

Comparative Effect of Cold Hydro Stem-Bark Extract of *Erythrophleum Suaveolens* on Gastrointestinal Muscle of Rabbit Jejunum (*Oryctolagus Cuniculus*)

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Abstract Detailed investigations on plant materials especially such that are already in use especially by tradio-practionals should not be taken with levity. The effect of cold water crude extract of stem-bark of *Erythrophleum suaveolens* on the activity of an isolated rabbit jejunum was studied. Reference drugs (Adrenaline and Isoprenaline) were used both in the presence and absence of *E. suaveolens* extract. Preliminary pharmacological investigation of the extract revealed inhibitory effects. However, the relaxative effect of the extract on isolated smooth muscle was confirmed from its cumulative response on Rabbit jejunum in which there was a graded inhibition of the jejunal contraction even up to 95% - 95.5%. The result of the study therefore suggest that the extract has the potential of been develop as an anti-motility agent as a remedy for GIT system related problems.

Keywords: *Erythrophleum suaveolens*, *Oryctolagus cuniculus*, Gastrointestinal Muscle, Jejunum, Inhibitory effect

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1. Introduction

The knowledge of the effect(s) of substances to be used as medicines on different body systems is very vital in drug development vis – a vis drug safety [1]. *E. suaveolens* is a perennial tree of about 30 m in height, slightly buttressed, often low-branching and producing a dense spreading crown. The plant is one of the useful plants of west tropical Africa which is referred to by various names by natives [2-7]. As drinks, the bark is used as alcoholic and stimulant as well as laxative, abortifacient, antibiotics, and in the treatment of oedema, gout, rheumatism amongst others in the area of medicine [8]. Investigations carried out on the isolated ileum tissue of the guinea-pig (*Cavia porcellus*) by running a dose-response relationship of the agonist test drugs (Acetylcholine, Histamine, and Barium Chloride) in the presence of the cold water crude extract of stem-bark of *Erythrophleum suaveolens* ascertained antagonist nature of the extract with a shift to the right [9]. The determination of LD₅₀ on albino mice gave an insight into safety margin of *E. suaveolens* (223.8±0.05 mg/kg body weight) falling within the very toxic range as defined by Hodge and Sterner (1947) categorization [10].

It is a well-established observation that inhibition in the small intestine is mediated by α - and β -adrenoreceptors [11,12]. In the guinea-pig ileum, it would seem that the

actions of adrenaline and nor-adrenaline are mainly on neuronal elements [13,14,15], whereas the effect of Isoprenaline is mainly on the muscle [13]. Evidence, however showed that α -adrenoreceptors are also situated on the smooth muscle cells in the guinea-pig taenia coli and the rabbit small intestine, [16,17].

The foregoing findings have been further analyzed by examining the effects of phenoxy-benzamine and propranolol on the inhibitory actions of catecholamines on acetylcholine release and on the responses of the longitudinal muscle of the guinea-pig ileum to electrical stimulation. Preliminary reports of some of the results have been made to the Pharmacological and Physiological Societies [18,19,20] and to the International Symposium on Gastro-Intestinal Motility in September, 1967 [21]. According to Couper in 2007, in addition to neuronal muscarine receptors, the guinea pig Ileum contains postsynaptic muscarine receptors which mediate the contraction of the smooth muscle [22].

1.1. Statement of Problem

Investigations carried out on the isolated ileum tissue of the guinea-pig (*Cavia porcellus*) by running a dose-response relationship of agonist test drugs (Acetylcholine, Histamine, and Barium Chloride) in the presence of the cold water crude extract of stem-bark of *Erythrophleum*

suaveolens ascertained antagonist nature of the extract with a right shift [9].

Detailed investigations on plant materials especially such that are already in use especially by tradio-practionals should not be taken with levity. As a result of need for further confirmation of the blockade / inhibitory effect of cold water bark extract of *E. suaveolens* on other smooth muscles of the GIT.

1.2. Aims and Objective

The objective of this study is to investigate the effect of cold water extract of the stem-bark of *E. suaveolens* on the rhythmic activity of an isolated rabbit's jejunum in comparison with the activity of selected standard drugs.

2. Materials and Methods

2.1. Plant Preparation and Extraction

Stem-bark of *Erythrophleum suaveolens* were collected from Buruku Local Government area of Benue State, Nigeria. Identification and authentication were done by a plant taxonomist with the Federal School of Forestry, Mr Okonkwo Jos Plateau State, Nigeria and Professor S.W Husseni of the Department of Botany, University of Jos, Nigeria.

The bark was dried under the shade, in the Pharmacology Research Laboratory of the University of Jos, Nigeria. Sample was pulverized using wooden Mortar and Pestle according to the method of Ibrahim *et al.* (1984); Audu *et al.* (2001). The pulverized was stored at room temperature until required (Idyu *et al.*, 2014a). 100 g of powdered stem-bark of the plant was weighed out in 1000 ml capacity Pyrex glass beaker. This was dissolved in 200 ml of distilled water according to the method of Audu *et al.* (2001). The mixture was allowed to stand for 24 hours at ambient room temperature. Mixture was stirred with a glass rod and then filtered through Whatman number one filter paper, using suction pump. The filtrate was concentrated in a water bath at a temperature of $80 \pm 1.0^\circ\text{C}$ until a reddish, sticky extract was obtained. This gave a yield of 6.125 g of the extract from 100 g powdered sample. The recovered extract was stored in the Refrigerator at -4°C (Idyu *et al.*, 2014a). 1.0 g of crude water extract was weighed and dissolved in 10ml of distilled water to give a stock concentration solution of 1×10^{-1} g/ml (100 mg/ml). Other concentration used for the test were prepared by diluting 1 ml of stock solution in 9ml of distilled water (1:9) to give 1×10^{-2} g/ml. Various concentrations were obtained through serial dilutions of the series as appropriate throughout the experiment.

2.2. Animals and Tissue Preparation

Adult sized rabbits (3.8-4.5 kg) of both sexes *American chinchilla* (*Oryctolagus cuniculus*) were purchased in cages from the Veterinary Research Institute, Vom, Nigeria. These were allowed to acclimatize, fed with spinach, cabbages and clean water *ad libitum* for 7 days, maintained at NEV temperature ($26-28^\circ\text{C}$) and deprived of food 24 hours before commencement of experiment.

The rabbits were sacrificed by a blow to the head and exsanguination after which the abdomen was cut open and segment of the jejunum dissected, trimmed to remove

adhering mesentery, divided into 2-3 cm segments. The fresh tissue was then secured to a tissue holder and then suspended in a 50 ml isolated organ bath containing freshly prepared physiological solution (Tyrode), pH(7.4), aerated with 95% and 5% CO_2 oxygen and maintained at 37°C . The effects of Adrenaline, Isoprenaline and Extract were tested on strips of jejunum strips while responses were isometrically recorded on recording paper via student physiograph stimulator (Labotech ss-700 BD instrumentation india).

2.3. Reference Drugs and Reagents

The drugs and the reagents used were of standard analytical grade- Adrenaline (1×10^{-3} g/ml) and Isoprenaline (1×10^{-3} g/ml). The reference drugs were prepared by weighing out and dissolving in required volume of distilled water to give desired stock concentration. Various dilutions from stock were made for each experiment, while Sodium Chloride, Calcium Chloride, Magnesium Chloride, Sodium Hydrogen-Trioxocarbonate (IV), Sodium Dihydrogen Phosphate and Glucose for preparation of physiological salt solution. These were products of Sigma Chemical Company, Louis, USA, Burgoynes & Co, India, BDH Chemical Ltd. Poole, England, Kernel Chemicals, Germany and Hopkin & Williams Ltd. England (Idyu *et al.*, 2014b).

The reference drugs were prepared by weighing out and dissolving in required volume of distilled water to give desired stock concentration. Various dilutions from stock were made for each experiment.

2.4. Drugs and Crude Extract Investigations

Drug activities were investigated on the isolated jejunum tissue by way of arithmetic progression volume to obtain dose- responses using varying volumes (0.1ml, 0.2 ml, 0.4 ml and 0.8 ml): in the following order:

- Adrenaline (1×10^{-5} g/ml) alone
- Isoprenaline (1×10^{-5} g/ml) alone
- E. suaveolens* extract (1×10^{-2} g/ml)

3. Results

Figure 1, Figure 2, Figure 3 illustrate tracings obtained from administration of Adrenaline, Isoprenaline and of crude extract of stem-bark of *E. suaveolens* respectively. Tables and graphs 1, 2, 3 illustrate same while graph 4 shows the combined plot of the two standard drugs and extract.

3.1. Tracings Showing the Effect of Drugs on Rabbits Jejunum

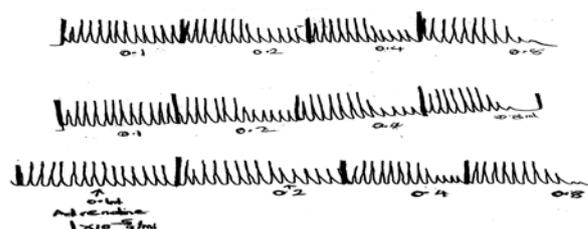


Figure 1. Adrenaline

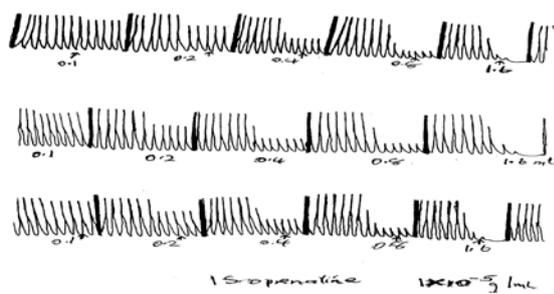
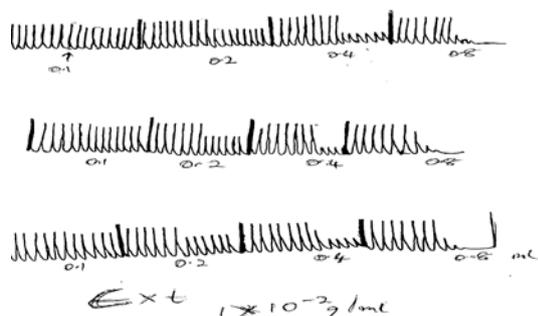


Figure 2. Isoprenaline

Figure 3. *E. suaveolens* Extract

3.2. Dose-response Relationship of Drugs on Rabbits Jejunum

Table 1. Adrenaline alone

| Conc. Of Adr. (g/ml) | Vol. of Adr. (ml) | FBC (g/ml) | Log FBC | Mean Inhibition (cm) (%) Max. |
|----------------------|-------------------|----------------------|---------|-------------------------------|
| 1×10^{-5} | 0.4 | 2×10^{-8} | -7.69 | 0.33 17.37 |
| 1×10^{-5} | 0.6 | 4×10^{-8} | -7.39 | 0.77 40.53 |
| 1×10^{-5} | 1.0 | 8×10^{-8} | -7.09 | 1.06 55.79 |
| 1×10^{-5} | 1.8 | 1.6×10^{-7} | -6.79 | 1.90 100.00 |

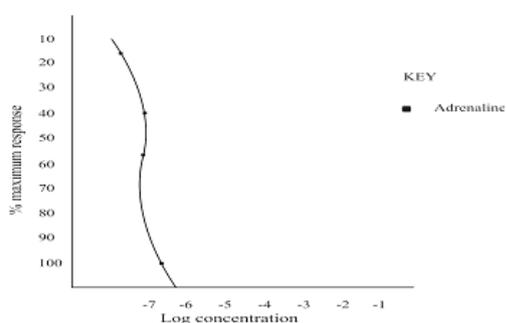
Table 2. Isoprenaline alone

| Conc. Of Isopr. (g/ml) | Vol. of Isopr. (ml) | FBC (g/ml) | Log FBC | Mean Inhibition (cm) (%) Max. |
|------------------------|---------------------|----------------------|---------|-------------------------------|
| 1×10^{-5} | 0.1 | 2×10^{-8} | -7.69 | 0.30 10.83 |
| 1×10^{-5} | 0.2 | 4×10^{-8} | -7.39 | 0.97 35.02 |
| 1×10^{-5} | 0.4 | 8×10^{-8} | -7.09 | 1.57 56.68 |
| 1×10^{-5} | 0.8 | 1.6×10^{-7} | -6.79 | 2.30 83.03 |
| 1×10^{-5} | 1.6 | 3.2×10^{-7} | -6.49 | 2.77 100.00 |

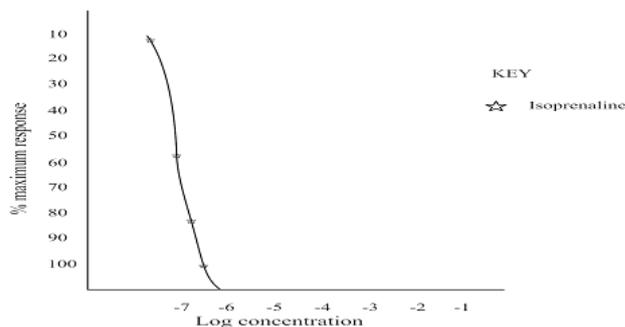
Table 3. Extract alone

| Conc. Of Extract (g/ml) | Vol. of Extract (ml) | FBC (g/ml) | Log FBC | Mean Inhibition (cm) (%) Max. |
|-------------------------|----------------------|----------------------|---------|-------------------------------|
| 1×10^{-2} | 0.1 | 2×10^{-5} | -4.699 | 0.17 8.95 |
| 1×10^{-2} | 0.2 | 4×10^{-5} | -4.39 | 0.70 36.84 |
| 1×10^{-2} | 0.4 | 8×10^{-5} | -4.09 | 1.27 66.84 |
| 1×10^{-2} | 0.8 | 1.6×10^{-4} | -3.80 | 1.90 100.00 |

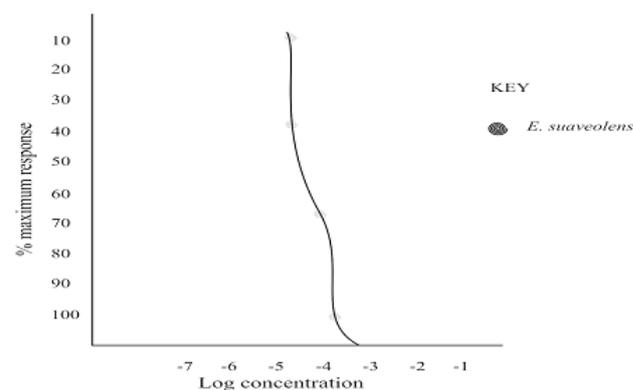
Graph 1:



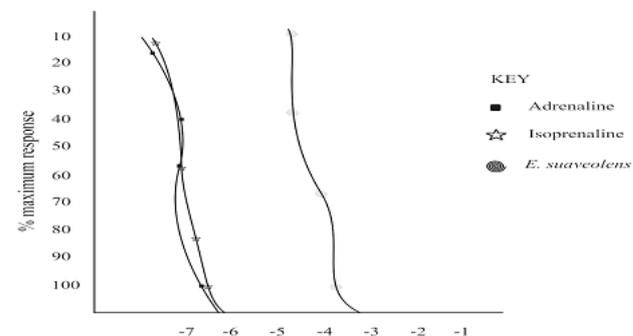
Graph 2:



Graph 3:



Graph 4:



4. Discussion

Effects of standard drugs and *E. suaveolens* on the isolated tissue are highlighted below:

4.1. Adrenaline

The effect of adrenaline on the isolated rabbit jejunum, which acts on the β_2 receptors, was gradual inhibition. At lower doses, the inhibition were minimal, thus a doses dependent inhibitory rhythmic activities as expected (Table 1; Figure 1; Graph 1).

4.2. Isoprenaline

The drug acts through the β_2 receptors on the rabbit jejunum. A gradual inhibition was observed also with minimal inhibition at lower doses and blockade of rhythmic activity of same isolated tissue at higher doses as expected (Table 2; Figure 2; Graph 2).

4.3. Extract

The effect of the *Erythrophleum suaveolens* extract on the isolated rabbit jejunum was also a gradual inhibition as at lower doses, the inhibition was minimal and at higher doses, reduced rhythmic activities, thus a blockade.

Preliminary pharmacological investigation of the extract revealed inhibitory effect agrees with Idyu 2014b. This suggests that the extract interfered with the mechanism(s) of the jejunal rhythmic activity. Extract has an anti-diarrheal tendency due to the inhibitory nature hence may contain flavonoid. The presence of flavonoid in plant extract could be responsible for their anti-diarrheal activities. This justifies the ethno medicinal use of the plants [22].

The therapeutic effect could also be due to its anti-motility and anti-secretory properties. A comparison of pre- and postsynaptic activities of drugs in one and the same tissue has been carried out previously in experiments on peripheral adrenergic neuroeffector junctions [15]. Fozard and Mushcholl found similar potencies for pre- and postsynaptic effects of a series of muscarinic agonists in the perfused rabbit heart. They, therefore, concluded that similar receptors mediate inhibition of arterial tension, ventricular rate and neuronal nor-adrenaline release [23].

5. Conclusion

The gradual inhibitory effect at lower doses and minimal / reduced rhythmic activities exhibited by the cold water bark extract of *E. suaveolens* on the isolated rabbit jejunum compares with that of the standard drugs (Adrenaline and Isoprenaline) thus, portray dose dependent inhibitory rhythmic activities. However, the relaxative effect of the extract on isolated smooth muscle was confirmed from its cumulative response on Rabbit jejunum in which there was a graded inhibition of the jejunal contraction even up to 95% - 95.5%. The result of the study therefore suggest that the extract has the potential of been develop as an anti-motility agent as a remedy for GIT system related problems.

5.1. Recommendation

Further studies on phytochemistry and confirmation on the anti-diarrheal activities as well as the effect on other smooth and skeletal muscles are recommended.

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Conflicting Interest

No conflict of interest.

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