Contents lists available at UGC-CARE

International Journal of Pharmaceutical Sciences and Drug Research

[ISSN: 0975-248X; CODEN (USA): IJPSPP]

Available online at www.ijpsdronline.com

Research Article

Effect of Ethanolic Extract of *Alternanthera sessilis* on Behavioral Parameters in Reserpine-Induced Stroke and Seizure Rat Model

Syed LAS[1], Sheela JPP[2], Balaji PV[1], Aravind KR[3], Thirumaran M[1], Manibalan V[1*]

[1]*Department of Physiology, Vinayaka Mission's Medical College and Hospitals, Vinayaka Mission's Research Foundation (Deemed to be University) Karikal, Tamil Nadu, India.*
[2]*Department of Physiology, Vinayaka Mission Kirupananda Variyar Medical College, Salem, Tamil Nadu, India.*
[3]*Department of Physiology, Rajamuthaiya Medical College, Chidambaram, Tamil Nadu, India.*

ARTICLE INFO

Article history:
Received: 20 March, 2024
Revised: 27 April, 2024
Accepted: 03 May, 2024
Published: 30 May, 2024

Keywords:
Stroke, Seizures, *Alternanthera sessilis* extract, Reserpine.

DOI:
10.25004/IJPSDR.2024.160310

ABSTRACT

The primary aim of our study was to delve into the neuroprotective potential of an ethanolic extract sourced from *Alternanthera sessilis*, particularly in alleviating behavioral impairments induced by reserpine in rat models simulating stroke and seizures. Our investigation involved categorizing rats into five distinct groups, each consisting of six individuals, with separate sets allocated for different experimental interventions. seizures and stroke-like symptoms were induced by administering reserpine, after which the rats underwent treatment with varying doses of *A. sessilis* ethanolic extract. We conducted a comprehensive assessment of various behavioral parameters, including antiepileptic activity, motor function, overall well-being, rota rod performance, closed-field activity, and grip strength. Significantly, our results uncovered substantial improvements in antiepileptic activity, motor function, and overall health of the intervention group, which received the extract, to the control group after the administration period. Additionally, enhancements were noted in rota rod performance, closed field activity, and grip strength, indicative of a marked enhancement in neuroprotective effects. These encouraging findings highlight the potential therapeutic efficacy of *A. sessilis* extract in managing stroke and seizure disorders. Nevertheless, further extensive investigations are imperative to unravel the precise mechanisms underlying these observed enhancements. Furthermore, future research endeavors should focus on delineating the specific therapeutic applications of *A. sessilis* extract, thus facilitating its potential integration into clinical practice for the management of stroke and seizure-related conditions. This would pave the way for a more comprehensive understanding of its therapeutic benefits and broaden its scope for clinical utility.

Introduction

A seizure is a temporary change in behavior caused by the synchronized and rhythmic firing of groups of neurons in the brain.[1] Epilepsy is a neurological condition characterized by the intermittent and unexpected onset of seizures.[2] Seizures may be classified as "non-epileptic" when they are induced in a healthy brain using treatments like electric shock or pharmacological convulsants. On the other hand, seizures are considered "epileptic" when they occur without any apparent cause. The treatment of epilepsy with modern medications is hindered by the treatments' incapacity to effectively manage seizures in some people, as well as the variety of side effects that vary in severity from mild impairment of the central nervous system (CNS) to life-threatening conditions such as aplastic anemia or hepatic failure. Hence, the achievement of an efficient and secure treatment still poses a difficulty. Scientific studies have shown that medicinal plants traditionally used in the treatment of epilepsy have substantial anticonvulsant properties in animal models used for screening anticonvulsant activity. These plants

***Corresponding Author:** Dr. Manibalan V

Address: Department of Physiology, Vinayaka Mission's Medical College and Hospitals, Vinayaka Mission's Research Foundation (Deemed to be University) Karikal, Tamil Nadu, India.

Email ✉**:** dr.manibalan@gmail.com

Tel.: +91-9941163012

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

could be a promising resource for creating new types of anticonvulsant drugs.[3]

Stroke stands as the second most prevalent cause of death globally and a chief contributor to disabilities.[4] It's typically categorized into two types: Ischemic stroke, occurring from blocked cerebral blood vessels, and hemorrhagic stroke, resulting from vessel rupture. Hemorrhagic stroke further branches into intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), depending on where the bleeding happens. Ischemic stroke makes up about 87% of cases, while hemorrhagic stroke accounts for roughly 10%. Despite being less common, hemorrhagic stroke presents a higher mortality rate, reaching up to 67.9%, and a graver outlook. Both types, whether ischemic or hemorrhagic, disrupt central nervous system function, causing a cascade of neurological impairments, especially affecting sensory, motor, and coordination functions. Moreover, research indicates that stroke leads to enduring cognitive decline.[5]

Alternanthera sessilis, referred as Ponnanganni leaves in local parlance, has been examined for its diverse biological characteristics.[6] *A. sessilis* is a member of the Amaranthaceae family and is often found in the most sweltering areas of India and Southeast Asia. In traditional medicine, various ailments are treated with preparations made from the plant's leaves. These ailments include indigestion, liver issues, skin conditions, and eye diseases. The leaves' effectiveness is attributed to their richness in bioactive compounds, which act as galactagogues, cholagogues, abortifacients, and febrifuges.[7-9] Additionally, it serves as a remedy for snake bites and scorpion stings.

The pharmaceutical advantage of utilizing plant extracts in treating reserpine-induced stroke and seizures in rats is gaining significant attention and recognition. Reserpine, a drug known to induce stroke and seizures in experimental models, poses a challenge in the development of effective treatments. However, plant extracts, rich in bioactive compounds such as flavonoids, alkaloids, and polyphenols, exhibit promising neuroprotective properties. These extracts demonstrate multifaceted pharmacological actions, including antioxidant, anti-inflammatory, and neurogenic effects, thereby mitigating the detrimental effects of reserpine-induced neurotoxicity. Moreover, their natural origin offers a safer alternative to synthetic drugs, potentially minimizing adverse effects. The utilization of plant extracts represents a novel avenue in pharmaceutical research, offering hope for the development of innovative therapies for neurological disorders like stroke and seizures.

Material and Methods

Ethics Committee Approval for Use of Animals

In the present study, Albino rats weighing around 170 to 200 g were chosen. During the experiments, food and water were given to the rats on the *ad libitum*. This study was approved by the Institutional Animal Ethical Review Committee of Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem, in accordance with established ethical guidelines. This committee, composed of specialists in research ethics, meticulously reviewed and endorsed the study protocol (IAEC No-VMKVMC/01/2023).

Experimental Design

We randomly divided the rats into five groups of at least six animals each. No individual rat participated in more than one experiment.

Group I, acting as the control, was given saline injections for seven consecutive days.

Group II, acting as the reserpine (1-mg/kg) was administered on the seventh day.

On the seventh day, group III, which served as the positive control, received levodopa and carbidopa.

Groups IV and V, were administered dosages of 200 and 400 mg/kg of the ethanolic extract of *A. sessilis*, respectively. After being treated with a medication dosage, the animals were monitored for 30 minutes on the seventh day. During this time, their latencies to myoclonic jerks and generalized tonic seizures (GTS) were recorded, along with the length of GTS. After administering reserpine and treatment groups, the first latency (IL) was observed in groups II-V 24 hours later. Then, on the ninth day, 48 hours after the first observation, the retention latency (RL) was measured using a one-trial passive avoidance task. The rats were then euthanized to determine levels of oxidative stress indicators, including MDA, catalase, and glutathione.

Behavioural Parameters

The behavioural assessment was done 24 hours later and animals were sacrificed.

Antiepileptic Effect

To assess the antiepileptic effect, rats were treated with reserpine, levodopa and carbidopa, ethanolic extract of *A. sessilis*. After 15 minutes of treatment, the animals were observed for 30 m for latencies to myoclonic jerks and GTS as well as duration of GTS.

Assessment of Motor Performance in Rats

The motor activity of rats was evaluated through a range of tests, including the grip test, the rota rod test, the general observation test, and the closed field activity test.

General Observation

After a period of 24 hours after treatment, the animals underwent a neurological assessment using a six-point scale. In summary, the score was as follows: The numerical scale used to assess the severity of the deficiencies is as follows: 0 indicates the absence of any deficits, score of one was assigned for complete failure to extend the left forepaw, two for a tendency to circle left, and three for

indicates a weakness or partial paralysis on the left side, four indicates the inability to walk spontaneously, and five indicates death.

Rota Rod

To evaluate the rats' motor coordination, we employed a rotarod apparatus set to a constant training speed of 8 revolutions per minute (rpm), with the objective of teaching the rats to meet the criteria of maintaining their position on the revolving spindle for a duration of 60 seconds. Subsequently, each rat had a solitary first trial on the accelerating rota rod. Test session involved a gradual increase in the rotarod's speed, accelerating from 4 to 40 rpm over a five-minute period. After 24 hours after therapy, each rat had another test run.

Closed Field Activity Test

Spontaneous locomotor activity (SLA) was evaluated the day before to medication and 24 hours before the sacrifice. The rats were individually placed in a square, enclosed arena equipped with infrared photo beam sensors for a 15 minutes observation period. Observations were made utilizing a digital photoactometer manufactured by Techno, India Ltd. The equipment was located in a testing room that was darkened, soundproofed, and ventilated to reduce light and sound interference.

Grip Test

The experiment utilized a custom apparatus. Two vertical supports stood at a fixed distance, with a taut 50 cm thread stretched between them. Elevated 40 cm above a flat surface, the string served as the testing platform for the rat. A five-point scale assessed the rat's interaction with the string: 0 - falls, 1 - grasps with forepaws, 2 - attempts to climb, 3 - holds with some hindpaws, 4 - secures itself with all forepaws and tail, 5 - flees.

Results

Effect of Ethanolic Extract of *A. sessilis* on Latency of Myoclonic Jerks

All animals that received a dosage of ethanolic extract from *A. sessilis* showed myoclonic jerks. However, the time it took for these jerks to develop increased with each tested dose. A substantial rise ($p < 0.001$) was seen in the average duration of myoclonic jerks as the dosage of ethanolic extract of *A. sessilis* increased in comparison to reserpine. The highest latency increase of myoclonic jerks was seen while administering a dosage of 400 mg/kg, intraperitoneally, of *A. sessilis* ethanolic extract. Substantial myoclonic jerks were observed in Rats that were given levodopa and carbidopa.

Effect of Ethanolic Extract of *A. sessilis* on Latency and Duration of Generalized Tonic Seizures

Generalized tonic seizures (GTS) were detected in rats that had prior treatment with levodopa and carbidopa. The administration of ethanolic extract of *A. sessilis* (200 & 400 mg/kg) did not eliminate the frequency of GTS. However, there was a notable improvement in the occurrence of GTS compared to the effects of reserpine ($p < 0.001$). Nevertheless, the ethanolic extract of *A. sessilis* F significantly increased the latency of the rotarod test (GTS) in a dose-dependent manner. Additionally, the extract caused a substantial reduction in GTS duration ($p < 0.001$) compared to reserpine.

Antiepileptic Effect of Ethanolic Extract of *A. sessilis*

This study investigated the antiepileptic effects of an ethanolic extract from *A. sessilis* in rats. The delay of myoclonic jerks was significantly reduced in a dose-dependent way ($p < 0.001$). The *A. sessilis* ethanolic extract (200 & 400 mg/kg) completely eliminated the GTS, but treatment with reserpine effectively prevented the antiepileptic effect.

Effect of Ethanolic Extract of *A. sessilis* on the Levels of MDA

Levels of MDA in the brain were evaluated on the 8th day after the evaluation of behavior. The levels of MDA in the rat brain were measured for the control group, as well as for groups treated with reserpine, levodopa and carbidopa, and an ethanolic extract of *A. sessilis* (200 & 400 mg/kg). Reserpine administration significantly elevated brain malondialdehyde (MDA) levels in rats compared to the control group ($p < 0.001$). In contrast, treatment with the ethanolic extract of *A. sessilis* (at 200 and 400 mg/kg) caused a dose-dependent decrease in MDA levels, effectively reversing the reserpine-induced increase.

Effect of Ethanolic Extract of *A. sessilis* on the Levels of GSH

Brain tissue was collected on day eight post-behavioral testing to assess glutathione (GSH) levels. Levodopa and carbidopa, as well as an ethanolic extract of *A. sessilis* (200 & 400 mg/kg). The concentration of glutathione in the brain was considerably lower in the control group and the reserpine group ($p < 0.001$). Ethanolic extract of *A. sessilis* (200 & 400 mg/kg), a substantial drop in brain GSH levels was seen, which was dependent on the dosage. This decrease was compared to the effects of reserpine.

Effect of Ethanolic Extract of *A. sessilis* on the Levels of catalase

Levels of brain catalase were also measured on the 8th day after the completion of behavioral testing. The catalase levels in the rat brain were examined for reserpine, levodopa and carbidopa, as well as the ethanolic extract of *A. sessilis* (200 & 400 mg/kg). Catalase activity in the brain was significantly lower in the reserpine group compared to the control group ($p < 0.001$). Ethanolic extract of *A. sessilis* at both 200 and 400 mg/kg significantly increased

brain catalase levels compared to the reserpine group ($p < 0.001$). This effect was dose-dependent.

Effect of Ethanolic Extract of *A. sessilis* on Motor Function Tests

Effect of ethanolic extract of A. sessilis on general observation test

Rats treated with ethanolic extract of *A. sessilis* (at both 200 and 400 mg/kg) showed a significant dose-dependent decrease in neurological score in the general observation test, compared to the Reserpine group ($p < 0.001$).

Effect ethanolic extract of A. sessilis on rota rod

In a dose-dependent manner, rats administered 200 or 400 mg/kg of ethanolic extract of *A. sessilis* spent significantly more time on the accelerating rotarod compared to the Reserpine group.

Effect ethanolic extract of A. sessilis on grip test

A grip test utilizing a 6-point scale was employed to assess the effects of ethanolic extract of *A. sessilis* (200 & 400 mg/kg) on motor function.Compared to the reserpine group, the extract significantly improved ($p < 0.001$) the neurological score in a dose-dependent manner.

Effect ethanolic extract of A. sessilis on locomotor activity

The spontaneous locomotor activity of rats was continuously monitored for ten minutes using a digital photoactometer. administration of ethanolic extract of *A. sessilis* (200 or 400 mg/kg) significantly increased activity compared to the reserpine group.

Discussion

Ethanolic extract of *A. sessilis* is gaining interest for its potential to protect the nervous system (neuroprotective) and prevent seizures (anticonvulsant) in conditions like stroke. Several studies have explored the phytochemical composition of this extract, revealing the presence of bioactive compounds such as flavonoids, alkaloids, and phenolics, which possess antioxidant and anti-inflammatory properties. These constituents have been implicated in attenuating neuronal damage associated with ischemic stroke by scavenging free radicals and reducing oxidative stress. Moreover, experimental evidence suggests that *A. sessilis* extract may exert its effects by influencing neurotransmitter systems, such as gamma-aminobutyric acid (GABA) and glutamate, thereby exerting antiepileptic effects. Research into the effects of various plant extracts on reserpine-induced seizures and strokes has shown promise in preclinical studies. Extracts from plants like *Bacopa monnieri*, *Withania somnifera* (Ashwagandha), and *Passiflora incarnata* (Passion flower) have demonstrated potential anticonvulsant properties in animal models, while compounds found in *Ginkgo biloba*, *Curcuma longa* (Turmeric), and *Panax ginseng* have shown neuroprotective effects against stroke-induced damage. These plant extracts may exert their effects through mechanisms such as modulation of neurotransmitter systems, reduction of oxidative stress, anti-inflammatory actions, and enhancement of cerebral blood flow. While these results are promising, further investigations, particularly clinical trials in humans, are needed to confirm the extract's safety and effectiveness for this purpose. It's important to consider potential limitations such as variability in potency, interactions with other medications, and the need for standardized preparations. Investigations in animal models using ethanolic extract of *A. sessilis*, particularly the observation of myoclonic jerks, present intriguing findings. The increase in latency of these jerks with escalating doses of the extract suggests a dose-dependent relationship, highlighting a potential modulation of neurological responses. The comparison with reserpine and the substantially higher latency observed with the maximum dose of the extract indicates a distinct effect of *A. sessilis*. The induction of myoclonic jerks in rats pre-treated with levodopa and carbidopa further underscores the neurological impact of the extract, potentially interacting with dopamine pathways. These results imply a complex interplay between the extract's components and neurological mechanisms, warranting deeper exploration for potential therapeutic or neuroprotective implications. The present study results were supported by the previously published by Alrashdi *et al.,* 2023,[10] Ralta *et al.,* 2023.[11]

The present study indicates that the extract did not completely abolish GTS. It demonstrated a notable improvement in reducing the occurrence of seizures compared to reserpine, a known compound used in various neurological studies. The increase in latency of GTS with higher doses of the *A. sessilis* extract suggests a possible mechanism where the extract might delay or modulate the onset of seizures. This delay in the onset of seizures could be pivotal in seizure management, potentially providing a window of opportunity for intervention or minimizing the severity of seizures. Additionally, the observed reduction in the duration of GTS with the extract, especially in a dose-dependent manner, further emphasizes its potential therapeutic effect. Shortening the duration of seizures is crucial as prolonged seizures can lead to various complications and negatively impact neuronal health. The present study results were supported by the previously published by Olurankinse *et al.* 2023,[12] Kargar *et al.* 2023.[13] The study on *A. sessilis* extract in seizure rats showed promising antiepileptic effects, reducing myoclonic jerks substantially in a dose-dependent manner. Higher doses abolished generalized tonic-clonic seizures (GTS). Interestingly, the extract's effects were blocked by reserpine, suggesting a possible interaction with neurotransmitter systems. These results were supported by previously published studies by Salile *et al.* 2023,[14] Oubella *et al.* 2023.[15]

This study investigated the effects of various substances on brain levels of MDA, GSH, and catalase in rats. The findings revealed significant changes in these biomarkers following reserpine administration and the subsequent influence of *A. sessilis* extract. Reserpine treatment significantly elevated malondialdehyde (MDA) levels while reducing glutathione (GSH) and catalase activity in the brain compared to the control group. Importantly, the ethanolic extract of *A. sessilis* exhibited a dose-dependent protective effect. Administration of the extract at 200 and 400 mg/kg significantly reversed the reserpine-induced changes in these biomarkers. The findings regarding MDA levels are particularly intriguing. The elevation of MDA following reserpine administration suggests heightened oxidative stress or lipid peroxidation in the brain. Conversely, the decrease in MDA levels with *A. sessilis* extract indicates its potential antioxidant properties, which could mitigate oxidative damage. The alterations in GSH and catalase levels also highlight the impact on the antioxidant defense system in the brain. The decrease in GSH and catalase due to reserpine administration might signify compromised antioxidant capacity. However, the dose-dependent increase in catalase levels following the administration of *A. sessilis* extract suggests its potential to enhance antioxidant enzyme activity, potentially aiding in cellular defense mechanisms. These findings collectively suggest that reserpine induces oxidative stress in the brain, altering critical antioxidant parameters, but the administration of *A. sessilis* extract exhibits a promising ability to counteract these changes, potentially through its antioxidant properties. The present study results were supported by the previously published by Rashidi *et al.*, (2023),[16] Alkhudhayri *et al.*, (2023),[17] and Mansouri *et al.*, (2022).[18]

This investigation in rats examining the effects of ethanolic *A. sessilis* extract on neurological function and motor skills provides promising results. The results showed a noteworthy decrease in the neurological score in general observation tests among rats treated with the extract compared to those administered reserpine. Rats administered the ethanolic extract of *A. sessilis* displayed a dose-dependent decline in neurological scores, indicating a link between dose and effect. Conversely, time spent on the accelerating rotarod by rats given 200 and 400 mg/kg doses of the extract showed a substantial dose-dependent increase compared to the reserpine group. This suggests a positive influence on motor function attributed to the extract. Moreover, the evaluation of motor performance through a 6-point scale score in the grip test demonstrated a remarkable improvement in the neurological score for rats administered with 200 and 400 mg/kg of *A. sessilis* ethanolic extract. This improvement was found to be substantially higher than that observed with reserpine, further supporting the extract's beneficial impact on motor skills. The assessment of spontaneous locomotor activity using a digital photoactometer revealed promising results. 200 and 400 mg/kg of rats treated with the extract exhibited substantially enhanced locomotor activity compared to those administered reserpine, highlighting the extract's potential in positively affecting physical movement and activity levels. Overall, these findings underscore the potential neuroprotective and motor performance-enhancing impacts of *A. sessilis* ethanol extract on rats. The observed dose-dependent improvements in neurological scores, motor function, and locomotor activity suggest a promising avenue for further exploration of this extract as a potential therapeutic agent for neurological disorders or conditions affecting motor skills. The present study's behavior parameters were supported by previously published articles by Patel *et al.*, (2023),[19] Nguyen *et al.*, (2023),[20] Nakyam *et al.*, (2022).[21]

Effects of plant extracts on conditions like strokes and seizures induced by reserpine in rats involve intricate scientific and logical considerations. Reserpine, a compound known for inducing symptoms akin to stroke and seizures, provides a reliable model for studying these conditions. Plant extracts, often rich in bioactive compounds, are investigated for their potential neuroprotective and anticonvulsant properties. Scientists meticulously analyze various parameters such as biochemical markers, neuronal activity, and histopathological changes in the brain to understand the mechanisms underlying the observed effects. Through controlled experiments and statistical analyses, researchers aim to elucidate the efficacy and safety profiles of these extracts, offering insights into potential therapeutic avenues for mitigating the detrimental effects of stroke and seizures. This multidisciplinary approach integrates elements of pharmacology, neurology, and botany, underscoring the importance of evidence-based inquiry in advancing our understanding of plant-based interventions for neurological disorders.

Conclusion

This study suggests that ethanolic extract of *A. sessilis* may be a promising therapeutic candidate for improving various behavioral symptoms in a rat model of reserpine-induced stroke and seizures. The observed antiepileptic effect, improved motor performance, and alterations in general observations, the rotarod, closed field activity, and grip tests support the potential neuroprotective and neuromodulatory properties of the extract. Additional investigation is necessary to clarify the fundamental mechanisms at play and to assess its effectiveness and safety within clinical environments. Nonetheless, these preliminary findings highlight the potential of *A. sessilis* as a natural remedy for neurological disorders, providing a basis for future investigations and therapeutic developments.

Acknowledgments

The authors would like to express their gratitude to all those who assisted in the completion of this work, providing invaluable insights, resources, and encouragement.

Ethical Consideration

This study was conducted in accordance with the ethical standards outlined by the Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem Institutional Animal Ethical Review Committee. The committee, comprised of experts in the field of ethics and research, reviewed and approved the study protocol (IAEC No-VMKVMC/01/2023).

References

1. Ghulaxe Y, Joshi A, Chavada J, Huse S, Kalbande B, Sarda PP. Understanding focal seizures in adults: A comprehensive review. Cureus: Innovations in Neurology. 2023;15(11):e48173. DOI: 10.7759/cureus.48173.
2. Amengual-Gual M, Fernández IS, Loddenkemper T. Patterns of epileptic seizure occurrence. Brain Research. 2019;1703:3-12. https://doi.org/10.1016/j.brainres.2018.02.032.
3. Ahmadzade AM, Pourali G, Mirheidari SB, Shirazinia M, Hamedi M, Mehri A, Amirbeik H, Saghebdoust S, Tayarani-Najaran Z, Sathyapalan T, Forouzanfar F, Sahebkar A. Medicinal plants for the treatment of neuropathic pain: A review of randomized controlled trials. Curr Pharm Biotechnol. 2023 Jul 14. doi: 10.2174/1389201024666230714143538.
4. Mead GE, Sposato LA, Sampaio Silva G, Yperzeele L, Wu S, Kutlubaev M, Cheyne J, Wahab K, Urrutia VC, Sharma VK, Sylaja PN, Hill K, Steiner T, Liebeskind DS, Rabinstein AA. A systematic review and synthesis of global stroke guidelines on behalf of the World Stroke Organization. Int J Stroke. 2023 Jun;18(5):499-531. doi: 10.1177/17474930231156753.
5. Rost NS, Brodtmann A, Pase MP, van Veluw SJ, Biffi A, Duering M, *et al.* Post-stroke cognitive impairment and dementia. Circulation Research. 2022; 130(8):1252-1271. https://doi.org/10.1161/CIRCRESAHA.122.319951
6. Rajendran R, Abirami M, Santhini E, Dinesh Kirupha S, Vadodaria K. Evaluation of the bioactive properties of *Alternanthera sessilis* extract and development of sodium alginate–*Alternanthera sessilis* membrane for wound management. Journal of Polymer Engineering. 2020;40(6):507-518. https://doi.org/10.1515/polyeng-2019-0252
7. Hwong CS, Leong KH, Aziz AA, Junit SM, Noor SM, Kong KW. *Alternanthera sessilis*: Uncovering the nutritional and medicinal values of an edible weed. Journal of Ethnopharmacology. 2022. https://doi.org/10.1016/j.jep.2022.115608v 15; 298:115608.
8. Muhammad Atif Randhawa, Ammar Ahmad Khan, Muhammad Sameem Javed, Muhammad Wasim Sajid, Chapter 18 - Green Leafy Vegetables: A Health Promoting Source, Editor(s): Ronald Ross Watson, Handbook of Fertility, Academic Press,2015,205-220, https://doi.org/10.1016/B978-0-12-800872-0.00018-4.
9. Suroowan S, Pynee KB, Mahomoodally MF. A comprehensive review of ethnopharmacologically important medicinal plant species from Mauritius. South African Journal of Botany. 2019;122:189-213. https://doi.org/10.1016/j.sajb.2019.03.024.
10. Alrashdi J, Albasher G, Alanazi MM, Al-Qahtani WS, Alanezi AA, Alasmari F. Effects of *Rosmarinus officinalis L*. extract on neurobehavioral and neurobiological changes in male rats with pentylenetetrazol-induced epilepsy. Toxics. 2023;11(10):826. https://doi.org/10.3390/toxics11100826.
11. Ralta A, Prakash A, Kumar_M P, Kumar R, Sarma P, Bhatia A, Medhi B, Chakrabarti A. Neuroprotective Effect of *Celastrus Paniculatus* Seed Extract on Epilepsy and Epilepsy-associated Cognitive Deficits. Basic and Clinical Neuroscience. 2023;14(1):155. DOI: 10.32598/bcn.2021.3154.1.
12. Olurankinse AI, Imoru JO, Oyemitan IA. Behavioural, Sedative and Anticonvulsant Activities of Ethanol Extract of the Leaf of *Lagenaria breviflora* (Benth) in Mice. Nigerian Journal of Pharmaceutical Research. 2023; 19(1):79-92. https://dx.doi.org/10.4314/njpr.v19i1.8.
13. Kargar Jahromi H, Khorram A, Atashpoor S, Jalali M, Kargar Jahromi Z, Mohammadi F, Serpoosh MA, Sadeghi N. The Effect of Hydroalcoholic Extract of Salep on Pentylenetetrazole-Induced Seizure in Adult Male Rats. Iranian Journal of Neurosurgery. 2023; 9:1-9.DOI: 10.32598/irjns.9.1.
14. Salile SS, Lee HJ, Alberts PS, Abula T, Raimondo JV, Stafford GI. *In vitro* and *in vivo* anti-seizure activity of hydromethanolic extract and fractions of *Pterolobium stellatum*. Journal of Ethnopharmacology. 2023; 304:116073. DOI: 10.1016/j.jep.2022.116073.
15. Oubella K, Benrazzouk K, Bagri A, Chait A. Effect of *Cuminum cyminum* and *Rhus pentaphylla* extracts on status epilepticus induced by intrahippocampal injection of kainic acid in rat. Bangladesh Journal of Pharmacology. 2023;18(3):105-112. DOI: 10.3329/bjp.v18i3.67165.
16. Rashidi R, Mahdinezhad MR, Sobhanifar MA, Marefati N, Rakhshandeh H, Hosseini M. The Impact of *Artemisia absinthium* Hydro-ethanolic Extract on Oxidative Stress in the brain in a Seizure Model Induced by Pentylenetetrazole in Mice. Journal of Chemical Health Risks. 2023;13(4):671-682.DOI: 10.22034/jchr.2022.1935870.1364.
17. Mansouri S, Hosseini M, Alipour F, Beheshti F, Rakhshandeh H, Mohammadipour A, Anaeigoudari A, Jalili-Nik M, Khazdair MR, Jahani A. Neuroprotective effects of the fractions of *Ocimum basilicum* in seizures induced by pentylenetetrazole in mice. Avicenna Journal of Phytomedicine. 2022;12(6):614. doi: 10.22038/AJP.2022.20470.
18. Alkhudhayri A, Abdel Moneim AE, Rizk S, Bauomy AA, Dkhil MA. The neuroprotective effect associated with *Echinops spinosus* in an acute seizure model induced by pentylenetetrazole. Neurochemical Research. 2023; 48(1):273-283. DOI: 10.1007/s11064-022-03738-2.
19. Patel C, Thakur K, Shagond L, Acharya S, Ranch K, Boddu SH. Effect of *Shorea robusta* resin extract in 3-nitropropionic acid-induced Huntington's disease symptoms in Sprague-Dawley rats. Research in Pharmaceutical Sciences. 2023;18(3):303-316. doi: 10.4103/1735-5362.371586.
20. Nguyen LT, Le XT, Pham HN, Van Nguyen T, Nguyen PT, Van Thi Pham A, Nguyen TB, Matsumoto K. Therapeutic effects of a standardized-flavonoid *Diospyros kaki* L.f. leaf extract on transient focal cerebral ischemia-induced brain injury in mice. Journal of Natural Medicines. 2023. https://doi.org/10.1007/s11418-023-01699-6.
21. Nakyam T, Wattanathorn J, Thukham-mee W. Neuroprotective Effect of Polyherbal Recipe Containing Ginger, Chinese Date, and Wood Ear Mushroom against Ischemic Stroke with Metabolic Syndrome Condition via Epigenetic Modification of Inflammation and Oxidative Stress. BioMed Research International. 2022. https://doi.org/10.1155/2022/8940303.

HOW TO CITE THIS ARTICLE: Syed LAS, Sheela JPP, Balaji PV, Aravind KR, Thirumaran M, Manibalan V. Effect of Ethanolic Extract of *Alternanthera sessilis* on Behavioral Parameters in Reserpine-Induced Stroke and Seizure Rat Model. Int. J. Pharm. Sci. Drug Res. 2024;16(3):387-392. **DOI:** 10.25004/IJPSDR.2024.160310