https://dx.doi.org/10.4314/jpb.v15i1.9
Vol. 15 no. 1, pp. 70-77 (March 2018)
http://ajol.info/index.php/jpb

Journal of
PHARMACY AND BIORESOURCES

Sedative and anticonvulsant evaluation of *Tapinanthus globiferus* A. Rich (*Loranthaceae*) in mice and chicks

Mustapha H. Abdullahi[1*], Helen O. Kwanashie[2], Nuhu M. Danjuma[2] and Aliyu M. Musa[3]

[1]Department of Pharmacology and Therapeutics, Bayero University, Kano. Nigeria.
[2]Department of Pharmacology and Therapeutics, [3]Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria. Nigeria.

Received 24th August 2017; Accepted 20th February 2018

Abstract
Tapinanthus globiferus is mistletoe that is used in folklore for the management of sleep disorders and epilepsy, amongst others. This study was designed to evaluate the sedative and anticonvulsant properties of the ethanol extract of *T. globiferus* in mice and chicks. The extract was screened for its sedative activity and effect on motor coordination using diazepam-induced sleep and beam-walk assay respectively; while anticonvulsant property was screened, using maximal electroshock (MES), pentylenetetrazole (PTZ)- and strychnine (STN)-induced seizure test models. Experiments were conducted in mice except MES which was conducted in day old cockerels, with all drug administered by intraperitoneal route. Data was analysed using ANOVA followed by Dunnett's post-hoc test. The extract produced a significant ($p \leq 0.05$) and dose-dependent decreased in the onset and increased in the duration of diazepam-induced sleep at doses of 87.5, 175 and 350 mg/kg and also produced significant ($p \leq 0.05$) increase in number of foot slips and the time spent on beam at the highest dose of 350 mg/kg, compared to control. However, the extract had no effect on the onset of seizure compared to the control in both PTZ and STN-induced seizures and offered no protection against STN and MES-induced seizure. The results indicated that the ethanol extract of *T. globiferus* possesses sedative effects in mice and minimum or no anticonvulsant properties in mice and chicks.

Keywords: *Tapinanthus globiferus*, Electroshock, Pentylenetetrazole, Strychnine

INTRODUCTION

Tapinanthus globiferus commonly known as mistletoe (English), *Kauchin kadanya* (Hausa), *Eme-emi afomo* (Yoruba), and *Osisi/Okwuma osa* (Igbo) in Nigeria, is semi-parasitic that mostly grows on a large number of tree species such as *Vitellaria paradoxa* in West Africa and belong to the family of *Loranthaceae* [1]. In West Africa, mistletoes are found on many tree crops of economic importance including the shea butter tree (*Vitellaria* Gaertn. *F.*), the Neem tree (*Azadirachta indica L.*), Citrus species, especially sweet orange (*Citrus sinensis* L.) and grape (*Citrus paradise* L.), cocoa (*Theobroma cacao* L.) and rubber (*Hevea brasiliensis* Muell Arg.) [2]. Some pharmacological studies on the various mistletoes extract revealed that, the extract possess hypotensive, hypoglycaemic, antilipidaemic, antioxidant, anti-inflammatory and antimicrobial properties [3-5]. *T. globiferus* have been used in traditional medicine in the management of hypertension, insomnia, epilepsy, pain relief, tinnitus and trypanosomiasis [6]. Fresh leaves of *T.*

[*] Corresponding author. *E-mail*: am.huguma@yahoo.com *Tel*: +234 (0) 8065541850
ISSN 0189-8442

globiferus crushed in cold water served as remedies for tumour in South-western Ethiopia [7]. A mixture of one handful each of fresh leaves of *T. globiferus* and root bark of *Boswellia odorata* macerated in 5L of local beer and taken orally for two weeks daily are used to treat Syphilis in the Ebolowa region of Cameroon [8]. *T. globiferus* and *Treculia africana* mixture were observed to have good postprandial sugar lowering effect [4]. There is little or no scientific information on the sedative and anticonvulsant activity of *T. globiferus*. Hence, this study was designed to evaluate the sedative and anticonvulsant properties of the ethanol extract of *T. globiferus* in mice and chicks.

EXPERIMENTAL

Plant collection and extraction. Fresh *Tapinanthus globiferus* (mistletoe) of *Vitellaria paradoxa* tree (host) was collected from Huguma village of Takai L.G.A, Kano State, Nigeria. The plant was identified and authenticated in the Herbarium unit of the Department of Biological Sciences, Ahmadu Bello University Zaria, Nigeria by comparing with existing voucher specimen number 1052. The plant was dried under shade until constant weight, crushed and pounded into fine powder using pestle and mortar. Powdered material (1500 g) was used for the extraction in 75% ethanol and the extraction was carried out using Soxhlet extractor. The extract was concentrated using water bath at 60^{o}C.

Experimental animals. Mice (weighing 20 – 25 g) were obtained from animal House of the Department of Pharmacology and Therapeutics, Ahmadu Bello University, Zaria. Animals were kept in a well-ventilated room, fed with a pelletized grower mash (Vital feeds, Plc Jos) and water provided *ad libitum* while day old cockerels (weighing 28-30 g) were obtained from the National Animal Production and Research Institute (NAPRI) Shika, Zaria.

Chemicals and equipment. Drugs/chemicals and equipment were obtained from reputable scientific supplies such as F. Hoffmann-La Roche Ltd, Basel, Switzerland (Diazepam and Phenobarbitone), Sanofi-Sythelabo Ltd, UK (Sodium valproate), Sigma Aldrich Inc. USA (Pentylenetetrazole), Sigma Chem. Co. USA (Ethanol and Strychnine), Dana Plc Nigeria (Normal saline), Parke-Davis and Co. Ltd, Detroit, M.I. (Phenytoin sodium) and Ugo Basile, Model No. 7801, Comerio, VA, Italy (Electroconvulsive machine).

Diazepam-induced sleeping time in mice. The method of [9] was used. Twenty-four mice of either sex were divided into four groups of six each. The first group served as control and was treated with normal saline (10 ml/kg, body weight *i.p.*). The second, third and fourth groups were treated with graded doses of *T. globiferus* ethanol extract (87.5, 175 and 350 mg/kg, body weight *i.p* respectively). Thirty minutes post treatment, mice in all groups received 25 mg/kg body weight of diazepam *i.p.* Mice were placed individually in cages. The onset and duration of sleep were determined for each mouse. The interval between the loss and recovery of righting reflex were observed and considered as the duration of sleep.

Beam walking assay. The beam walking assay was carried out according to the method of [10]. The beam was made of wood (8 mm in diameter and 60 cm long) elevated 30 cm above the bench by metal supports. Mice were trained to walk from a start platform along a ruler (80 cm long and 3 cm wide) elevated 30 cm above the bench by metal supports to a goal box. Three trials were made for each mouse, such that the mice tested would be aware that there was a goal box that could be reached. Thirty trained mice were divided into five groups of six each. The first group received 10 ml/kg body weight normal saline *i.p*. The second, third and fourth groups received the extract at doses of 87.5, 175 and 350 mg/kg, body weight *i.p* respectively. The

fifth group received diazepam (1 mg/kg body weight, *i.p*). Thirty minutes post-treatment, each mouse was placed on the beam at one end and allowed to walk to the goal box. Mice that fall were returned to the position they fell from, mouse was allowed to spend a maximum of 60 second on the beam. The number of foot slips (one or both hind limb slipped from the beam) and time spent to reach the goal box was recorded.

Pentylenetetrazole (PTZ)-induced convulsion test in mice. The method of [11] was adopted. Thirty mice were divided into five groups of six each. First, second and third groups were treated with graded doses of *T. globiferus* ethanol extract (87.5, 175 and 350 mg/kg, body weight *i.p* respectively). Fourth and fifth groups received sodium valproate (200 mg/kg) and normal saline (10 ml/kg) respectively (*i.p*). Thirty minutes after *i.p* treatment, mice in all groups received 100 mg/kg body weight of PTZ subcutaneously (s.c.) and observed for 30 minutes for the onset and incidence of seizures. An episode of tonic extension of the hind limbs, which persisted for a minimum of 30 seconds, was taken as threshold convulsion. Lack of threshold convulsion during 30 minutes of observation was regarded as protection.

Strychnine-induced convulsion test in mice. The method of [12] was adopted. Thirty adult mice of either sex were divided into five groups of six each. Groups I, II and III received 87.5, 175 and 350 mg/kg, *i.p* body weight of *T. globiferus* ethanol extract respectively. Mice in group IV, served as control and received normal saline (10 mg/kg *i.p*) while group V, received phenobarbitone (30 mg/kg *i.p*). Thirty minutes after *i.p* treatment, mice in all groups received 1.2 mg/kg body weight of Strychnine nitrate s.c. and they were observed for a period of 30 minutes for the onset and incidence of convulsion. Prevention of tonic hind-limb extension within 30 minutes was considered as an indication of anticonvulsant activity. Seizure was manifested as tonic hind limb extension and the ability of the extract to prevent the feature or prolong the latency or onset of tonic hind limb extension was taken as an indication of anticonvulsant activity.

Maximal electroshock-induced convulsion test in chicks. The method of [13] was adopted. Fifty chicks were divided into five groups of ten (10) each. Group I were given 10 ml/kg *i.p.* normal saline and Group II received 20 mg/kg *i.p.* phenytoin. Groups III, IV and V received extract at doses of 87.5, 175 and 350 mg/kg (*i.p.*) respectively. Thirty minutes later, maximal electroshock was delivered to each chick to induce seizure using an Ugo Basile electro-convulsive machine (Model No. 7801) connected with corneal electrodes to the eyelid of each chick. The parameters used were 80 mA (current), 100 Hz (frequency), 0.8 s. (shock duration) and 0.6 ms (pulse width). Time of recovery from seizures was recorded. The episodes of tonic extension of the hind limbs were regarded as full convulsion while lack of tonic extension of the hind limbs was considered as protection.

Statistical analysis. Results were expressed as the Mean ± Standard error of mean (Mean ± SEM) and the differences between means were considered significant when $p \leq 0.05$. The significant differences were carried out using one - way analysis of variance (ANOVA) followed by Dunnett's Post-hoc test.

RESULTS

Diazepam-induced sleep in mice. The ethanol extract of *T. globiferus* produced a significant ($p \leq 0.05$) and dose dependent decrease in the time of onset of sleep at the tested doses (87.5, 175 and 350 mg/kg) and increase in the duration of diazepam-induced sleep at 175 and 350 mg/kg compared to control (Fig. 1).

Beam walk test in mice. The ethanol extract of *T. globiferus* at dose of 350 mg/kg offered significant ($p \leq 0.05$) increase in the time spent to reach the goal box and number of foot slips, but at the doses of 87.5 and 175 mg/kg, the extract did not significantly increase the number of foot slips compared to normal saline treated group (control). Diazepam (1 mg/kg) significant ($p \leq 0.05$) increase the time spent to reach the goal box and number of foot slips compared to the control group (Fig. 2).

Pentylenetetrazole (PTZ)- induced convulsion test in mice. The ethanol extract of *T. globiferus* at doses of 175 and 350 mg/kg showed 33.33 % and 16.67 % protection respectively against subcutaneous pentylenetetrazole-induced seizure in mice. An insignificant ($p \geq 0.05$) delay in the onset of seizure was observed at the tested doses (87.5, 175 and 350 mg/kg) when compared to the control group treated with 10 ml/kg normal saline. Sodium valproate (200 mg/kg) produced 66.67 % protection against PTZ-induced convulsion and mortality in mice (Table 1).

Strychnine-induced convulsion test in mice. The ethanol extract of *T. globiferus* did not protect mice against strychnine induced convulsion at all tested doses (87.5, 175 and 350 mg/kg) but insignificantly ($p \geq 0.05$) prolonged the onset of convulsion at dose of 350 mg/kg when compared to the control group. Phenobarbitone (30 mg/kg) used as positive control produced 100 % protection against both convulsion and mortality induced by subcutaneous administration of 1.2 mg/kg strychnine (Table 2).

Maximal electroshock-induced convulsion in chicks. The ethanol extract of *T. globiferus* offered no protection against hind limb tonic extension (HLTE) in maximal electroshock-induced convulsion in chicks at all tested doses (87.5, 175 and 350 mg/kg).

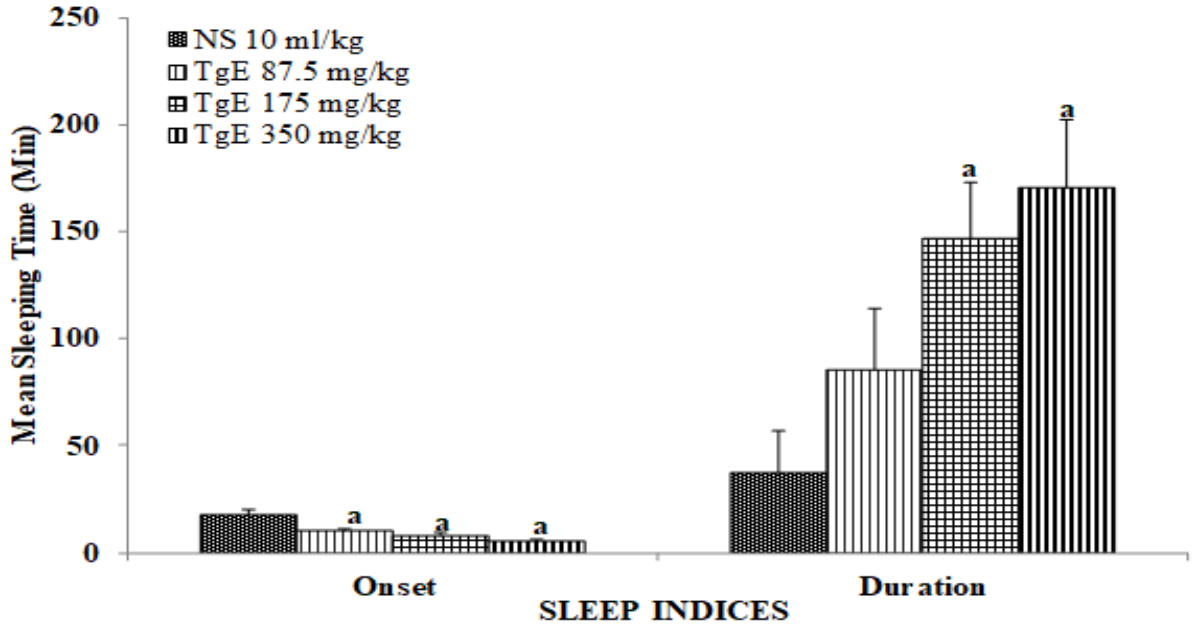

Fig 1: Effect of ethanol extract of *Tapinanthus globiferus* on onset and duration of diazepam-induced sleep in mice. [a]P≤0.05 compared to NS; One-way ANOVA followed by Dunnett's Post-hoc test. n=6; Data = Mean ±SEM; diazepam (25mg/kg); route of administration = intraperitoneal; TgE = *Tapinanthus globiferus* ethanol extract; NS = Normal saline

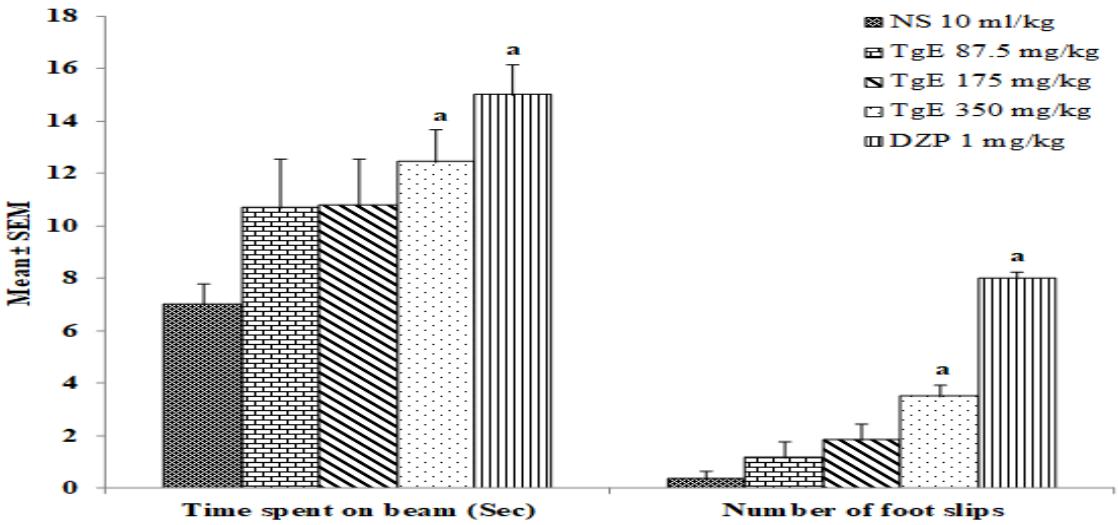

Fig 2: Effect of ethanol extract of *Tapinanthus globiferus* on time spent and number of foot slips in Beam Walk Test in mice. [a]P≤0.05 compared to NS; One-way ANOVA followed by Dunnett's Post-hoc test. n=6; Data = Mean ±SEM; route of administration = intraperitoneal; TgE = *Tapinanthus globiferus* ethanol extract; NS = Normal saline; DZP = diazepam

Table 1: Effect of ethanol extract of *Tapinanthus globiferus* on pentylenetetrazole-induced convulsion in mice

Treatment (mg/kg)	Mean onset of seizure (min)	Quantal protection	% protection	% mortality
NS 10 ml/kg	4.50±0.43	0/6	0.00	83.33
TgE (87.5)	5.67±0.88	0/6	0.00	66.67
TgE (175)	5.00±1.90	2/6	33.33	50.00
TgE (350)	5.83±1.78	1/6	16.67	33.33
SV (200)	3.33±2.17	4/6	66.67	16.67

No significant difference between control and treated groups, one way ANOVA followed by Dunnett's Post-hoc test. n = 6, Data = Mean ± SEM, route of administration = intraperitoneal, TgE = *Tapinanthus globiferus* Ethanol Extract, NS = Normal saline, SV = Sodium valproate, Pentylenetetrazole (100 mg/kg s.c).

Table 2: Effect of ethanol extract of *Tapinanthus globiferus* on strychnine-induced convulsion in mice

Treatment (mg/kg)	Mean onset of convulsion (min)	Quantal protection	% protection	% mortality
NS 10 ml/kg	3.67 ± 0.21	0/6	0.00	100
TgE (87.5)	3.17 ± 0.48	0/6	0.00	100
TgE (175)	3.50 ± 0.43	0/6	0.00	100
TgE (350)	4.17 ± 0.60	0/6	0.00	100
PBT (30)	0.00 ± 0.00[a]	6/6	100	0

[a]P ≤ 0.05 compared to NS, One way ANOVA followed by Dunnett's Post-hoc test. n = 6, Data = Mean ± SEM, Route of administration = intraperitoneal, TgE = *Tapinanthus globiferus* Ethanol Extract, NS = Normal saline, PBT = Phenobarbitone, Strychnine (1.2 mg/kg s.c).

Table 3: Effect of ethanol extract of *Tapinanthus globiferus* on maximal electroshock-induced convulsion in chicks

Treatment (mg/kg)	Mean recovery time (min)	Quantal protection	% protection	% mortality
N/saline (10 ml/kg)	5.40 ± 1.15	1/10	10	0
TgE (87.5)	7.20 ± 0.79	0/10	0	0
TgE (175)	5.90 ± 0.59	0/10	0	0
TgE (350)	6.00 ± 0.87	0/10	0	0
PNT (20)	0.00 ± 0.00[a]	9/10	90	0

[a]P ≤ 0.05 compared to NS, One way ANOVA followed by Dunnett's Post-hoc test. n = 6, Data = Mean ± SEM, Route of administration = intraperitoneal, TgE = *Tapinanthus globiferus* Ethanol Extract, NS = Normal saline, PNT = Phenytoin.

Similarly, there was no significant ($p \geq 0.05$) difference in the recovery time at all tested doses of the extract compared to normal saline treated group (control). Phenytoin (20 mg/kg) produced 90 % protection against HLTE (Table 3).

DISCUSSION

The ethanol extract of *Tapinanthus globiferus* showed a depressant effect on the central nervous system. This action was demonstrated by its effects on diazepam-induced sleep, beam-walk assay, maximal electroshock test (MEST), pentylenetetrazole (PTZ) and strychnine (STN)-induced seizure. Diazepam-induced sleep test is used to illustrate central nervous system active property of drug [14]. However, the pharmacological test of sedative, hypnotics, tranquilizers, neuroleptics as well as antidepressants is based on the potentiation of sleeping time induced by barbiturates or other sedative agents. The ethanol extract of *T. globiferus* significantly ($p \leq 0.05$) reduced the onset and prolonged the duration of sleep induced by diazepam in a dose dependent manner. The potentiation effects of the extract on diazepam-induced sleep, suggests that the extract have central nervous system depressant activity and possibly sedative property. Beam-walking assay is used to test the effect of substance on motor coordination in laboratory animals [10] and also to screen for peripheral neuromuscular blockade [15]. Beam walking assay is a sensitive model for detecting sedative dose [16]. The number of foot slips in beam walking assay is a sensitive measure in detecting benzodiazepine-induced motor coordination deficits in mice and may be more useful in predicting doses that could cause sedation in clinical settings [10]. The significant effects of the extract at highest dose and diazepam on foot slips in beam walking test revealed the sedative activity of the extract. The effects of the extract on diazepam-induced sleep and beam walking assay showed that, the extract have sedative activities which may be acting via central mechanisms and peripheral neuromuscular blockade respectively. Diazepam-induced sleep is a model used to assess sedative activity while beam walking assay to distinguish central and peripheral activity [15]. The ability of the *T. globiferus* extract to potentiate diazepam-induced sleep and increase number of foot slips may confirmed its depressant activity. The *T. globiferus* extract might have produced its depressant effects through activation of the receptors of endogenous neurotransmitters such as dopamine, norepinephrine, serotonin, gamma amino butyric acid (GABA), histamine or neuropeptides. Alternatively, that the extract potentiates the sedative property of diazepam and it may act by interacting with GABA-mediated synaptic transmission [17]. Diazepam acts at the level of the limbic, thalamic and hypothalamic regions of the CNS through potentiation of GABA. GABA is known to be an important inhibitory neurotransmitter in the brain. GABA interacts with GABA-receptors ($GABA_A$, $GABA_B$ and $GABA_C$-receptor). However, $GABA_A$-receptor controls the opening of chloride channel for the entering of chloride anions resulting in the neuronal hyperpolarisation [18].

The ethanol extract of *T. globiferus* prolonged the mean onset of acute seizure induced by chemical convulsants (PTZ and STN) and offered minimum protection against PTZ-induced seizure. The extract increased onset of convulsion in both PTZ and STN may reveal that the plant has a weak anticonvulsant property that delayed the occurring of convulsion due to the PTZ or STN and may suggest that the extract might possess an element of anticonvulsant properties. PTZ-induced seizure is a model of screening agents with activity against petit mal epilepsy [19]. Sodium valproate and ethosuximide are useful in the management of

absence seizure and inhibit PTZ-induced seizure [20]. Prolongation in onset of seizure in the PTZ model provided evidence that extract can be effective in absence seizure [19]. Pentylenetetrazole act as selective antagonist that blocks the inhibitory effects of GABA at $GABA_A$ receptors and STN acts as a selective and competitive antagonist that block the inhibitory effects of glycine at all glycine receptors. GABA is the major inhibitory neurotransmitter in the brain while glycine is inhibitory neurotransmitter in the spinal cord [21]. The minimum effect produced by the extract may probably act through GABAergic inhibitory mechanism by blocking the effects of PTZ on the receptors. The extract offered no protection in chicks against MEST (non-chemical convulsant). Maximal electroshock test is used primarily for compounds that are effective in grand mal epilepsy [22]. Hence, the extract is ineffective in generalized tonic clonic seizures and may be effective in the management of absence seizure.

Conclusion: The results of the study showed that the ethanol extract of *T. globiferus* contained active constituents, which have sedative effects and weak or minimum anticonvulsant properties in mice and also gave scientific justification for the use of the plant in the management of sleep disorder and convulsion as claimed in traditional medicine.

REFERENCES

1. Burkill, H.M. (2000). *Useful Plants of West Tropical Africa*. (2nd ed.) Royal Botanic Gardens, Kew England, 5: Pp. 548-560.

2. Adesina, S.K., Illoh, H.C., Johnny, I.I. and Jacobs, I.E. (2013). African mistletoes (*Loranthaceae*); Ethnopharmacology, Chemistry and Medicinal values. *Afr. J. of Trad., Compl. and Alt. Med.*, pp 161-170.

3. Jadhav, N., Patil, C.R., Chaudhari, K.B., Wagh, J.P., Surana, S.J. and Jadhav, R.B. (2010). Diuretic and natriuretic activity of two mistletoes species in rats. *Pharmacog. Res.*, pp 50-57.

4. Ogbonnia, S. O., Anyika, E.N., Mbaka, G.O., Utah, P., Ugwu, D., Nwakakwa, N. and Ota, D.A. (2012). Antihyperglycaemic and antihyperlipidaemic effects of aqueous ethanol extract of *Tapinanthus globiferus* leaves and *Treculia Africana* root bark and their mixture on alloxan diabetic rats. *Agr. and Bio. J. N. America*, 3(6), 237-246.

5. Samba, M., Cheikh, A., Abdullahi, M.V., Hadou, A., Boumediana, A.I., Kaihil, A., Deida, M. V., Dieng, S., Essassi, E.M. and Minnih, M.S. (2015). Ethnobotanic study, phytochemical screening, anti-oxidant and anti- bacterial activities of *Tapinanthus pentagonia*. *J. Chem. and Pharmaceu. Res.*, 7(4), 1604-610.

6. Abedo, J.A., Jonah, A., Abdullahi, R., Mazadu, M., Idris, H., Muhammed, H., Shettima, F., Ombugadi, S., Dauda, M., Garba, J., Abdulmalik, U. and Kagu, B. (2013). Comparative Studies of *In vitro*, *In vivo* Trypanocidal Activity and Phytochemical Screening of *Tapinanthus globiferus* and *Gongronema latifolium. Int. J. of Animal and Vet. Adv.*, 5(3), 120-124.

7. Yineger, H. and Yewhalaw, D. (2007). Traditional medicinal plant knowledge and use by local healer in Sekoru District, Jimma Zone, South-western Ethiopia. *J. Ethnobio. and Ethnomed.*, 3, 24-30.

8. Noumi, E. and Eloumou, M.E.R. (2011). Syphilis ailment; Prevalence and Herbal Remedies in Ebolowa subdivision (South region, Cameroon). *Int. J. Pharm. Biomed. Sci.* 2(1), 20-28.

9. Rakotonirina, S.V., Ngo Bum, E., Rakotonirina, A. and Bopelet, M. (2001). Sedative properties of the decoction of the rhizome of *Cyperus articulates*. *Fitoterapia*, 72, 91-95.

10. Stanley, L.J., Lincoln, J.R., Brown, A.T., McDonald, M., Dawson, R.G. and Reynolds, S.D. (2005). The mouse beam walking assay offers improved sensitivity over the mouse rotarod in determining motor coordination deficits induced by benzodiazepines. *J. Psychopharm.*, 19, 221-227.

11. Swinyard, E.A., Woodhead, J.H., White, H.S. and Franklin, M.R. (1989). General principles: Experimental selection, quantification and evaluation of anticonvulsants. In: Levy, R.H., Matson, R.H., Meldrum, B., Penry, J.K. and Dreifuss, F.E. (Eds.). *Antiepileptic Drugs*, Third Edition, Raven Press, New York, Pp. 85-102.

12. Porter, R.J., Cereghino, J.J. and Gladding, G.D. (1984). *Antiepileptic Drug Development*,

Livingstone. Elsevier Science Limited. Pp. 515-557.

13. Swinyard, E.A. and Kupferberg, H.J. (1985). *Antiepileptic drugs*: detection, quantification and evaluation. *Federal Proceedings*, 44, 39-43.

14. Vogel, G.H. (2008). Psychotrophic and neurotrophic activity In: Vogel, G. H. (Ed) *Drug discovery and Evaluation: Pharmacological Assays*, Springer-Verlag Berlin Heidelberg New York, pp. 566-874.

15. Ya'u, J., Abdulmalik, U.A., Yaro, A.H., Chindo, B.A., Anuka, J.A. and Hussaini, I.M. (2011). Behavioural properties of *Balanites aegyptiaca* in rodents. *J. Ethnopharmacol.*, 135, 725 – 729.

16. Magaji, M.G., Yaro, A.H., Musa, A.M., Anuka, J.A., Abdu-Aguye, I. and Hussaini, I.M. (2012). Central depressant activity of butanol fraction of *Securinega virosa* root bark in mice. *J. Ethnopharm.*, 141, 128–133.

17. Tanko, Y., Ezekiel, I., Okpanachi, A.O., Goji, A.D.T., Ndebi, H., Musa, K.Y. and Mohammed, A. (2009). Behavioural Effects of Hydro-methanolic Crude Extract of Aerial Part of *Indigofera pulchra* in mice. *J. Bio. Sci.*, 1(3), 89-93.

18. Mirshafa, S.A., Azadbakht, M. and Ahangar, N. (2013). Study of Antidepressant and Sedative-Hypnotic Activity of Hydroalcoholic Extract of *Asperugo procumbens* L. Aerial Parts in Mice. *Ira. J. Pharmaceut. Res.*, 12(3), 529-535.

19. Garba, K. and Yaro, A.H. (2015). Anticonvulsant actions of ethanol stem bark extract of *Trichilia roka* (*Meliaceae*) in mice and chicks. *J. Phytopharmacol.*, 4(4), 231-234.

20. McNamara, J.O. (2006). Pharmacotherapy of the epilepsies In: Goodman and Gilman's, Brunton, L.L., Lazo, J.S. and Parker, K.L. (Eds.); *The Pharmacological Basis of Therapeutics*, (11th ed.), McGraw-Hill Medical Publishing Division, New York, pp. 501-526.

21. Rang, H.P., Dale, M.M. and Ritter, J.M. (1998). Antiepileptic drugs and centrally acting muscle relaxants In: Rang, Dale and Ritter, (Eds.). *Pharmacology* (3rd ed.), Churchill Livingstone, Longman Group, London, pp. 596-608.

22. Rang, H.P., Dale, M.M., Ritter, J.M. and Moore, P.K. (1995). Chemical transmission and drug action in the Central Nervous System In: Rang and Dale (Eds.). *Pharmacology* (3rd ed.). Churchill Livingstone, New York, pp. 473 – 512.