



## **Anticonvulsant Potential of Dichloromethane Extract of *Aspilia africana* Leaf in Mice**

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### **Authors' contributions**

*This work was carried out in collaboration between both authors. Author KJO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors HDK and KJO managed the analyses of the study. Author HDK managed the literature searches. Both authors read and approved the final manuscript.*

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### **ABSTRACT**

**Aim:** The study was carried out to determine the anticonvulsant potential of dichloromethane leaf extract of *Aspilia africana*.

**Study Design:** Three seizure models namely: Pentylentetrazole (PTZ), strychnine (STC) and maximal electroshock (MES) were used, motor coordination behavior of the animals were also assessed.

**Place and Duration of Study:** The study was carried out between the months of October and November, 2017 at Pharmacology laboratory, Department of Pharmacology and Toxicology, Faculty of Pharmacy, Niger Delta University, Bayelsa State, Nigeria.

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**Methodology:** The powdered leaves of *A. africana* (2000 g) were extracted with 10 liters of 100% dichloromethane. Doses of 25, 50, 100 and 200 mg/kg were administered to the test animals.

**Results:** The chemical models, STC & PTZ showed 50% & 100% survival respectively. The delayed onset of seizure suggested anti-seizure potential of dichloromethane extract of *A. Africana* leaf with the maximal latency period of seizure recorded in the 25 mg/kg dose within the following chemical models, this was significant,  $P = .05$  compared to the normal control. The MES method showed that at doses of 25 & 50, 100 mg/kg, the animals were 66.7% & 50% free of hind limb tonic extension (HLTE). Furthermore, there was reduced motor coordination potential at 25 mg/kg by 68.5%, which was significant at the level of,  $P = .05$ , compared to healthy control.

**Conclusion:** From the preceding, it can be seen that the dichloromethane leaf extract of *A. Africana* has antiseizure potential.

**Keywords:** *A. africana*; antiseizure; pentylenetetrazole (PTZ); strychnine (STC); maximal electroshock (MES).

## 1. INTRODUCTION

Convulsion is a chronic neurological condition with history across all ages, race and gender with prevalence variance across countries; it is characterised by uncontrolled muscle contraction and relaxation of the affected body part resulting to bladder and bowel incontinent [1]. In a convulsion is often a symptom of an epileptic seizure, so the term convulsion is commonly used as a synonym for seizure. However, not all epileptic seizures lead to convulsions, and not all convulsions are caused by epileptic seizures [2,3].

It is the third most common chronic neurological disorders characterised by seizures after stroke and Alzheimer's disease [4,5]. According to the WHO, 2017 fact sheet report about 50 million people suffers epilepsy worldwide especially 75-80% of the population live in developing countries with little or no access to medical services or treatment [6, 7]. The prevalence of epilepsy in Nigeria is about 6.2 to 20.8 per 1000 [8,9]. However, it has been reported not less than 30% of epileptic seizure that is associated with individuals and does not have seizures control even with the best available medications [10,5,11,6]. Furthermore, undesirable side effects such as psychosis, agitations, aggression, allergies, sedation, blood dyscrasias, teratogenesis, changes in mood, memory problems and intolerance of anticonvulsant drugs are clinically often rendered as treatment difficult. Thus, search for new, safer and affordable antiepileptic drugs are geared towards naturally-occurring compounds, which is thought to belong to new structural, chemical classes of especially from herbal sources.

Several authorities acknowledge that natural products remained the keystone in drug

discovery and maintained the essential role in antiepileptic seizure even in the future [12]. Various medicinal plants are known for their anticonvulsant value, and their extracts are imperative source of chemicals for the development of better and safer drugs for the treatment of epilepsy as earlier stated. Leaves of *Solanum Nigrum* may be beneficial in producing anti convulsive property amongst mammalian entity. Several studies on the same plant also excavate the fact that, except anti-convulsion *A. Africana*, also posses effects against moderate haematopoiesis [13]. Similarly, the use of herbal medicine in the management of epilepsy is widely accepted among rural dwellers in most Nigerian communities, and their efficacies are well acclaimed [14]. Some of these medicinal plants remain unexplored for their value as sources of antiepileptic drugs and therefore, research is encouraged to validate the folkloric claims of these medicinal plants to provide scientific evidence of their safety and efficacy [6].

The plant *Aspilia africana* (wild sunflower), also called iodine or haemorrhage plant because of its characteristics, is said to be an *Asteraceae* species and was evaluated for its potential chemoprotective bioactivities among others.

### 1.1 Justification to the Study

No available literature indicating antiseizure potential as well as other related behavioural changes evaluation of non-polar dichloromethane extract of *A. africana* leaf extracts as at the time of this study it is found that leaf extracts of *A. africana* are much more sensitive in controlling out the seizure. Thus, its property suggests flavonoids, and tannins pull as revealed in kinds of literature. The study was established following the antiepileptic territorial

claim of *A. africana* leaves among the Joinkrama People of the Engenni ethnic nationality of Ahoada West Local Government Area of Rivers State, Nigeria.

## 2. MATERIALS AND METHODS

### 2.1 Plant Material and Preparation of *Aspilia africana* Extraction

Fresh leaves of *Aspilia africana* were sourced from Wilberforce Island rainforest around the Niger Delta University, Bayelsa State, Nigeria. On the 17th of February, 2017, and were authenticated by DR. Gideon Alade of the Department of Pharmacognosy and Herbal Medicine, Faculty of Pharmacy, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria. The voucher specimen of the plant leaves were prepared and deposited at the Herbarium Unit of the same department, NDUP 098. Fresh leaves of *A. africana* were collected, air-dried for 14 days and made a powder using an industrial grinder. The powdered leaf of *A. africana* (2000 g) was extracted cold in 10 litres dichloromethane (100%). The mixture was filtered and the filtrate concentrated using a rotary evaporator at a maximum temperature of 45°C. The total dried extract obtained from the 2000 g powdered leaves of *A. Africana* was 51.9 g given 2.6% w/w yield of dichloromethane. The semi-solid paste of the dichloromethane extract of *A. Africana* leaf was stored in the refrigerator at 4°C till needed for use. The study dose was established based on preliminary data that proof ratio 1/33 of the LD50 (6.6 g/kg) safe in mice [15,16] using intraperitoneal route (i.p); hence 200, 100, 50 and 25 mg/kg applied in the study. The semi-solid paste of the dichloromethane extract was dissolved in 20% of tween80, and as such, the subjects in control group received 20% tween80 normal saline.

### 2.2 Experimental Animals

One hundred and eight (108) male mice weighed between 23 g, and 30 g were obtained from the animal house of the Department of Pharmacology, College of Health Sciences, University of Port Harcourt, Nigeria. Those were acclimatised for two weeks at the Animal Breeding and Research Unit, Department of Pharmacology and Toxicology, Faculty of Pharmacy, Niger Delta University, Wilberforce Island Bayelsa State, Nigeria. The animals were kept under conducive laboratory conditions and

fed with standard animal feed (Grower's pelletized), and water ad libitum. The principle of laboratory animal care as prescribed by the National Institute of Health-NIH (publication No. 85-23) guidelines and procedures [17,18] were followed in this study. The research study approval was subjected to the Postgraduate Research Ethical Committee, University of Port Harcourt, Nigeria.

### 2.3 Administration of Extract

The extract was administered to the male mice respectively through the i.p route. The volume of extract administered intraperitoneally was ten mL/kg in all cases. The i.p route was used in this study because it is considered to be faster, more consistent in its outcome and is readily reproducible as it bypasses enteral route metabolic effects (first pass result). This route is preferred in the central nervous system related studies because of the possibility of interference of metabolic processes with the test agents given through the oral course as well as maintain regular route of administration for both extract and the chemical substances [19]. The dichloromethane extract as non-polar extract was made i.p applicable via dissolution of the semi-solid extract in 20% tween80 including 20% tween 80 normal salines for a control group.

### 2.4 Anti-seizure Study Design

The study design was adapted from three methods of seizure induction of the *in vivo* animal model as described by Kasthuri et al. [20].

### 2.5 Maximum Electroshock-induced Convulsion in Mice

The method of Swinyard and Kupferberg [21] and Browning [22] was employed. Thirty-six (36) male mice were randomly allotted into six groups of six mice each (n=6). The first group received i.p ten mL per body weight 20% tween 80 normal saline and the second group received i.p 60 mg/kg phenobarbitone (analytical grade) while the third, fourth, fifth and sixth group received 25, 50, 100 and 200 mg of the dichloromethane extract per kg body weight i.p respectively. Thirty minutes later, maximum electroshock was administered to induce a seizure in the mice using Ugo Basile electroconvulsive machine (Model 18182 v 220) with an electrode clipped to each ear of the mice. The current, shock duration, frequency and pulse width set and maintained at 60 mA, 2.0 s, 100

pulses per second and 2.0 ms respectively. Abolition of hind limb tonic extension (HLTE) was considered protection from electroshock [23].

## 2.6 Strychnine-induced Convulsion in Mice

The method of Porter et al. [24] was employed. As stated in the MES method earlier, the first group received i.p 10 mL per body weight 20% tween 80 normal saline and the second, third, fourth, and fifth group receive i.p 25, 50, 100 and 200 mg per body weight and the sixth group received i.p 1.0 mg/kg of diazepam (Swipha Nig. Ltd.). Thirty minutes later, mice in all the groups received i.p 2.0 mg/kg of strychnine (Sigma chemicals Co. St Luis U.S.A). Abolition of tonic extensor jerks of the hind limbs was considered an anticonvulsant indicator in strychnine-induced convulsions.

## 2.7 Pentylentetrazole (PTZ) Induced Convulsion in Mice

The method of Swinyard et al. [25] was employed. As treated in the STC method, thirty minutes later, male mice in all the groups receive i.p 80 mg/kg pentylentetrazole (Sigma chemicals Co. St Luis U.S.A). An absence of an episode of clonic spasm of at least 5 seconds duration indicated the extract's ability to abolish the pentylentetrazole seizure stimulation.

## 2.8 Motor Coordination Evaluation

Test for motor coordination and motor planning potential of *A. africana* leaf extract of dichloromethane in thirty-six (36) male mice were adopted from Swinyard and Kupferberg [21] using Ugo Basile, Italy Rota Rod (for mice 47600 V04). The rotarod is set at 6 revolutions per minute (rpm) for 120 s with baseline record established by placing each of the mice on the rotarod for at least 120 s constant grip were selected, weighed and divided into the healthy control group, phenobarbitone group and test groups of 25, 50, 100 and 200 mg/kg respectively. Thirty minutes after the controls and test extract have been administered. The falling time from the rotating rod was recorded for each mouse per group.

## 2.9 Method of Data Analysis

The laboratory data were expressed as mean, standard error of the mean ( $M \pm SEM$ ). Statistical

difference for parametric data was determined by one-way analysis of variance (ANOVA) followed by a post hoc test (Student Newman-Keuls Test, SNK). Difference considered statistically significant with  $P=0.05$  for all comparisons. Computer software Graph pad PRISM<sup>®</sup> version 5.00 was used for the analysis.

## 3. RESULTS AND DISCUSSION

### 3.1 Survival Rate

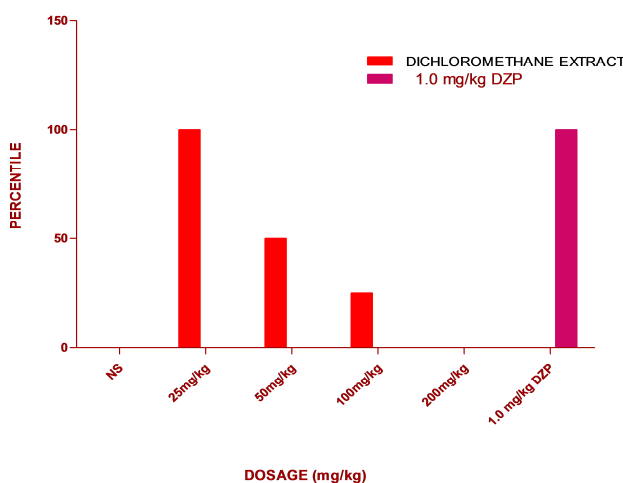
The chemical methods of seizure stimulation revealed survival rate of the subjects from seizure exposure for at least 24 h. The PTZ seizure survival rate suggests 100% protection in lowest dose, 25 mg/kg of *A. africana* leaf extract of dichloromethane as seen in Fig. 1 showing survival rate in treatment descending order. The STC method of seizure stimulation revealed a unique pattern in the survival rating of the exposure of the subject to seizure unlike the PTZ method, survival was observed in the highest dose of the plant extract at 25% protection over 24 h with 200 mg/kg while 25, 50 mg/kg rating 50% survival along the standard group as seen in Fig. 2.

### 3.2 Maximal Electro-Shock

The plant extract was evaluated using the incidence of HLTE seizure revealing 66.7% protection of forfeiture in the lowest dose, 25 mg/kg of dichloromethane extract of *A. africana* leaf with the mid doses, 50, 100 mg/kg suggesting 50% protection against HLTE seizure, see Table 1.

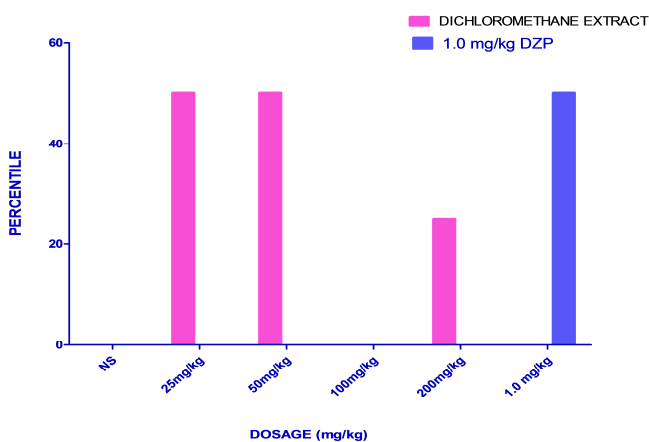
### 3.3 Seizure Latency Period

The dichloromethane extract of *A. africana* leaf was evaluated of latency period using the chemical method of seizure stimulation. The STC method showed unique pattern in Fig. 3 similar to Fig. 2. The Fig. 3 revealed decreased latency periods in dose depended on pattern except at the high dose, 200 mg/kg. The test group, 25 mg/kg and standard group responded equally linked to the glycine receptor inhibitory mechanism of STC besides of the fact that the test substance is un-purified and doesn't suggest glycine/acetylcholine substrate. Fig. 4 showed dose independence pattern with the highest latency period of over 300 s seen at the lowest dose yet.



**Fig. 1. Survival rate after PTZ induced convulsions at different doses of dichloromethane extract of *A. africana* leaf**

NS = 20% tween80 Normal saline, DZP = Diazepam.



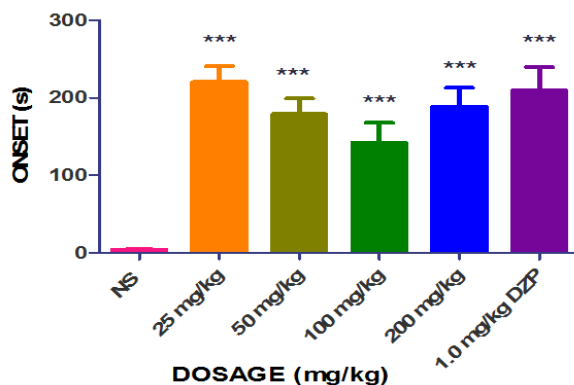
**Fig. 2. Survival rate after STC induced convulsions at different doses of dichloromethane extract of *A. africana* leaf**

NS = 20% tween80 Normal saline, DZP = Diazepam

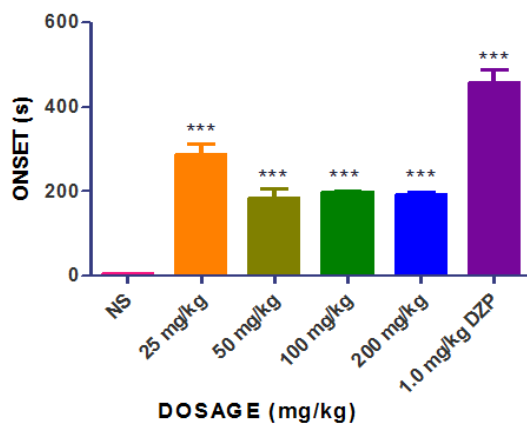
**Table 1. MES evaluation of dichloromethane extract of *A. africana* leaf**

| Treatment | Dose      | Incidence of HLTE seizure (%) |
|-----------|-----------|-------------------------------|
| NS        | 10 mL/kg  | 100                           |
| PHB       | 60 mg/kg  | 0*                            |
| DEAA1     | 25 mg/kg  | 33.3*                         |
| DEAA2     | 50 mg/kg  | 50                            |
| DEAA3     | 100 mg/kg | 50                            |
| DEAA4     | 200 mg/kg | 66.7                          |

N=6, \* denotes significant  $P = .05$  compared to normal control value, NS= 20% tween 80 Normal saline, PHB = Phenobarbitone, DEAA = Dichloromethane extract of *A. africana*



**Fig. 3. Effects of dichloromethane extract of *A. africana* leaf on STC induced seizure onset**  
 Data analysed using Newman-Keuls Multiple Comparison Test showed, \*\*\* denotes statistically significant ( $P=0.01$ ). S = Seconds, NS = 20% tween80 Normal saline, DZP = Diazepam



**Fig. 4. Effects of dichloromethane extract of *A. africana* leaf on PTZ induced seizure onset**  
 Data analysed using Newman-Keuls Multiple Comparison Test showed, \*\*\* denotes statistically significant ( $P=0.01$ ). S = Seconds, NS = 20% tween80 Normal saline, DZP = Diazepam

**Table 2. Motor coordination evaluation of dichloromethane extract of *A. africana* leaf**

| Treatment | Dose      | Rota rod performance (s) | % inhibition of motor coordination |
|-----------|-----------|--------------------------|------------------------------------|
| NS        | 10 mL/kg  | 120.0 ± 0.0              | 0                                  |
| PHB       | 60 mg/kg  | 85.0 ± 24.0              | 29.2                               |
| DEAA1     | 25 mg/kg  | 37.8 ± 7.4               | 68.5*                              |
| DEAA2     | 50 mg/kg  | 53.8 ± 10.3              | 55.2                               |
| DEAA3     | 100 mg/kg | 59.8 ± 18.0              | 50.2                               |
| DEAA4     | 200 mg/kg | 63.3 ± 22.7              | 47.3                               |

*N* = 6. Values are presented as the Mean ± SEM, NS = 20% tween80 normal saline, PHB = Phenobarbitone, DEAA = dichloromethane extract of *Aspilia africana*; \* denotes Significant  $P=0.05$  compared with the normal saline control group (one-way ANOVA followed by Newman-Keuls Multiple Comparison Test)

### 3.4 Discussion

Dichloromethane extract of *A. africana* leaf prove potent against seizure at 100% (PTZ method) and 50% (STC method) survival rate within 24 h of exposure remarkable in the lowest dose. 25

mg/kg as shown in Figs. 1 & 2. The MES method suggests protection against HLTE seizure at 66.7% observed in the lowest dose, 25 mg/kg and 50% in both mid doses 50 mg/kg and 100 mg/kg, see Table 1. This study outcome contrast an evaluation of anticonvulsant activity study by

Kar et al. [26] as well as Gollapalle et al. [27] and similar to Nazifi et al. [6]. The latency period was further used to evaluate the anti-seizure potential of *A. africana* leaf extract of dichloromethane using the strychnine and pentylenetetrazole methods also show delayed onset (increased latency period) of seizure with the least delayed onset period of 180 s observed in the mid dose, 100 mg/kg. The lowest dose, 25 mg/kg revealed the highest delayed onset period of over 200 s as shown in Fig. 3 with statistical significant ( $P = .05$ ) when compared with the normal control group. The pattern of response observed in Fig. 3 & 2 above, showed a unique resemblance of "U" shape pointing to increase latency period response in descending dose order with sudden increase latency period of seizure in the highest dose, 200 mg/kg with the standard group and the highest response of the test group, 25 mg/kg rated almost same because of the suggestive mechanism of action of strychnine, implicating glycine receptor inhibition rather than GABA receptor inhibition as mostly known of some other chemical agents used in seizure stimulation. The preliminary study and survival/lethal evaluation of the plant extract indicated gross mortality at higher doses above 200 mg/kg and survival at low dose less than 200 mg/kg (see Fig. 2) which also suggests body weight of the animal subject (mice) is incapable of accommodating high dose of the dichloromethane extract of *A. africana* leaf in the STC method contrary to recent study by Kemelayefa and Kagbo [28] but the Fig. 3 response is similar to a PTZ method study by Nazifi et al. [6]. Furthermore, the pattern of anticonvulsant potential can be said to be due to *A. africana* leaf phytoconstituents, [15] with flavonoids well known scientifically for its GABAergic activity. The dose independent pattern seen in this study may be attributed to the fact that the test substance is crude drug, unpurified as such is subject to biochemical compromises. This study outcome appears similar to anticonvulsant evaluation study by Nazifi et al. [6]; Kemelayefa and Kagbo [28]. The crude drug, *A. africana* leaf extract of dichloromethane tested positive to reduced motor coordination using rota rod means of evaluation complimenting the various methods of seizure evaluation in this study. The mean value of the treated groups with *A. africana* leaf extract of dichloromethane showed calmness among the doses with 25 mg/kg statistically significant ( $P = .05$ ) compared to the normal control (see Table 2 above). Further expression was made by estimating percentage of motor coordination

inhibition which appears similar to the mean score. This is a clear pointer of anxiolytic, sedative and antiseizure potentials with the earlier not scientifically measured in this study but apparent. It is also interesting to note that the reduced muscular tone was more pronounced in the test substance (dichloromethane extract of *A. africana* leaf) than the standard drug, phenobarbitone see Table 2 above. The mean value of the motor evaluation also showed dose independence. This can be attributed to the fact that the test substance are not pure compounds corresponding with antiseizure group of drugs recommended per seizure model used in this study and several other plant extracts studies especially similar to that of the Nazifi et al. [6]; Kemelayefa and Kagbo [28] including other studies with similar pattern of outcome compared to an evaluation of central nervous system effect study by Lidianne et al. [29] as well as *in vivo* sedative and muscle relaxants activity study by Rauf et al. [30].

#### 4. CONCLUSIONS

The study suggests the antiseizure potential of *A. africana* leaf extract of dichloromethane as well as reduced motor coordination pointing to strong relaxant potential as evidenced scientifically. The study has also expressed *A. africana* leaf extract to be sensitive to seizure control at the lowest dose 25 mg/kg in the electrical and chemical methods as well as reduced motor coordination. Future recommendations involve several beneficial effects of herbal clusters in remedy generation for various neural disorders, where sensory and motor paths are tried to keep in control to rule over the movement & posture mechanisms.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2015;84(16):1705-1713.  
DOI: 10.1212/wnl.0000000000001487
- Fisher R, Van E, Boas W, Blume W, Elger C, Genton P, Lee P, Engel J. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia*. 2005;46(4):470–2.  
DOI: 10.1111/j.0013-9580.2005.66104.x
- Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, Engel J, Forsgren L, French JA, Glynn M, Hesdorffer DC, Lee BI, Mather GW, Moshé SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S. ILAE official report: A practical clinical definition of epilepsy. *Epilepsia*. 2014;55(4):475–82.  
DOI: 10.1111/epi.12550
- Paul R. Carney. The textbook of nanoneuroscience and nanoneurosurgery. 2013;333–350. [ISBN: 978-1-4398-4941-5]
- Aliyu M, Mumammad A, Isma'il M, Muhammad J, Kamal Magaji GM. Phytochemical screening and anticonvulsant studies of ethyl acetate fraction of *Globimetula braunii* on laboratory animals. *Asian Pacific Journal of Tropical Biomedicine*. 2014;4(4):285–289.
- Nazifi AB, Danjuma NM, Temidayo OO, Jamilu Ya'u. Anticonvulsant activity of methanol stem bark extract of *Boswellia dalzielii* Hutch. Burseraceae in mice and chicks. *African Journal of Pharmacology and Therapeutic*. 2017;6(2):64-71.
- World Health Organization, WHO. Epilepsy fact sheet updated; 2017. Megiddo I, Colson A, Chisholm D, Dua T, Nandi A, Laxminarayan R. Health and economic benefits of public financing of epilepsy treatment in India: An agent based simulation model. *Epilepsia Official Journal of the International League against Epilepsy*; 2016.  
DOI: 10.1111/epi.13294
- Banerjee PN, David F, Hauser WA. The descriptive epidemiology of epilepsy-a review. *Epilepsy Research*. 2009;85(1):31-45.  
DOI: 10.1016/j.eplepsyres.2009.03.003
- Osakwe C, Alo C. Epilepsy prevalence, potential causes and social beliefs in Ebonyi state and Benue state, Nigeria. *Epilepsy Research*. 2014;108(2):316-326.  
DOI: 10.1016/j.eplepsyres.2013.11.010
- Yemitan OK, Adeyemi OO. Antiepileptogenic and anticonvulsant actions of *Dalbergia saxatilis* (Hook, F.) in sub-toxic chemical kindling and toxic convulsant models. *European Journal of Medicinal Plants*. 2013;3(2):288-296.  
DOI: 10.9734/ejmp/2013/3334
- National Institute of Neurological Disorders and Stroke, NINDS. The epilepsies and seizures: Hope through Research, National Institute of Neurological Disorders and Stroke (NINDS), U.S. National Institutes of Health (NIH), *Nature*. 2016;399(6738Suppl):15–A22.
- Malami S, Kyari H, Danjuma NM, Ya'u J, Hussaini IM. Anticonvulsant properties of methanol leaf extract of *Laggera aurita* Linn. F. (Asteraceae) in laboratory animals. *Journal of Ethnopharmacology*. 2016;191:301-306.  
doi: 10.1016/j.jep.2016.06.035
- Noel N. Wannang, Joseph A. Anuka, Helen O. Kwanashie, Steven S. Gyang, Asa. *Health Sci*. 2008;8(2):74–79.. Available: [https://www.ncbi.nlm.nih.gov/pubmed/?term=Auta%20A%5BAuthor%5D&cauthor=true&cauthor\\_uid=19357754](https://www.ncbi.nlm.nih.gov/pubmed/?term=Auta%20A%5BAuthor%5D&cauthor=true&cauthor_uid=19357754), [https://www.ncbi.nlm.nih.gov/pubmed/?term=Auta%20A%5BAuthor%5D&cauthor=true&cauthor\\_uid=19357754](https://www.ncbi.nlm.nih.gov/pubmed/?term=Auta%20A%5BAuthor%5D&cauthor=true&cauthor_uid=19357754)"Auta. "Anti-seizure activity of the aqueous leaf extract of *Solanum nigrum* linn (solanaceae) in experimental animals " <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2584323/>
- Kazeem. Available: [https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831), [https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831), [https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831), [https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ajeigbe%20KO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831) Ajeigbe Seyi



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- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Enitan%20SS%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Enitan%20SS%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)" Enitan,Dayo
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)Rotimi
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Omotoso%20DR%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)Omotoso, Olayemi
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)Olutobi
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)
- [https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor\\_uid=24311831](https://www.ncbi.nlm.nih.gov/pubmed/?term=Oladokun%20OO%5BAuthor%5D&cauthor=true&cauthor_uid=24311831)
- Oladokun, Acute effects of aqueous leaf extract of *Aspilia africana* C.D. Adams on Some Haematological Parameters in Rats", Afr. Med. 2013;10(5):236–243.
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847411/>, J
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847411/>, TraditHYPERLINK
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847411/>, Complement
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847411/>, Altern,
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847411/>
15. Oko OOK, Agiang EA. Phytochemical activities of *Aspilia africana* leaf using different extractants. Indian Journal of Animal Sciences. 2011;81(8):814–818.
  16. Etoa FXT Lieou C, Nkegoum B, Pieme CA, Dzeufiet DPD. Acute and subacute toxicity of *Aspilia africana* leaves. African Journal of Traditional, Compensatory and Alternative Medicine. 2007;4(2):127-134. DOI: 10.4314/ajtcam.v4i2.31203
  17. Guide for the care and use of laboratory animals, DHEW publication No.(NIH) 85-23, Revised, Office of Science and Health Reports, DRR/NIH, Bethesda, MD 20892; 1985.
  18. Michael FWF, Altman DG. Guidelines for the design and statistical analysis of experiments using laboratory animals. Institute of Laboratory Animal Research Journal. 2002;43:244-258.
  19. DeCarvalho RSM, Duarte FS, De-Lima TC. Involvement of GABAergic nonbenzodiazepines anticonvulsants. Epilepsy Research. 2011;12:87-110.
  20. Kasthuri S, Karthigadevi K, Manjulakshmi PSK. A review: Animal models used in the screening of antiepileptic drugs. International Research Journal of Pharmaceutical and Applied Sciences. 2013;3(3):18-23.
  21. Swinyard EA, Kupferberg HJ. Antiepileptic drugs: Detection quantification and evaluation. Federation Proceedings-Journals. 1985;44:39-43.
  22. Browning R. The electroshock model, neuronal network and antiepileptic drugs. In: Druggs for control of epilepsy: Actions on neuronal networks in seizure disorders, (Faingold CL, Fromm GH Eds.) CRC Press. Boca Rton, FL. 1992;195-211.
  23. Imoru OJ, Oyemitan IA, Ilesanmi OR. Evaluation of anticonvulsant activity of aqueous leaf extract of *Telfairia occidentalis* in mice European. Journal of Medicinal Plants. 2015;5(3):272-280. DOI: 10.9734/ejmp/2015/13665
  24. Porter RJ, Cereghino JJ, Gladding GD, Hessie BJ, Kupferberg HJ, Scoville B, White BG. Antiepileptic drug development program. Cleveland Clinic Quarterly. 1984;51(2):293-305.
  25. Swinyard EA, Woohead JH, White HS, Franklin MR. General principles: Experimental selection, quantification and evaluation of anticonvulsants. In Antiepileptic Drugs, 3<sup>rd</sup> edition. Levy RH, Mattson B, Melrum JK, Dreifuss FE. (Eds). New York, Raven Press. 1989;30-39.
  26. Kar DM, Rout SK, Moharana L, Majumdar S. Evaluation of anticonvulsant activity of hydroalcoholic extract of *Mussaenda philippica* on animals. Journal of Acute Disease. 2013;46-50. DOI: 10.1016/S2221-6189(14)60010-X
  27. Gollapalle L, Viswanatha MV, Venkataranganna N, Bheema L, Prasad GA. Evaluation of anti-epileptic activity of leaf extracts of *Punica granatum* on experimental models of epilepsy in mice.

- Journal of Intercultural Ethnopharmacology. 2016;5(4):415-421.  
DOI: 10.5455/jice.20160904102857
28. Kemelayefa OJ, Kagbo HD. Anticonvulsant potential of ethanolic extract of *A. africana* leaf in mice. Journal of Applied Life Science International. 2018;16(2):1-7.  
DOI: 10.9734/jalsi/2018/38808
29. Lidianne ML, Campelo SG, De-Lima CM, Feitosa RM, De-Freitas. Evaluation of central nervous system effects of Citrus Limon essential oil in mice. Rev. Bras. Farmacogn. Brazilian Journal of Pharmacognosy. 2010;4:1-6.
30. Rauf A, Ghias U, Bina SS, Haroon K. *In vivo* sedative and muscle relaxants activity of *Diospyros lotus* L. Asian Pacific Journal of Tropical Biomedicine. 2015;5(4):277-280.

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