocation and the intestine exsanguinated. The small intestine was ligated both at the pyloric sphincter and at the ileocaecal junction, its contents were expelled into a graduated measuring cylinder, the volume and the weight of the intestinal contents were recorded according to the methods of Dicarlo et al., (1994) and Robert et al., (1976).

Small intestinal transit

Both sexes of male and female albino rats fasted for 24hrs, but allowed free access to water were used for the experiment. The rats were weighed and randomized into nine groups of six rats each. Group I received 10 ml/kg distilled water orally and 30 minutes later 1ml of charcoal meal orally. Groups II-IV, received 43.3, 86.6 and 173.2 mg/kg of ESE of C. lutea p.o. and 1ml of charcoal meal p.o. one hour after extract administration. Groups V-VII, received ESE (86.6 mg/kg p.o.); and 15 minutes later Diphenoxylate (0.5 mg/kg p.o.), Isosorbide dinitrate (150 mg/kg p.o.) and Yohimbine (1 mg/kg i.p.). Charcoal meal (1 ml p.o.) was administered to each group 30 minutes later. Group VIII-X, received Diphenoxylate (0.5 mg/kg p.o.), Isosorbide dinitrate (150 mg/kg p.o.), Yohimbine (1 mg/kg i.p.) and charcoal meal (1 ml p.o.) 30 minutes after the drugs administration to established mechanism antidiarrheal effects of extract. After 30 min, animals were killed by cervical dislocation, and the intestines were removed carefully without stretching and placed lengthwise on dissecting board. The length of the intestine (pyloric sphincter to cecum) and the distance travelled by the charcoal head as a percentage of total length were evaluated for each animal animal, and group means were compared and expressed as percentage inhibition (Lutterodt, 1989).

Statistical analysis

The results were expressed as the mean value ± SEM and significant was determined by Tukey’s Kramer multiple comparison (Linton et al., 2007). A probability level of less than 0.05 was considered significant.

Results

Phytochemistry

Analytical HPLC-PAD chromatogram recorded at 280 nm of the compounds of ethanolic stem extract of C. lutea after SPE clean-up is shown in Figure 1. The peaks are fingerprint of UV spectra and characteristic of bioactive compounds present in the ESE of C. lutea. A preliminary phyto-chemical screening gave positive test for saponins, polyphenols and glycosides.

Table 1: Cation content (mg/g) of Carpolobia lutea aqueous stem extract

<table>
<thead>
<tr>
<th>Samples</th>
<th>Cation content (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SEM</td>
<td>Na</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------</td>
</tr>
<tr>
<td></td>
<td>0.180 ± 0.020</td>
</tr>
</tbody>
</table>
The results of the elemental and anionic analysis of the plant stem-bark extract are shown in Tables 1 and 2. The results indicate that it contains significant amounts of cations which ranged from 0.05 ± 0.001 mg/g (for copper) to 1.00 ± 0.01 (for potassium). Heavy metal ion content (lead and mercury) were < 0.001. Anion contents of the plant ESE includes: PO$_4^{2-}$, SO$_4^{2-}$, CL$^-$, F$^-$, and NO$_3^-$ as shown in Table 2. The results indicate that the ESE contains phosphate (33.50 ± 7.09), sulphate (7.19±3.29), chloride (0.90±0.02), nitrate (0.97 ±0.02) and fluoride (< 0.2) mg/g of stem extract. The most abundant anions are phosphate and sulphate. The pH of the ESE was estimated as 4.6 ± 0.05.

**Table 2: Anionic content (mg/L)/pH of Carpolobia lutea ethanolic stem-bark extract**

<table>
<thead>
<tr>
<th>Samples</th>
<th>PO$_4^{2-}$</th>
<th>SO$_4^{2-}$</th>
<th>CL$^-$</th>
<th>F$^-$</th>
<th>NO$_3^-$</th>
<th>pH of ESE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SEM</td>
<td>3.35±7.09</td>
<td>7.19±3.29</td>
<td>0.90±0.02</td>
<td>&lt;0.200</td>
<td>4.6±0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3: Effects of ethanolic stem extract (ESE) of C. lutea on Castor oil-induced diarrhea in rats**

<table>
<thead>
<tr>
<th>Treatment (Dose mg/kg)</th>
<th>Onset time of stooling (mins)</th>
<th>Solid stool (g)</th>
<th>Semi-solid stool (g)</th>
<th>Watery stool (g)</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>32.30 ± 1.90</td>
<td>0.62 ± 0.25</td>
<td>0.78 ± 0.38</td>
<td>8.49 ± 0.92</td>
<td>0%</td>
</tr>
<tr>
<td>ESE 43.3</td>
<td>28.17 ± 2.07</td>
<td>0.62 ± 0.28</td>
<td>0.44 ± 0.24</td>
<td>4.59 ± 0.24</td>
<td>46%</td>
</tr>
<tr>
<td>ESE 86.6</td>
<td>28.33 ± 2.96</td>
<td>0.71 ± 0.23</td>
<td>0.63 ± 0.27</td>
<td>3.25 ± 0.36</td>
<td>62%</td>
</tr>
<tr>
<td>ESE 173.2</td>
<td>27.83 ± 2.07</td>
<td>1.05 ± 0.21</td>
<td>0.90 ± 0.28</td>
<td>2.22 ± 0.13</td>
<td>74%</td>
</tr>
<tr>
<td>ESE 86.6 + Diph 0.5</td>
<td>120.00 ± 3.66</td>
<td>0.96 ± 0.43</td>
<td>0.61 ± 0.24</td>
<td>0.44 ± 0.24</td>
<td>95%</td>
</tr>
<tr>
<td>ESE 86.6 + Yoh (1)</td>
<td>121.00 ± 7.00</td>
<td>1.42 ± 0.24</td>
<td>1.28 ± 0.27</td>
<td>1.26 ± 0.27</td>
<td>85%</td>
</tr>
</tbody>
</table>

Significance relative to control: *p<0.05, †p<0.01, ‡p<0.001; ns= not significant. Values represent mean ± SEM (n=6). Diph = Diphenoxylate; Yoh=Yohimbine.

**Table 4: Effects of ethanolic stem extracts of C. lutea on intestinal fluid accumulation in rats.**

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>Weight of intestinal content (g)</th>
<th>Volume of intestinal content (ml)</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.76 ± 0.37</td>
<td>1.98 ± 0.37</td>
<td>0.00%</td>
</tr>
<tr>
<td>ESE 43.3</td>
<td>1.40 ± 0.27</td>
<td>1.70 ± 0.20</td>
<td>20.40%</td>
</tr>
<tr>
<td>ESE 86.6</td>
<td>0.80 ± 0.27</td>
<td>1.10 ± 0.23</td>
<td>52.00%</td>
</tr>
<tr>
<td>ESE 173.2</td>
<td>0.97 ± 0.11</td>
<td>1.25 ± 0.18</td>
<td>45.00%</td>
</tr>
<tr>
<td>Morphine 5</td>
<td>0.72 ± 0.16</td>
<td>1.18 ± 0.18</td>
<td>59.20%</td>
</tr>
</tbody>
</table>

Significance relative to control: ns= not significant Values represent mean ± SEM (n=6).

**Table 5: Effects of ethanolic stem extract of C. lutea on normal intestinal transit in rats.**

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>Peristaltic index</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>77.79 ± 2.88</td>
<td>0.00%</td>
</tr>
<tr>
<td>ESE 43.3</td>
<td>63.59 ± 1.79</td>
<td>18.25</td>
</tr>
<tr>
<td>ESE 86.6</td>
<td>48.02 ± 2.13</td>
<td>38.27</td>
</tr>
<tr>
<td>ESE 173.2</td>
<td>54.05 ± 1.67</td>
<td>50.52</td>
</tr>
<tr>
<td>ESE + Diph 86.6 + 0.5</td>
<td>75.86 ± 3.61</td>
<td>2.48</td>
</tr>
<tr>
<td>ESE + IDN 86.6 + 150</td>
<td>64.00 ± 2.12</td>
<td>17.70</td>
</tr>
<tr>
<td>ESE + Yoh 86.6 + 1.00</td>
<td>68.1 ± 1.92</td>
<td>12.36</td>
</tr>
<tr>
<td>Diph 0.5</td>
<td>51.76 ± 3.72</td>
<td>33.46</td>
</tr>
<tr>
<td>IDN 150</td>
<td>66.19 ± 2.15</td>
<td>14.91</td>
</tr>
<tr>
<td>Yoh 1.00</td>
<td>47.86 ± 2.67</td>
<td>38.48</td>
</tr>
</tbody>
</table>
Significance relative to control: *p<0.05; †p<0.01; ‡p<0.001; values represent mean ± SEM (n=6). ESE; Ethanolic stem extract of the various dose range of the extract, Diph; Diphenoxylate, IDN; Isosorbide nitrate, Yoh; Yohimbine

Acute toxicity (LD₅₀)

The crude extracts produced mortality at the dose of 1500 mg/kg i.p. The crude ESE was found to be slightly toxic. The LD₅₀ was calculated to be 866.025 mg/kg. The lowest dose (43.3 mg/kg), middle (86.6 mg/kg) and highest dose (173.2 mg/kg), utilised for this bioassay is estimated from 1/20th, 1/10th and 1/5th of LD₅₀ (866.025 mg/kg).

Effect on Castor oil-induced diarrhea

The ESE of *C. lutea* (43.3-173.2 mg/kg), significantly (p<0.001) reduced the number of wet stool (purging frequency) of diarrheal episodes as shown in the Table 3 below. The effect of ESE of *C. lutea* on onset time (Figure 2) reveals only significant effect on watery stool. The extract alone does not have significant effects on onset time of diarrheal, weight of solid and semi-solid stool but only watery stool when compared to the control. The ESE produce a dose dependent inhibition of watery stool with the highest dose of the extract (173.2 mg/kg), producing 74.0% inhibition of diarrheal (wet) stool but no significant effect on solid and semi-solid stool. The middle dose of extracts (86.6 mg/kg) plus 0.5 mg/kg Diphenoxylate or 1 mg/kg Yohimbine produced a marked increase in onset time of stooling and a reduction in diarrheal stool but no significant effect on solid and semi-solid stool. The pure drug morphine (5 mg/kg) prolonged the onset time in diarrheal stool in a statistical significant manner (p<0.001) and exhibited 90% inhibition of diarrhea.

![Fig 2: Effect of *C. lutea* stem extract onset time in castor induced diarrhoea](image)

**Effect on Castor oil-induced fluid accumulation (Intestinal fluid accumulation)**

Castor oil-induced water and electrolyte accumulation in intestinal loop was antagonised in a dose dependent manner (p>0.05) when compared to the control Table 4). The doses of ESE of *C. lutea* (43.3-173.2 mg/kg) were found to inhibit fluid accumulation by 20-45% while the pure drug, morphine exhibit 59% inhibition.

**Effect on small intestinal transit**

The administration of ESE of *C. lutea* (43.3-173.2 mg/kg), significantly reduced the intestinal propulsive movement of charcoal head in dose dependent manner (p<0.05 - 0.001) when compared with the control group. The percentage inhibitions of intestinal transit in *C. lutea* pre-treated groups (43.3-173.2 mg/kg), are 18.25 %, 38.27% and 30.52% respectively. The elucidation of mechanism of anti-diarrhoeal effects of ESE was reveal by combination of the middle dose of ESE (86.6 mg/kg) with Diphenoxylate (0.5 mg/kg); ESE (86.6 mg/kg) with Isosorbide dinitrate (150 mg/kg) and ESE (86.6 mg/kg) with Yohimbine (1 mg/kg). The pure drugs antagonizes the intestinal transit time producing marked reduction of inhibition of diarrheal to 2.5%, 17.7% and 12.5% respectively. The result is shown in Table 5.

**Discussion**

Many plants with anti-diarrhoeal activities are widely distributed in Nigeria and have been reported by Soladoye et al., (2010), but very few have been subjected to pharmacological screening and elemental analysis. Human health could benefit maximally from nature if the correct amounts of the elements are taken in its ionic varieties in the right form and at the right time. The medicinal values of some plant species used in homeopathic system has been traced to the presence of Ca, Cr, Cu, Fe, Mg, Ca, K and Zn in plants (Perma et al., 1993). Elements have been reported to play major role as co-factors of various enzymes and in various metabolic processes (Mayer and Yykchky, 1989). The ESE of *C. lutea* contain high amount of potassium compared to other element. The potassium may exist as potassium phosphate or sulphate. Potassium replacement during acute diarrhea prevents below-normal serum concentrations of potassium, especially in children, in whom stool potassium losses are higher than in adults (Black et al., 2003) and it is a constituent in oral rehydration salt.
This research work revealed that ESE of *C. lutea* contains pharmacologically active substance(s) which mediates antidiarrheal properties by inhibition of intestinal motility through muscarinic, α-adrenoceptor and nitrous oxide dependent pathway. This was not the case on castor oil-induced diarrheal in which the inhibition of diarrheal by the extract was potentiated by either diphenoxylate or yohimbine through a mechanism yet to be elucidated. α2-adrenergic agents mediating reduction of diarrheal through increase in intestinal transit time may have special role in diabetics with chronic diarrhoea, in whom autonomic neuropathy can lead to loss of noradrenergic innervations (Jafri and Pasricha, 2001). The bioactive and elemental substances present in the extract could play major role in diarrheal management. These investigations gave credence to wide patronage of stem-bark extract in illicit gin or ethanol otherwise called ‘akpatashi’ in the ethnomedicinal management of chronic diarrhea in diabetes by the Effiks of Nigeria.

**Acknowledgement**

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Declaration of interest

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