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Anticonvulsant Activity of *Hippocratea welwitschii* Oliv. (Celastraceae) Root Extracts on Chicks and Swiss Mice

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ABSTRACT

Dried roots of *Hippocratea welwitschii* are a prevalent traditional medication for the management of epilepsy in the traditional 'Ukanafum' system of medicine in the Akwa Ibom, South Southern, Nigeria. Various extracts of the root of the plant namely: n-hexane, ethyl acetate, methanolic, aqueous and crude extracts were subjected to anticonvulsant evaluation using the maximal electroshock test (MEST) in chicks, subcutaneous pentylenetetrazole (scPTZ) and strychnine induced seizures test in mice. The neurotoxic potential of the extracts was assessed using beam walking assays in mice. The n-hexane (250 mg/kg), methanol (250 mg/kg) and aqueous (125 and 250 mg/kg) extracts produced 30% protection against seizure induced by MEST. The methanol extract (250 mg/kg) and crude extract (125 mg/kg) showed 80% and 70% protection in the scPTZ test, respectively. Similarly, the aqueous extract at 125 mg/kg protected 60% of the mice against seizure induced by strychnine. In the beam walking assay test, only the methanol extract produced a significant ($p < 0.05$) increase in the number of foot slips and the time taken to complete the task. In conclusion the various extracts of the root of *Hippocratea welwitschii* demonstrated anticonvulsant activity and deserve further study on the isolation and elucidation of the anticonvulsant active compounds and possible mechanism of anticonvulsant action.

***Keywords*:** Epilepsy, *Hippocratea welwitschii*, Seizure, Strychnine, Pentylenetetrazole, Beam Walking Assay

Introduction

Epilepsy is a central nervous system (neurological) disorder in which nerve cell activity in the brain is disturbed, causing frequent or recurrent seizures, sensations and sometimes loss of awareness.[1] It is a chronic non-communicable disease of the brain that affects people of any gender, age and geographic region.[2] Approximately 1% of the general population in western societies suffers from some sort of epilepsy while up to 10 % will have at least one seizure during their life times.[3] According to the World Health Organization, approximately 50 million people live with epilepsy worldwide, 80% being from low-income countries.[4]

Conventional treatment of epilepsy consists mainly of anticonvulsant medications.[5] Antiepileptic drugs accomplish seizure reduction by suppressing neuronal intrinsic or synaptic excitation (usually mediated by the neurotransmitter glutamate) and promoting synaptic inhibition (usually mediated by the neurotransmitter gamma-amino- butyric acid or GABA).[6] Currently available antiepileptic drugs do not affect epileptogenesis and are associated with serious side effects, including teratogenicity, hepatotoxicity and adverse effects on cognition and behavior.[7]

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Almost all the currently available antiepileptic drugs are associated with drug interaction making it difficult to attain easy seizure control.[8] There is an urgent need for the development of newer antiepileptic agents with better safety and efficacy profile.

Much of modern medicine, particularly pharmaceuticals, has been developed through the study of natural products. Up until the 1800's the treatment and prevention of diseases was largely performed through the application of medicinal plants.[9] Traditional medicines have not only been the bedrock from which newer medicinal agents are launched but also a therapeutic resort for hard-to cure illnesses. This is the reason why developing countries still rely on them to resolve her health needs, especially in cases where synthetic medicines cannot provide relief from hard to-cure illnesses. About 80 percent of the African population depends on traditional remedies as they do not have access to adequate orthodox medicine.[10] Plants form the basis of a sophisticated traditional medicine from antiquity to date and humans have long relied on naturally occurring substances for medical purposes.[11] Plants, in particular, have played a leading medical role in most cultures. The importance of plants as one of the natural sources of drugs cannot be over-emphasized as about 25% of the drugs prescribed worldwide come from plants.[12]

The plant *Hippocratea welwitschii*, is a shrub of closed, primary or mature secondary forest or in thickets of secondary shrub from Guinea to western Cameroon and widespread across Africa to Angola, Uganda and Tanzania.[13] It belongs to the family of the Celastraceae (also known as staff vine or bitter sweet family). It is a shrub or climber of closed, primary or mature secondary forest. It is called different names by the natives in different parts of Africa; the Igbo tribe of south-eastern Nigeria call it '*obulumgbede*', while it is known as '*Nya worouruambombo*' in Efik, or '*Nya worouruambombi*' in Ibibio both of which literally means 'coming out of the fattening room into the market while the Yoruba tribe in south – western Nigeria know it as '*ijan*'.[14] Several parts of the plant have been reported to have ethno medicinal uses and among such, is in south-south Nigeria where the root of the

plant is claimed to be used effectively in the management of epilepsy. There has been inadequate scientific data to support the use of the plant in the management of epilepsy; hence this study is aimed at providing such. The anticonvulsant properties of crude extracts of *Hippocratea welwitschii* have been carried out and reported in this paper as a means of validating the traditional claims.

Materials and Methods

Collection and Identification of Plant Materials

Hippocratea welwitschii roots were collected by farmers in Ukanafum Local Government Area of Akwa Ibom state (south south Nigeria) in August 2021. It was identified and authenticated by plant taxonomists at the Department of Pharmacognosy and Environmental Medicine, University of Nigeria, Nsukka (UNN), with Voucher reference number PCG/UNN/0305. A voucher specimen was deposited for further reference in the herbarium section of UNN. The plant material was cleaned and air dried at room temperature under the shade, after which they were chopped into pieces and milled into powder with the aid of an electric hammer mill (model TRAPP TRF 80 Hammer mill foliage) and subsequently stored in a moisture free environment until required for further use.

Preparation of the Extracts

The crude extract of the plant material was obtained by boiling 150 g of the powdered sample in water for 6 h, filtered and the filtrate freeze dried to yield a crispy dark brown powder. Hexane, ethyl acetate, methanol and aqueous, extracts were obtained through successive cold maceration. The powdered plant sample (1 kg) was soaked in adequate hexane in a stoppered glass container and tightly covered. The mixture was left for 3 days at room temperature with periodic daily stirring and then the extracts finally filtered through cotton wool and Whatman 125 mm filter paper No. 1. The extract obtained was concentrated using rotary evaporator model Stuart RE 300B W13 at reduced pressure and temperature (40ºC) to obtain the hexane extract of the sample. The residue was subjected to same procedure serially using ethyl acetate, methanol and water to obtain ethyl acetate, methanol and aqueous extracts respectively. The dried extracts were later kept in tightly stoppered bottles in a refrigerator (at 4ºC) until required for further analysis.

Animals

Locally bred adult Swiss mice of either sex weighing 20±2 g were obtained from the Animal House Facility of the Department of Pharmacology and Therapeutics, Ahmadu Bello University Zaria, Nigeria. Day old ranger cockerels (30±5) g were obtained from Zarm farms, Kwara state, Nigeria. The mice, maintained on standard rodent faced and water *ad libitum*, were housed in polypropylene cages at ambient environmental condition throughout the study. The experimental protocol was duly approved by the Ahmadu Bello University committee on Animal use and care (Reg. No. ABUCAUC 2017/018).

Acute Toxicity Study

The median lethal doses (LD_{50}) of the various extracts of *Hippocratea welwitschii* was performed according to OEDC protocols 423. The extracts were administered orally in the range of 1000, 2000, 5000 mg/kg to mice of either sex. The animals were individually observed during the first 30 min for signs and symptoms of toxicity including deaths in each group within 24 hours after treatment.[7]

Maximum electroshock-induced seizure in chicks

The method previously described by Swinyard and Kupferberg,[15] (1985) as modified by Sayyah *et al.*[16] (2002) was used in this study. Fifty (50) one-day old white ranger cockerels were randomly divided into five groups each comprising of ten chicks. The first, second and third groups received 125, 250 and 500 mg/kg crude extract orally. The fourth group was given normal saline equivalent to the vehicle given with the extract while the fifth group was given 20 mg/kg Phenytoin. The maximal electroshock was performed using Ugobasile electro convulsive machine (Model 7801) connected to Claude Lyons stabilizer with corneal electrodes placed on the upper eyelids of the chicks to induce seizure in the chicks via delivering an electric current of 90 mA and shock duration of 0.80 s. The frequency and pulse width were set and maintained at 200 pulse per second and 0.8 ms respectively. The ability to prevent the chicks against tonic hind limb extension (THLE) or to reduce the recovery time was considered as an indication of anticonvulsant activity.[17] Maintaining the positive and negative controls, the method was repeated for residual aqueous, methanol, ethyl acetate and n-hexane extracts (125, 250 and 500 mg/kg).

Pentylenetetrazole-induced Seizure in mice

The method of Swinyard *et al.*[17] (1989) was employed. Fifty mice were divided into five groups each containing ten mice. The first group received normal saline (10 ml/kg). The second, third and fourth groups received 125, 250 and 500 mg/kg crude extract orally. The fifth group received 200 mg sodium valproate per kg body weight. Pentylenetetrazole (PTZ 85 mg/kg) was subcutaneously administered in all mice after one-hour post treatment, mice were observed over a period of 30 minutes for an episode of clonic spasm. The ability of the extracts to protect the animals against clonic spasm was considered as index of protection. The same method was repeated for the residual aqueous, methanol, ethyl acetate and n-hexane extracts (125, 250 and 500 mg/kg) with the same positive and negative controls.

Subcutaneous strychnine-induced seizure in mice

Fifty mice were divided into five groups each containing ten mice. The crude extract was administered orally using feeding cannula in accurate does of 125, 250 and 500 mg/kg to the first, second and third groups respectively. The fourth group received normal saline equivalent to the vehicle given with the extract while the fifth group was given 20 mg/kg phenobarbitone. One-hour post -treatment, mice in all the groups received 1.5 mg strychnine per kg. The number of mice exhibiting convulsions as well as the onset of tonic convulsions was recorded. Abolition of tonic hind limb extension within 60 minutes after strychnine administration was considered an indicator of anticonvulsant activity. Maintaining the positive and negative controls, the same method was repeated for the residual aqueous, methanol, ethyl acetate and n-hexane extracts (125, 250 and 500 mg/kg).[18]

Mouse Beam Walking Assay in mice

The beam walking assay described by Stanley *et al.*[19] (2005) was adopted to evaluate motor coordination deficit as an index of neurotoxicity. Mice were individually trained to walk on a ruler 80 cm long and 3 cm wide elevated 30 cm above the bench by metal support to a goal box. Three trials were conducted for each mouse, and were meant such that the mouse tried would be conscious that there was a goal box that could be reached. The goal box was a Perspex glass cage (with wood chippings beddings) with a small hole at the bottom. The mice that successfully walked along the ruler were randomly grouped into five groups each containing ten mice. The first group received normal saline (10 ml/kg), i.p. The second, third and the fourth groups received the extracts at doses of 125, 250 and 500 mg/kg body weight respectively. The fifth group received diazepam (2 mg/kg body weight). Each mouse was placed on the beam at one end and allowed to walk to the goal box after one-hour post- treatment. Mice that fell were returned to the position they fell from, with a maximum time of 60 s allowed on beam. The number of foot slips (one or both hind limb slipping from the beam) was recorded with the aid of a tally counter. The time taken to complete the task was also recorded. The same method was repeated for the residual aqueous, methanol, ethyl acetate and n-hexane extracts (125, 250 and 500 mg/kg) while maintaining the positive and negative controls.

Statistical Analysis

Values were expressed as Mean ± S.E.M. Data were analyzed using One-Way ANOVA followed by Dunnet post hoc t-test for multiple comparison. Ap value < 0.05 was considered significant.

Results and Discussion

The anticonvulsant activity results of the extracts of *Hippocratea welwitschii* were determined using electrically induced (MEST) in chicks, chemically induced (PTZ) and Strychnine induced convulsion. The motor coordination was determined using the Beam Assay in mice. In MEST, the extracts administered orally 60 min before electro convulsions, abolished in a non dose-dependent manner the threshold for MEST-induced seizures in mice (Table 1). The aqueous (125 and 250 mg/kg), n-hexane (250 mg/kg) and methanol (250 mg/kg) extracts afforded 30% protection against tonic hind limbs extension. Phenytoin (30 mg/kg) protected 80% of the chicks from seizure.

In PTZ-induced convulsion, *Hippocratea welwitschii* extracts prolonged the onset time of the clonic spasm, myoclonic jerk and tonic extension ($p < 0.05$) in non dose-dependent manners (Table 2). At doses of 125 mg/kg and 250 mg/kg, the crude and methanol extracts provided 80% and 70% maximum protection respectively (Table 2). They also, gave a non dose dependent protection against the hind limbs and loss of the righting reflex with tonic fore limb seizures and reduced animal deaths in all the extracts tested compared to the control by at least 10%. However, phenobarbitone administered as standard drug had recorded no death of the tested animals in this analysis in the dose of 30 mg/kg I.P.

In *strychnine*-induced seizure test, the aqueous (500 mg/kg) and methanol extracts (250 mg/kg) prolonged the onset time of the tonic hind limb extension. The administration of aqueous extracts (125, 250 and 500 mg/kg) afforded a dose-dependent protection 60, 30 and 20%, and 20, 30 and 30% against mortality respectively. Phenobarbitone at a dose of 30 mg/kg produced 20% protection against strychnine induced seizures with no mortality recorded in the animals tested.

Beam walking was used to relate the fine motor coordination and balance skills of the extracts and control mice. The tested and control mice walked along the beam types with ease. However, MeOH extracts at 500 mg/kg showed significant difficulty in crossing the beam and also made more foot slips as measured by the increase inactivity compared with control mice. In diazepam 0.2 mg/kg (positive control), the mice displayed a noticeable deterioration in performance with the mice taking significantly longer time to cross the beam, exhibiting a greater number of foot slips and failing to maintain balance on the surface of the beam.

The results of the phytochemical screening carried out on the root extract of *Hippocratea welwitschii* revealed saponins, flavonoids, alkaloids, phenols, tannins, oxalic, cyanide, glycocides and terpenoids. These constituents have been described to be responsible for different activities of plants.[20-21] The decline in the period of seizure by MEST (aqueous 125 and 250 mg/kg, n-hexane 250 mg/kg and methanol 250 mg/kg) and the abolition of PTZ (crude 125 mg/kg and methanol 250 mg/kg) and strychnine (aqueous 500 mg/kg and methanol 250 mg/kg) seizures are indication of central inhibition through the stimulation of the CNS inhibitory pathway.[22] The electroshock convulsions are characterized by the tonic limb flexion followed by tonic limb extension.[23] The elimination or suppression of the tonic extensor constituent of the electroshock convulsions as shown by the upsurge in the beginning and reduction in the duration of MEST by the aqueous (125 and 250 mg/kg), n-hexane (250 mg/kg) and methanol (250 mg/kg) extracts that exhibited a weak effect on hind limb tonic extension was a sign of its ability to prevent seizure spread[24] and suggest its efficacy against partial and generalized seizures. MEST test identifies sodium channel blockers as such as carbamazepine, lamotrigine, oxcarbazepine, phenytoin and valproate with activity against generalized tonic clonic seizures[25] or agents that block glutamatergic neurotransmission mediated by n-methyl-d-aspartate (NMDA) receptors.[26] An anticonvulsant effect in the MEST model further shows the ability of the extracts to weakly inhibit seizure discharge within the brain suggests them to be partially effective in treating generalized tonic-clonic and partial seizures. The extracts protected the mice against PTZ and significantly reduced the onset of myoclonic jerks and tonic seizures. It is extensively believed that pentylenetetrazole causes convulsions by blocking the main GABAergic inhibitory pathways.[27] Standard anticonvulsant drugs such as barbiturates, benzodiazepines and phenobarbitone demonstrate their effects through enhancement of GABA mediated inhibition pathway in the brain.[28] Seizures produced by pentylenetetrazole can also be stopped by drugs such as ethosuximide and gabapentin via an interaction with voltage operated T-type Ca^{2+}channels.[29]

Table 1: Effect of Crude, Methanol, Aqueous, Ethyl Acetate and n-Hexane Extracts on MEST

Sample	Treatment (mg/kg)	Mean recovery period (min)	Quantal protection	% Protection
Control	0	14.38 ± 3.96	1/10	10.0
Aqueous extract	500	14.67 ± 3.83	2/10	20.0
Aqueous extract	250	8.79 ± 2.48	3/10	30.0
Aqueous extract	125	7.24 ± 1.58	3/10	30.0
EtOAc extract	500	12.05 ± 2.97	0/10	0.0
EtOAc extract	250	9.52 ± 2.04	1/10	10.0
EtOAc extract	125	8.60 ± 2.61	1/10	10.0
n-Hexane extract	500	8.16 ± 1.47	1/10	10.0
n-Hexane extract	250	5.98 ± 0.37	3/10	30.0
n-Hexane extract	125	7.66 ± 0.99	2/10	20.0
Crude extract	500	6.46 ± 0.72	1/10	10.0
Crude extract	250	6.11 ± 1.21	1/10	10.0
Crude extract	125	8.37 ± 0.89	1/10	10.0
MeOH extract	500	5.27 ± 1.08*	1/10	10.0
MeOH extract	250	8.58 ± 1.72	3/10	30.0
MeOH extract	125	8.33 ± 3.15	1/10	10.0
Standard	30	6.67 ± 0.14	8/10	80.0

Values are expressed as Mean ± S.E.M., * = $p<0.05$ as compared to control – One-way ANOVA followed by Dunnett's and Tukey's post hoc tests, n = 10

Table 2: Effect of Crude, Methanol, Aqueous, Ethyl Acetate and n-Hexane Extracts on PTZ-Induced Seizures

Sample	Treatment (mg/kg)	Onset of jerking (min)	Onset of myoclonic spasm (min)	% protection against tonic limb extension	Time of tonic limb limb extension (min)
Control	0	5.90 ± 0.62	9.91 ± 1.15	0.0	10.29 ± 1.09
Aqueous extract	500	6.05 ± 0.95	10.76 ± 2.14	40.0	12.69 ± 2.29
Aqueous extract	250	7.84 ± 1.04	13.53 ± 1.54	20.0	13.60 ± 1.57
Aqueous extract	125	5.65 ± 0.75	12.58 ± 3.66	50.0	16.51 ± 2.72
EtOAc extract	500	5.47 ± 1.11	12.38 ± 2.52	10.0	13.20 ± 2.47
EtOAc extract	250	4.84 ± 0.46	9.36 ± 1.05	10.0	10.31 ± 1.15
EtOAc extract	125	7.30 ± 1.27	9.90 ± 1.26	30.0	9.70 ± 1.41
n-Hexane extract	500	5.81 ± 0.85	11.61 ± 1.02	20.0	12.13 ± 1.34
n-Hexane extract	250	6.54 ± 0.80	13.51 ± 2.06	40.0	9.13 ± 0.96
n-Hexane extract	125	4.68 ± 0.55	12.71 ± 1.01	30.0	14.27 ± 2.75
Crude extract	500	6.04 ± 0.73	15.46 ± 4.72	60.0	16.11 ± 4.48
Crude extract	250	4.76 ± 0.54	11.69 ± 2.27	50.0	11.73 ± 2.25
Crude extract	125	6.47 ± 1.25	5.31 ± 0.61	80.0	5.43 ± 0.62
MeOH extract	500	6.17 ± 0.90	9.47 ± 2.20	60.0	9.58 ± 2.19
MeOH extract	250	6.66 ± 1.01	9.61 ± 0.84	70.0	8.98 ± 0.90
MeOH extract	125	6.23 ± 1.43	10.31 ± 0.60	60.0	10.31 ± 0.60
Standard	200	7.20 ± 0.71	13.25 ± 4.66	70.0	–

Values are expressed as Mean ± S.E.M., No significant difference as compared to control – One-way ANOVA followed by Dunnett's and Tukey's post hoc tests, n = 10.

Table 3: Effect of Crude, Methanol, Aqueous, Ethyl Acetate and n-Hexane Extracts on Strychnine-Induced Seizures

Sample	Treatment (mg/kg)	Onset of jerking (min)	Onset of seizures (min)	% protection against seizures	Time of death (min)
Control	0	2.82 ± 0.16	3.08 ± 0.35	0.0	4.54 ± 0.34
Aqueous extract	500	5.92 ± 1.12**	8.90 ± 1.59**	20.0	16.02 ± 4.80*
Aqueous extract	250	6.04 ± 0.57**	6.29 ± 0.66	30.0	6.09 ± 0.31
Aqueous extract	125	5.83 ± 0.74*	6.50 ± 0.57	60.0	9.61 ± 1.13
EtOAc extract	500	3.03 ± 0.24	3.54 ± 0.19	0.0	3.68 ± 0.19
EtOAc extract	250	4.09 ± 0.86	6.36 ± 1.14*	0.0	7.64 ± 1.39
EtOAc extract	125	3.69 ± 0.36	5.88 ± 0.98	0.0	7.71 ± 1.18
n-Hexane extract	500	2.83 ± 0.42	3.81 ± 0.44	0.0	4.21 ± 0.42
n-Hexane extract	250	2.59 ± 0.26	3.81 ± 0.44	0.0	4.21 ± 0.42
n-Hexane extract	125	2.59 ± 0.26	4.10 ± 0.39	0.0	4.72 ± 0.22
Crude extract	500	4.77 ± 0.86	6.23 ± 1.44*	0.0	8.00 ± 1.69
Crude extract	250	2.99 ± 0.17	4.28 ± 0.28	0.0	6.28 ± 0.88
Crude extract	125	3.21 ± 0.16	5.98 ± 0.75	0.0	9.12 ± 1.47
MeOH extract	500	4.74 ± 0.32	5.12 ± 0.35	10.0	6.34 ± 0.77
MeOH extract	250	3.95 ± 0.39	6.50 ± 0.93*	0.0	6.83 ± 1.21
MeOH extract	125	3.95 ± 0.20	4.33 ± 0.17	0.0	8.45 ± 2.17
Standard	200	4.99 ± 0.71*	6.36 ± 0.94*	20.0	–

Values are expressed as Mean ± S.E.M., * = $p<0.05$, ** = $p<0.01$ as compared to control– One-way ANOVA followed by Dunnett's and Tukey's post hoc tests, n = 10.

Stimulation of the NMDA receptor system is also involved in the start and spread of PTZ-induced convulsions.[30] In this respect, drugs such as felbamate that decreases glutamate discharge by obstructing presynaptic NMDA receptors in the entorhinal cortex have shown anticonvulsant activity against pentylenetetrazole induced seizures.[31] The anticonvulsant effect demonstrated in this study by the extracts against seizures produced by PTZ might be attributed to either the obstruction of glutamatergic neuro transmission mediated by NMDA receptor, inhibition of T-type Ca^{2+}current or enhancement of GABAergic neurotransmission.[7] The aqueous extract dose dependently prevented strychnine seizure and also caused a reduction in death. The three doses of aqueous extracts produced 60%, 30% and 20% protection

against strychnine induced seizures and mortality. Strychnine produces seizures by antagonizing competitively the postsynaptic inhibitory effects of glycine and interact with the glycine-mediate inhibitory pathway.[32-33] High anticonvulsive of some barbiturates such as pentobarbitone and phenobarbitone are well known to be used against strychnine induced convulsions.[33] The result obtained point to the likelihood that, the extracts act straight by stimulation of some sites on glycine channels, indirectly through stimulation of GABAergic activities or stimulation of voltage dependent chloride channels.[34] The performance on the balance beam was used to assess the fine coordination and balance capability of the tested and control mice. The time taken and foot slips to cross the beam are very sensitive procedures of determining benzodiazepine-like drugs that produced motor coordination shortfalls and sufficiently forecast clinical sedation comprising GABAergic neurotransmission.[19] The functioning on the beam by the animals that received MeOH (500mg/kg) worsened with the mice taking significantly lengthier time to cross the beam, displaying a more number of foot slips and failing to maintain balance. Additionally, narrow beam walking, foot slipping errors and time taken to cross the beam were significantly increased in the group of animals treated with diazepam. Therefore, the increase in the number of foot slips observed in the study may be associated with the interaction of these agents with the GABA system to produce clinical sedation.[1]

Conclusion

On the basis of overall results of this study, *Hippocratea welwitschii* extracts have been found to possess anticonvulsant activity on the animal models investigated and these findings may lend credence to the ethno medicinal use of the plant in the management of epilepsy. Further work to establish the active chemical constituent(s) of the extracts and the definite mechanism of action is currently going.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Table 4: Effect of Crude, Methanol, Aqueous, Ethyl Acetate and n-Hexane Extracts on Beam Walking Assay

Sample	Treatment (mg/kg)	Mean time taken to reach goal post (min)
Control	0	16.71 ± 1.76
Aqueous extract	500	14..57 ± 1.67
Aqueous extract	250	14.14 ± 1.49
Aqueous extract	125	11.86 ± 1.34
EtOAc extract	500	11.86 ± 1.34
EtOAc extract	250	18.29 ± 7.22
EtOAc extract	125	16.75 ± 3.14
n-Hexane extract	500	22.43 ± 9.72
n-Hexane extract	250	14.86 ± 7.60
n-Hexane extract	125	11.86 ± 2.28
Crude extract	500	14.71 ± 1.20
Crude extract	250	13.71 ± 1.48
Crude extract	125	7.57 ± 0.81
MeOH extract	500	36.57 ± 10.11*
MeOH extract	250	19.29 ± 7.02
MeOH extract	125	13.57 ± 2.66
Diazepam	200	60.00 ± 0.00*

Values are expressed as Mean ± S.E.M., * = $p<0.05$ as compared to control – One-way ANOVA followed by Dunnett's and Tukey's post hoc tests, n = 10

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