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PHARMACOGNOSTIC EVALUATION, NEUROBEHAVIORAL AND ANALGESIC STUDY OF THE ETHANOL BARK EXTRACT OF *TERMINALIA IVORENSIS* A. CHEV (COMBRETACEAE)

Gina Flor C. Ramos¹, Nyerovwo Dian Onayomake¹ and *Emmanuel Ifeanyi Obeagu²

¹Department of Pharmacognosy, Faculty of Pharmacy, Madonna University Nigeria, Elele Campus, Rivers State, Nigeria

²Department of Medical Laboratory Science, Kampala International University, Uganda.

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Abstract

Terminalia ivorensis A. Chev (Combretaceae) is a medicinal plant used in folk medicine in the management of pain, rheumatic condition, gastroenteritis and as a tranquilizer in psychotic disorder. The sample was washed, air-dried and milled. The moisture content of the milled sample was measured 0.7%, Total ash value of 6.5%, Water extractive value of 3.5% and Alcohol extractive value of 1.45%. The crude extract was screened for the presence of some phytoconstituents and was found to contain Saponins, Flavonoids, Tannins, and traces of alkaloid. This study evaluated the pharmacognostic, neurobehavioral and analgesic activities of the ethanol bark extract of *T. ivorensis* (EBETI). Effects of EBETI (20, 40, and 60 mg/kg) on novelty-induced behaviours were determined using novelty induced rearing and grooming test and open field test. Analgesic property of EBETI (40, 60, and 80 mg/kg) was evaluated using acetic acid induced writhing, and tail immersion tests. The extract was administered once intraperitoneally. The LD₅₀ of EBETI was 89.44mg/kg. EBETI (20, 40, and 60 mg/kg) significantly reduced rearing and grooming as compared with controls. EBETI (40, 60, and 80 mg/kg) significantly inhibited abdominal constriction in writhing assay as compared with control. However, the extract could not alter response to thermal stimulus in tail immersion test. Therefore, EBETI is sedative and has

analgesic effect, thus supporting its folkloric use in pain management and as a tranquilizer.

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*Corresponding Author:- Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda.
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Introduction: -

Herbal medicine is an important part of health care in Africa. Herbs are widely exploited in the traditional medicine and their curative potential are well documented [1-7]. Therapeutics effects of many indigenous plants for several disorders have been described by several practitioners of traditional medicine and thereby improve quality of life, accessibility and affordability among rural population of tropical Africa [8]. Medicinal plant is any plant in which one or more of its organs contain substances that can be used for therapeutic purposes [9-12] and drug derived from natural sources play a significant role in the prevention and treatment of human diseases, it is estimated that 400,000 places such as Ghana. The bark is also harvested from the wild for local use as a medicine and dyestuff species of tropical plants have medicinal properties[13-19].

Terminalia ivorensis also known as Black afara is a large deciduous forest tree ranging in height from 15 to 46 meters. The bole is very straight with small buttresses and is sometimes also fluted. It can be branchless for up to 30 meters with a diameter from 2 - 4.75 meters in diameter. Mature trees are very flat topped with a wide horizontal canopy of evenly distributed foliage arising from the apex of the straight bole. It sometimes loses its vertical-growing leader, resulting in considerable variation in the height of mature trees. It is also cultivated as a shade tree in cacao plantations in some.

PLANT COLLECTION

Barks of *Terminalia ivorensis* were collected in May 2019 at 8pm at Madonna University Elele, Rivers state, Nigeria.

MICROSCOPY AND CHEMOMICROSCOPY EVALUATION

MICROSCOPY OF FRESH PLANT MATERIAL

The fresh bark sample was washed, cut into smaller pieces and placed into 70% chloral hydrate solution in a test tube in a water bath to clear the cells. The cleared bark sample was then placed on a slide and viewed under the microscope.

MICROSCOPY OF POWDERED BARK

A small quantity of powdered crude drug was placed on a slide and few drops of chloral hydrate solution were added to it. The mixture was passed across the flame of a Bunsen burner repeatedly until bubbles occurred and then allowed to cool for proper clearing of the sample.

CHEMOMICROSCOPY

The chemomicroscopy of the plant material was carried out under the following headings:

TEST FOR LIGNIN

Powdered bark mounted in a few drops of phloroglucinol and concentrated hydrochloric acid and observed under a microscope for a pink-red fibre colouration.

TEST FOR STARCH

Powdered bark mounted in a few drops of iodine solution and observed under the microscope for a blue black colouration. (Trease and Evans 2008)

TEST FOR CALCIUM OXALATE

Powdered plant mounted in a few drops of chloral hydrate and observed under a microscope for calcium oxalate crystals to disappear. (Trease and Evans 2008)

TEST FOR CUTIN

Powdered plant mounted in a few drops of Sudan III solution and observed under a microscope for a red colouration. (Trease and Evans 2008)

TEST FOR CELLULOSE

Powdered plant mounted in a few drops of iodine solution and 80% sulphuric acid solution and observed under a microscope for a blue-black colouration.

EXTRACTION

Air-dried three hundred gram (300g) of plant bark were pulverized and soaked in Absolute ethanol (700mL) for 48 h and then filtered with muslin cloth. The filtrate was then concentrated with a rotary evaporator to give a semisolid residue and evaporated to dryness to form solid residue. It was kept in the desiccator for further use. The dried extract was subsequently reconstituted in distilled water at appropriate concentrations for the various experiments. The weight of the dried extract was obtained using a sensitive weighing balance and the percentage yield was calculated.

PROXIMATE ANALYSIS**MOISTURE CONTENT DETERMINATION**

A porcelain crucible was placed in a muffle furnace for about 20 minutes at 35°C, cooled in desiccators for about 40 minutes and the crucible was weighed (W1), 3g of the sample was weighed into the preheated porcelain crucible and reweighed (W2) and then placed in the furnace for 2 hours. After 2 hours, the crucible was brought out and put in a desiccator to cool for 30 minutes and then reweighed (W3). After weighing the crucible was put back into the furnace for 30 minutes and brought out again, cooled in a desiccator for 30 minutes and reweighed (W4). This was done repeatedly until a constant weight was obtained.

TOTAL ASH VALUE

A porcelain crucible was placed in a muffle furnace for about 15 minutes at 35 c , cooled in a desiccator for about one hour and the crucible was weighed (W1). 3g of the sample is accurately weighed into the preheated porcelain crucible and reweighed (W2). The sample is ash in a muffle furnace at 650 c for 6 hours until the sample turns grey (white ash). The crucible is removed with a crucible tong, cooled in a desiccator and reweighed (W3). The percentage ash content is determined by the relationship.

ALCOHOL EXTRACTIVE VALUE

Two grams of the sample was macerated in 100mls of absolute ethanol for 24 hours and filtered. The filtrate was dried in the oven at the temperature of 105°c to obtain a constant weight dry extract which was cooled in a desiccator. The weight of the dried extract was determined and recorded (Inya-Agha, 2006).

PHYTOCHEMICAL ANALYSIS AND CHROMATOGRAPHIC ANALYSIS**TEST FOR CARBOHYDRATES**

One-half of the plant extract was boiled with 2ml of distilled water and filtered. Few drops of naphthol solution in ethanol (Molish reagent) was added to the filtrate and concentrated sulphuric acid was then gently poured down the side of the test tube to form a lower layer. A purple interfacial ring indicates the presence of carbohydrates.

TEST FOR PROTEINS

One-half gram of the extract dissolved with 200ml of distilled water, filtered and the filtrate was used for the following tests.

Million's test

To a little portion of the filtrate in a test tube, 2 drops of million's reagent was added. A white precipitate indicates the presence of proteins

TEST FOR TANNINS

One-half gram of the extract was boiled with 20ml of water, filtered and used for the following tests

Ferric chloride test

To 3ml of the filtrate, few drops of ferric chloride were added. Formation of a greenish black precipitate indicates the presence of tannins.

TEST FOR SAPONINS

200ml of distilled water was added to 0.5g of the extract and boiled on a hot water bath for 2minutes and filtered. The filtrate was allowed to cool and then used for the following tests

Frothing test

5ml of the filtrate was diluted with 15ml of distilled water and shaken vigorously. Formation of stable froth indicates the presence of saponins.

TEST FOR ALKALOIDS

Twenty ml of 3% sulphuric acid in 50% ethanol was added to 2g of the extract and heated on a boiling water bath for 10 minutes, cooled and filtered. 2ml of the filtrate was tested with few drops of Mayer's reagent (Potassium mercuric iodide solution), Dragendorff's reagent (Bismuth potassium iodide solution), and picric acid solution (1%). Alkaloids give milky precipitate with Mayer's reagent; reddish brown precipitate with Wagner's reagent; yellowish precipitate with picric acid and brick red precipitate with Dragendorff's reagent.

TEST FOR FLAVONOIDS

Four ml of the filtrate was shaken with 1ml of dilute ammonia solution. The layers were allowed to separate. A yellow colour in the ammoniacal layer indicates the presence of flavonoids.

CHROMATOGRAPHY**Thin layer chromatography**

A developing solvent (methanol to n-hexane 1:1) was poured into a TLC chamber covering the bottom of the chamber to a depth of 0.5cm. It is covered so that evaporation does not change the composition of the solvent. A precoated TLC plate which has been pre-cut was activated in an oven at 105 °c for 30 minutes then at 2cm from the bottom of the plate, 8 dots were made. The different extracts (water, methanol and n- hexane extracts) were then applied to the plate by using an applicator to quickly touch the plate with each extract on two dots after which they were left to dry for 10 minutes then they were carefully placed into the chamber. It was then allowed to develop. The TLC plate was then removed from the chamber when the solvent front was approximately 3.0cm from the top of the plate. After that was done, the solvent was allowed to evaporate from the TLC plate. The UV lamp was then turned on, and the colour of the spots noted. The distance travelled by the solvent and the solutes were both measured, and RF value calculated.

RF (retention factor) = Distance travelled by the solute/ Distance travelled by the solvent.

GAS CHROMATOGRAPHY EXTRACTION OF PHYTOCHEMICALS

5g of the sample was weighed and transferred in a test tube and 15ml of ethanol was added. The test tube was allowed to react in a water bath at 60°C for 60 minutes. After the reaction time, the reaction product contained in the test tube was transferred to a separating funnel. The tube was washed successfully with 20ml ethanol, 10ml of cold water, and 10ml of hot water and 3ml of hexane, which was all transferred to the funnel. This extracts were combined and washed three times with 10ml of 10%v/v ethanol aqueous solution. The solution was dried with anhydrous sodium sulphate and the solvent was evaporated. The sample was solubilized in 1000ul of hexane of which 200ul was transferred to a vial for analysis.

QUANTIFICATION BY GC-FID

The analysis of phytochemical was performed on a BUCK M910 Gas chromatography equipped with a flame ionization detector. A RESTEK 15-meter MXT-1 column (15m× 250 μm × 0.15μm) was used. The injector temperature was 280°C with split less injection of 2ul of sample and a linear velocity of 30cms⁻¹, Helium 5. 0pa.s was the carrier gas with a flow rate of 40mlmin⁻¹ and was kept at this temperature for 5min. The detector operated at a temperature of 320°C.

Phytochemical were determined by the ratio between the area and mass of internal standard and the area of the identified phytochemicals. The concentration of the different phytochemicals expresses in ug/g.

TEST ANIMALS SOURCING AND MATERIALS

TEST ANIMALS

Swiss male albino mice (20–25 g) used in this study was obtained from the laboratory animal centre of the pharmacology department, Madonna University, Nigeria. The animals were kept in well-ventilated and hygienic compartments, maintained under standard environmental conditions and fed with standard rodent pellet and water ad libitum.

REAGENTS AND SOLVENTS

Acetic acid (Frank, Anambra state), Acetylsalicylic acid (ASA) (MUTH Pharmacy), Diazepam (MUTH Pharmacy) and ethanol (Frank, Anambra state).

MATERIALS AND EQUIPMENTS

Plexiglas cage, beakers, measuring cylinder (50ml and 100ml), Rotatory evaporator, Water bath, and Syringes.

ACUTE TOXICITY TEST (LD50)

Lethal dose 50% is the dose of the substance that will kill half the test animals was determined using Lorke's method. The result is usually expressed in mg/kg. A single dose of the test substance was administered into the test animals by intraperitoneal route. Different groups of animals were given increasing doses of the test substances to see which dose will kill half of them.

Gram of the ethanol extract of Terminalia ivorensis was weighed and with the aid of a spatula and beaker, was solubilized in ml of water. The body weights of the animals were used to calculate the required dose in ml/kg. The equivalent dose in ml was administered to the animals intraperitoneally.

Mice with weights ranging from 22-30g were used. The preliminary test was carried out using 9 mice. They were divided into 3 groups was made up to 3 mice. A dose of 10, 100, 1000mg/kg were administered intraperitoneally to the groups respectively. They were observed for the lethal effect for 24hours and death was recorded for the groups given 100 and 1000mg/kg dose. The

remaining mice were grouped and given doses of 20, 40, and 80mg/kg respectively. They were observed for another 24hours for lethal effect and no death was recorded. The LD50 was then calculated as the geometric mean of the lowest dose showing death and the highest dose showing no death.

BEHAVIORAL STUDIES

Assessment of the effect of EBETI on Novelty-induced rearing (NIR) and grooming (NIG)

The behavioural profiles of albino mice under the influence of the extract were assessed singly in a white Plexiglas cage measuring (45 cm×25 cm×25 cm). Behavioural measurements were carried out after intraperitoneal administration of vehicle (distilled water, 10 mL/kg) to group (1) and different doses of EBETI (20, 40 and 60 mg/kg, i.p) to groups (2, 3 and 4) into mice (n=5). Animals were taken directly from their home cage and placed individually into an opaque Plexiglas observation chamber with only one side transparent for observation. Each animal was used only once, with the observation chamber cleaned with 70% ethanol after each assessment to remove olfactory cue from previous animal to the other. The time of the experiment was kept constant (9.00 am–1.00 pm) daily to avoid changes in biological rhythm. The behavioural components employed in this observational analysis were rearing and grooming. Diazepam (5 mg/kg, i.p.) administered to group (5) served as a reference drug. Frequency of rearing episodes was quantified by using a manual counter and a stop watch. The total frequency for the 30 min of observation time was summed up for each animal. Rearing was taken as the number of times the mouse was standing on its hind limb or with its forelimbs against the wall of the observation cage or in the free air. Grooming was taken as the number of body cleaning with paws, picking of the body and pubis with mouth and face washing actions.

Assessment of the effect of EBETI on locomotor activity in the open field

Motor activity was measured in an open field apparatus consisting a white Plexiglas box (28 cm×28 cm×25 cm) with a painted black grid dividing the floor into 16 (7×7 cm) equal squares. Animals were divided into 5 groups (n=5). Group (1) was given the vehicle (10 mL/kg, distilled water, i.p.), while groups (2, 3, and 4) received EBETI (20, 40, and 60 mg/kg, i.p.) respectively. Thirty minutes after administration of the extract, animals were placed singly in one of the corners of the box; the number of squares crossed with all 4 paws was counted for 5 min. The cage was cleaned with 70% ethanol at intervals when the animal is removed. Diazepam (5mg/kg, i.p.) administered to group (5), served as the reference drug.

ANALGESIC STUDY

Acetic acid-induced writhing test

Acetic acid-induced writhing in mice was carried out according to the method described by Koster et al. Animals were divided into 5 groups of 5 mice each. Group (1) received distilled water (10 mL/kg, i.p.), groups (2, 3, and 4) received EBETI (40, 60, and 80 mg/kg, i.p.) respectively while group (5) received acetylsalicylic acid (150 mg/kg, i.p.). Both the standard drug and the extract were administered 30 min before induction of nociception with 0.6% acetic acid (10 mL/kg, i.p.). Five minutes after administration of acetic acid, numbers of writhes were recorded for duration of 15 min.

Tail immersion test

The hot water-induced tail withdrawal reflex as a model of nociception was carried out according to the method of Janssen et al. Animals were divided into 5 groups of 5 mice each. Group (1) received distilled water (10 mL/kg, i.p.), groups (2, 3, and 4) received EBETI (40, 60, and 80 mg/kg, i.p.) respectively while group (5) received morphine (5 mg/kg, i.p.). Thirty minutes later, the tail of each animal (up to 5 cm) was dipped in water at 55.0±0.2°C. The time (in

seconds) taken by each animal to withdraw tail clearly out of the water was taken as the reaction time to pain. The cut-off time of 10 s was used to avoid tissue damage.

RESULTS

This chapter appraises the findings, analyses and discusses the results obtained from the experiments as described in the previous chapter. It presents results for macroscopic, microscopy, phytochemical screening, fluorescence, chromatography, neurobehavioral and analgesic study.

Table 1: Macroscopic and organoleptic description of strip bark of *Terminalia ivorensis*

Features	Appearance
Condition	Dried
Colour	Light brown
Odour	Characteristic odour
Texture	Rough
Shape	Curved

Table2: Macroscopic description of powdered *Terminalia ivorensis* bark

Features	Appearance
Condition	Dried
Color	Light brown
Odour	Characteristic smell
Texture	Smooth

Table 3: Proximate analysis of *Terminalia ivorensis*

PARAMETER	OCCURRENCE (%)
Moisture content	0.7
Total ash value	6.5
Water extractive value	3.5
Alcohol extractive value	1.45

The pictures below show the presence of different components in the powdered bark of *Terminalia ivorensis* when viewed under a microscope.

Table 4: Results of percentage yield

Weight of powder(g)	Volume of the solvent(ml)	Weight of disposable bottles(g)	Weight of disposable bottle + extract (g)	Weight of extract (g)	Percentage yield (%)
300	700	111.92	113.02	10.12	3.4

The tables show the different phytochemicals present in the ethanol bark extract of *Terminalia ivorensis*

Table 5: Phytochemical analysis of *Terminalia ivorensis*

S/N	TEST	OBSERVATION	OCCURRENCE
1	ALKALOIDS Dragendorff's reagent Mayer's reagent Wagner's reagent	Brick red cloudy solution Milky cloudy solution Reddish cloudy brown solution	Present in traces Present in traces Present in traces
2	PROTEIN Million's test	Brown precipitate	Present
3	CARBOHDRATE Molish test	Purple ring	Present
3	FLAVONOIDS Ammonium chloride	Yellow colour observed	Present
4	TANNINS Ferric chloride	Blue black precipitate	Present
5	SAPONINS Frothing test	Persistent froth	Present

Table 6: Chemomicroscopic results

S/N	TEST	OBSERVATION	INFERENCE
1	Lignin	Red/pink colouration	+
2	Starch	Blue black coloration	+
3	Calcium oxalate	Formation and disappearance of crystals	+
4	Cutin	Red color	+
5	Cellulose	Blue black coloration	+

The table and pictures below shows the result obtained after carrying out thin layer chromatographic technique on the ethanol bark extract of *Terminalia ivorensis*.

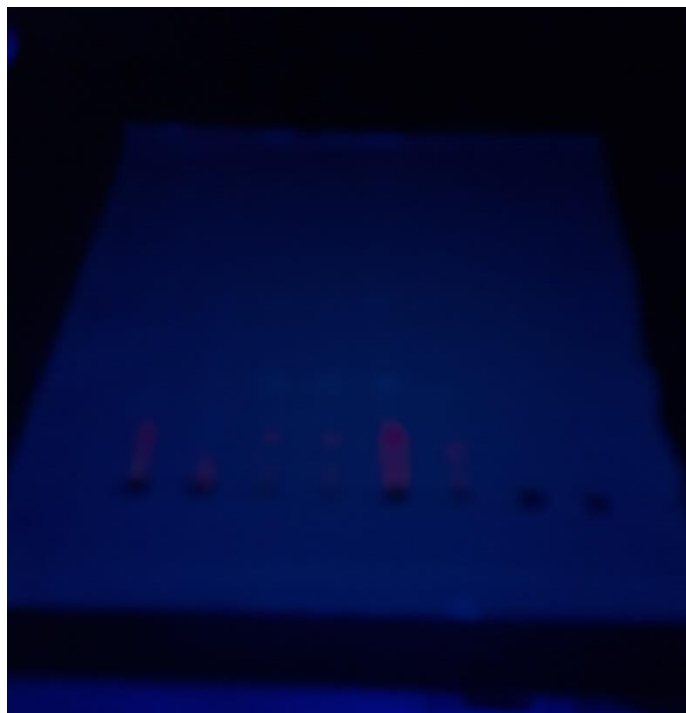


Plate 1: Photomicrograph of Thin layer Chromatography

Table 7: Result of Thin layer Analysis for Different fractions

S/N	Fractions	No of spot	Distance moved by spot (cm)	Distance moved by solvent(cm)	Retention Factors	High retention by Fraction (%)
1	Crude extract	3	7.8	8.0	0.98	98
2	Methanol	2	7.7	8.0	0.96	96
3	N-hexane	1	7.4	8.0	0.93	93
4	Water	1	7.0	8.0	0.88	88

The table below shows the result obtained from the gas chromatography carried out on bark extract of *Terminalia ivorensis*.

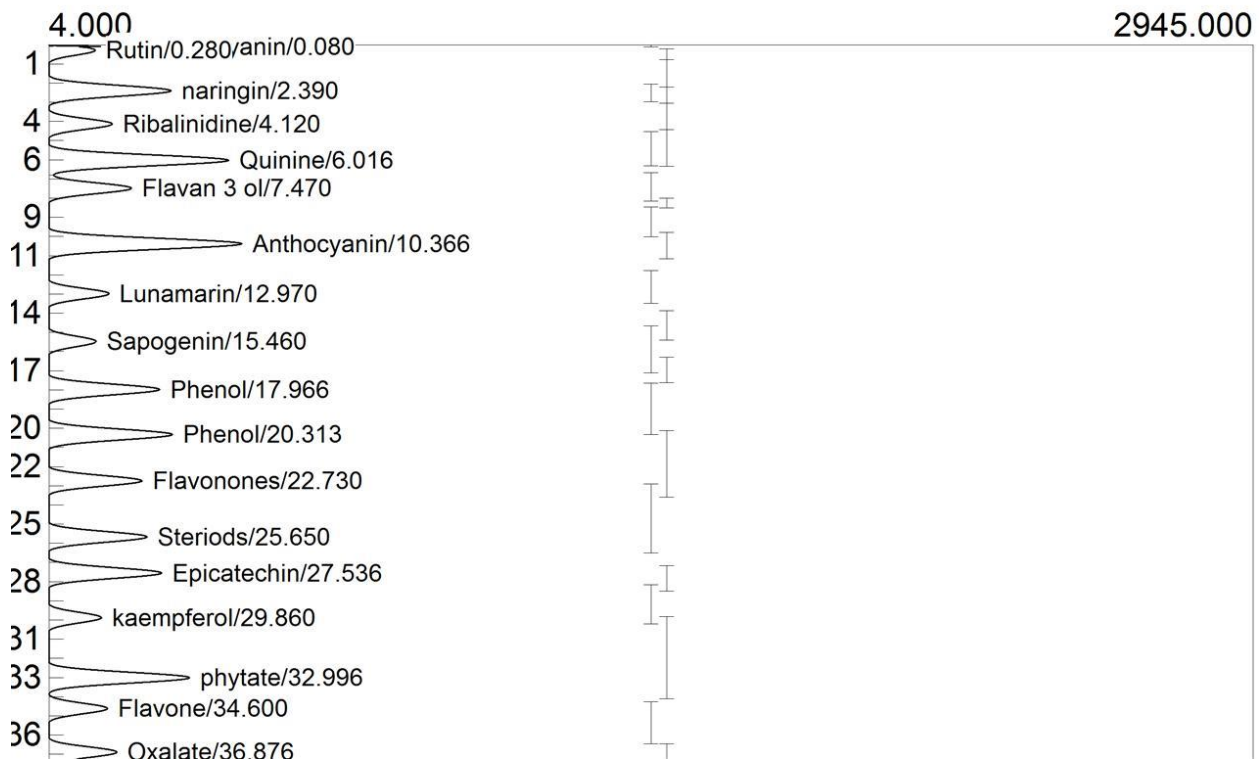
Lab name: Springboard Lab Awka
Client: Emma
Collected: 26/8/19
Method: Syringe Injection
Description: FID
Column: RESTEK 15METER MXT-1
Carrier: HELIUM AT 5 PSI
Data file: Emma sample A phytochemical analysis.chr ()
Sample: phytochemistry
Operator: David
Comments: TYPE YOUR COMMENTS HERE

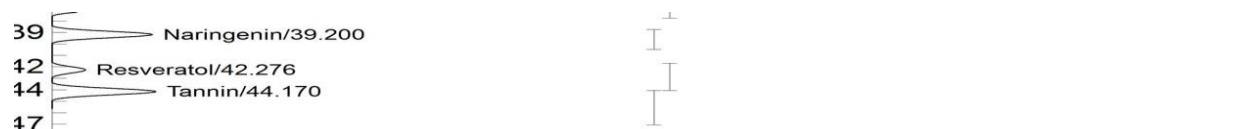
Temperature program:

Init temp	Hold	Ramp	Final temp
50.00	2.000	5.000	200.00
200.00	2.000	7.000	320.00
320.00	2.000	0.000	0.00

Events:

Time Event





Component	Retention	Area	Height	External	Units
Proanthocyanin	0.080	232.8066	139.940	4.3488	ppm
Rutin	0.280	3400.3980	117.455	2.1476	ug/ml
naringin	2.390	12252.8106	301.042	4.4071	ug/ml
Ribalinidine	4.120	6344.5478	157.568	6.3166	ug/ml
Quinine	6.016	18154.0688	442.689	21.7774	ug/ml
Flavn 3 ol	7.470	8442.9838	206.428	11.7573	ppm
Anthocyanin	10.366	19598.0668	476.646	70.0738	ug/ml
Lunamarin	12.970	6238.3258	152.341	0.4510	ug/ml
Sapogenin	15.460	4967.5639	121.273	11.7731	ug/ml
Phenol	17.966	11339.2568	276.424	13.4972	ppm
Phenol	20.313	12756.4840	307.630	15.1842	ppm
Flavonones	22.730	9573.1408	233.186	5.6605	ppm
Steriods	25.650	10008.8176	245.115	9.9532	ppm
Epicatechin	27.536	11458.0104	280.295	3.5833	ug/g
kaempferol	29.860	5478.4406	133.723	1.2115	ug/ml
phytate	32.996	14337.0482	348.877	32.0321	ug/ml
Flavone	34.600	6059.7940	147.836	3.8271	ug/ml
Oxalate	36.876	6988.5601	170.310	9.1439	ug/ml
Naringenin	39.200	10234.6024	249.263	5.3150	ug/ml
Resveratol	42.276	3473.1416	85.310	4.9270	ppm
Tannin	44.170	10509.6768	256.782	19.7575	ug/ml
		191848.5454		257.1453	

Parameters	Sample
Proanthocyanin	4.388
Rutin	2.1476
Naringin	4.4071
Quinine	21.7774
Flavn 3 ol	11.7573
Anthocyanin	70.0738
Lunamarin	0.4510
Sapogenin	11.7731
Sparteine	
Phenol	28.7880
Flavonones	5.6605
Steroids	9.9532
Epicatechin	3.5833
Kaempferol ppm	1.2115
Phytate	32.0321
Flavones	3.8271
Naringenin	5.3150
Resveratol	4.9270

Tannin	19.7575
Ribalinidine	6.3166
Catechin	-
Oxalate	9.1439

Table 8: Toxicological profile of Terminalia ivorensis

STAGE A	DOSE OF EXTRACT ADMINISTERED	NUMBER OF DEATH RECORDED
Group 1	10mg	0/3
Group 2	100mg	3/3
Group 3	1000mg	3/3
STAGE B		
Group 1	20mg	0/1
Group 2	40mg	0/1
Group 3	80mg	0/1

The EBETI (20, 40 and 60mg/kg, i.p.) showed dose dependent inhibitory effect on novelty-induced rearing and grooming in mice compared to control. A significant reduction in the frequency of rearing and grooming episodes was observed compared to control.

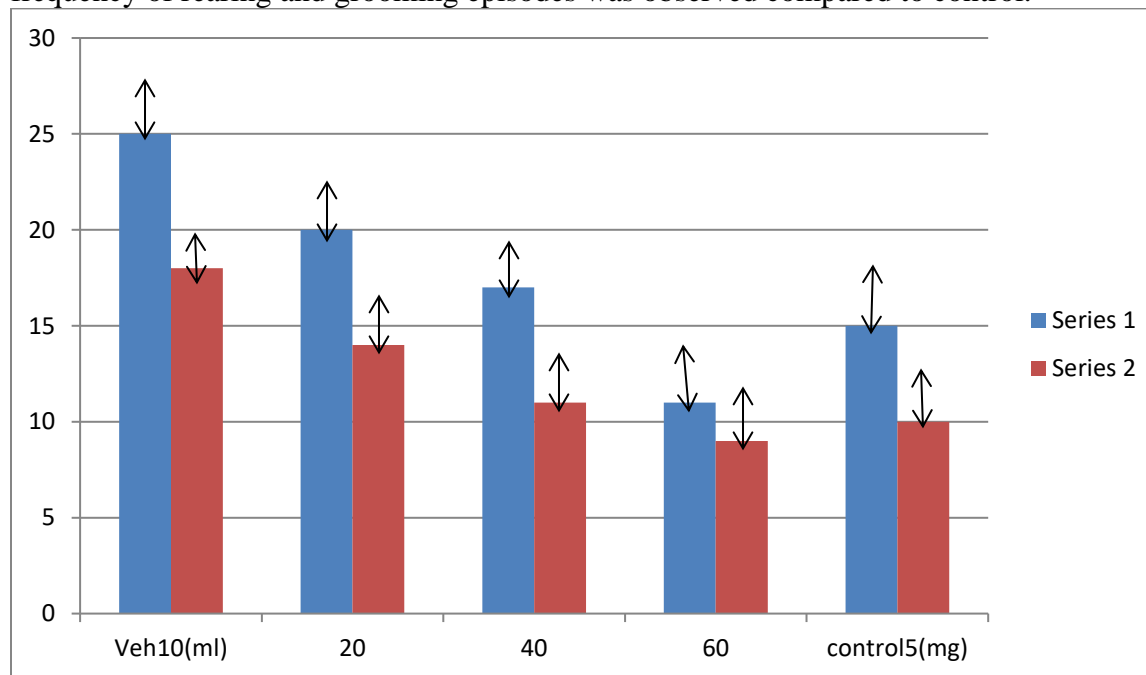


Figure 1: The EBETI (20, 40 and 60mg/kg, i.p.) reduced significantly spontaneous locomotor activity in a dose dependent manner compared to control. Diazepam also significantly reduced locomotor activity.

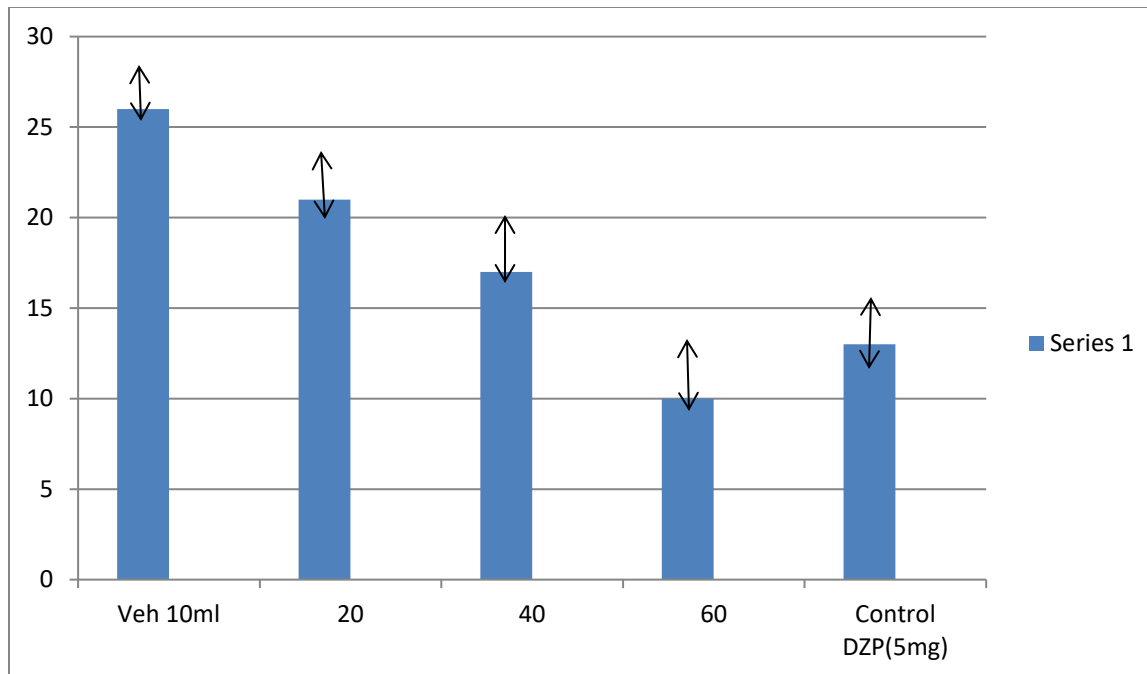


Figure 2: The EBETI (2.5–10 mg/kg, i.p.) produced significant inhibition of writhes (abdominal constrictions) in a dose-dependent manner compared to control. The effect of EBETI at 10 mg/kg and that of acetylsalicylate are comparable.

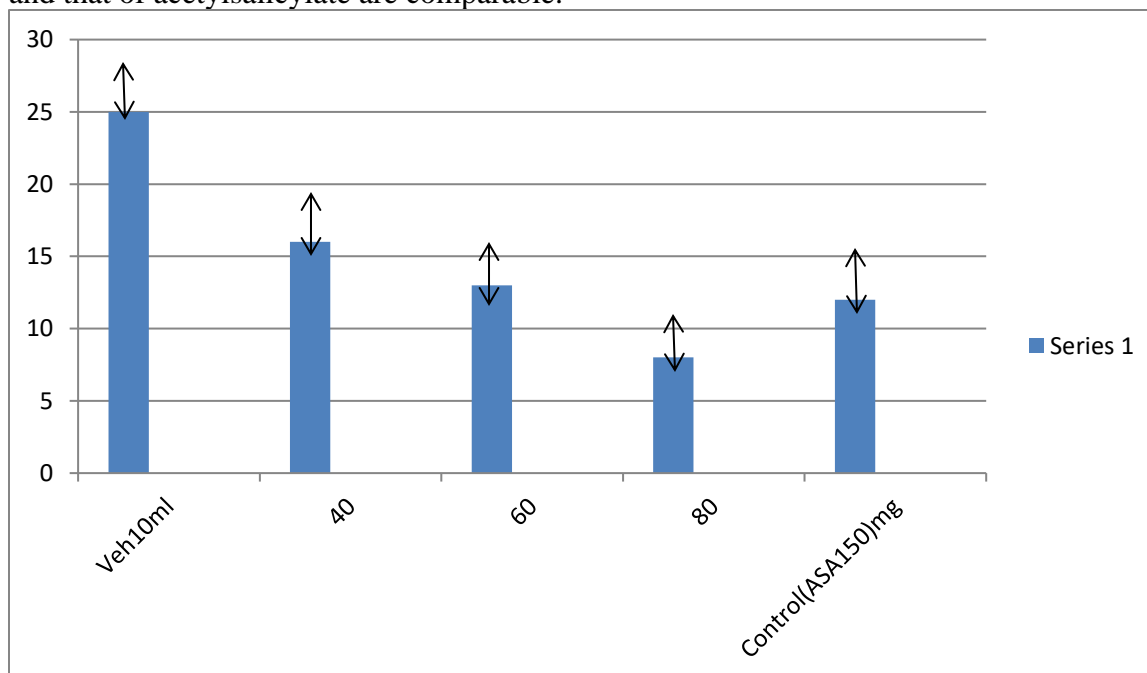


Figure 3

Table 9: Effect of EBETI on Tail Immersion Test

DOSE(mg/kg)	TIME ENDURED(seconds)
Vehicle (10ml)	2.4±0.157
40	3±0.005
60	3.7±2.209
80	4.3±1.542
Control(morphine5mg)	7.5±0.1026

DISCUSSION

This study evaluated the phytochemical properties of *Terminalia ivorensis* and effects of the extract on novelty-induced behaviours (rearing, grooming and locomotor activity). Rearing, a novelty-induced behaviour is employed by rodents as one of the strategies to explore a new environment for food, protection and possibly escape [20]. It has been described as a vertical locomotion in which animal can either stand on its hind limbs while raising up its forearms in the air or placing on the wall of the cage. This behaviour is considered as an index of central nervous system (CNS) excitation and can be employed to assess central nervous system stimulation and depression in animals. In this study, the extract demonstrated inhibitory effect on rearing thus suggesting its sedative property. Grooming is a maintenance behaviour primarily meant for the care of the body surface. It is elicited in animals in response to mild stress such as exposure to a novel environment. Its deactivating role in restoring homeostasis in animals exposed to novel environment-induced stress has been reported. It is described as face washing with forearms or body cleaning with mouth. The results indicate that the extract has dose dependent inhibitory effect on grooming behaviour suggesting its stress alleviating potential in a novel environment.

The need to discriminate pain in its peripheral and central components has led to the use of formalin as a noxious stimulus to induce nociception. Formalin pain model has been able to dissociate between inflammatory and non-inflammatory pains because of its characteristic biphasic pain responses. The initial response is derived from direct stimulation of nociceptors resulting in C-fiber firing. Subsequently, a delayed inflammatory reaction is observed in response to formalin-induced peripheral tissue damage. Central acting analgesics, such as morphine, have shown analgesic activity in both phases, whereas non-steroidal anti-inflammatory drugs and corticosteroids inhibit only the late phase. The extract inhibited nociception in this model significantly in both the 1st phase (neurogenic pain) and the 2nd phase (inflammatory pain). However, inhibitory effect of the extract on nociception is greater in the late phase suggesting more of peripheral action than central. Late phase activity hints on the possibility that the extract contains bioactive that exhibits anti-inflammatory property thus supporting the report of Iwu and Anyanwu [21] Antinociceptive effect of the extract was further evaluated with tail immersion test believed to be supraspinally integrated. This thermal nociceptive test is used to detect centrally acting analgesic and is more sensitive to opioids μ agonists. Although the extract inhibited neurogenic pain in formalin test, its failure to alter response to acute pain in thermal test precludes central opiate mechanism of action. The results suggest that the extract possesses analgesic activity probably mediated centrally and peripherally.

Conclusion

Terminalia ivorensis has demonstrated sedative property and has produced good analgesic effect in thermal and chemical models of nociception. This thus supports its use as a tranquilizer in psychosis and pain killer in folkloric medicine.

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