Journal of Complementary and Alternative Medical Research

10(1): 31-36, 2020; Article no.JOCAMR.58438
ISSN: 2456-6276

Neurohistological Study of the Interactive Influence of Ethanolic Leaf Extracts of *Sida acuta* and *Rauvolfia vomitoria* on the Hippocampus of Albino Rats

Kingsley A. Okon[1*], Enobong I. Bassey[1], Iboro E. Edet[1] and Grace U. Samuel[1]

[1]Department of Anatomy, Faculty of Basic Medical Sciences, University of Uyo, Uyo, Nigeria.

Authors' contributions

This study was carried out in collaboration among all authors. Author KAO designed the study, wrote the study protocol and the first draft of the manuscript. Authors GUS and IEE carried out all laboratories work. Authors KAO and EIB managed the literature searches and edited the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JOCAMR/2020/v10i130155
Editor(s):
(1) Dr. Sahdeo Prasad, Texas Tech University Health Sciences Center, USA.
Reviewers:
(1) Nadeem Kizilbash, Northern Border University, Saudi Arabia.
(2) H. K. Shreedhar, Visvesvaraya Technological University, India.
(3) Arthi Balasundaram, Sri Ramachandra University, India.
(4) Jyoti Prakash Pani, Krishna Mohan University Mathura, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/58438

Original Research Article

Received 14 April 2020
Accepted 19 June 2020
Published 21 July 2020

ABSTRACT

Aim: To provide information on the interactive influence of *Sida acuta* and *Rauvolfia vomitoria* on the hippocampus of albino rats using neurohistological parameter.
Methods: Thirty-five (35) female adult albino rats were used for the experiment. They were randomly divided into seven groups of five animals in each group. Group 1: The control group was given feed and water ad libitum for 28 days. Groups 2-7 served as the experimental groups. Group 2: Received 200 mg/kg body weight of *Sida acuta* leaf extract for 14 days. Group 3: Received 212.5 mg/kg body weight of *Rauvolfia vomitoria* leaf extract for 14 days. Group 4: Received 200 mg/kg body weight of *Sida acuta* and 212.5 mg/kg body weight of *Rauvolfia vomitoria* leaf extract for 14 days. Group 5: Received 200 mg/kg body weight of *Sida acuta* leaf extract for 14 days, then

**Corresponding author: E-mail: kingsleyokon407@gmail.com;*

212.5 mg/kg body weight of *Rauvolfia vomitoria* for the remaining 14 days. Group 6: Received 400 mg/kg body weight of *Sida acuta* leaf extract for 14 days, then 425 mg/kg body weight of *Rauvolfia vomitoria* for the remaining 14 days. Group 7: Received 600 mg/kg body weight of *Sida acuta* leaf extract for 14 days, then 850 mg/kg body weight of *Rauvolfia vomitoria* for the remaining 14 days.

Results: *Sida acuta* at the tested dose of 200 mg/kg body weight induced degeneration of pyramidal cells when compared to the control, *Rauvolfia vomitoria* at the tested dose of 212.5 kg/mg body weight exhibited neuroprotective effect, co-administration of both *Sida acuta* at 200 mg/kg body weight and *Rauvolfia vomitoria* at 212.5 mg/kg body weight and administration of *Rauvolfia vomitoria* after *Sida acuta at* increasing doses significantly reverse these changes to near normal when compared to the group that received 200 mg/kg body weight of *Sida acuta* for 14 days.

Conclusion: *Rauvolfia vomitoria* had the potential of ameliorating the neurodegenerative effect caused by the *Sida acuta* leaf extract on the pyramidal cells of the hippocampus albino rats.

Keywords: Rauvolfia vomitoria; Sida acuta; hippocampus; neurodegeneration.

1. INTRODUCTION

The use of medicinal plant is increasing exponentially around the globe; this has been attributed to the supposedly less adverse effect when compared to orthodox medicine [1]. Thus every year a number of persons turn to herbal medicine because they believe it is free from undesirable side effects [2]. In Africa/Nigeria, herbal medicines are commonly used for the treatment of mental and other disorders. This is probably due to the rising cost of orthodox drugs in the maintenance of personal health and well-being [3].

Sida acuta belong to the Malvaceae family [4]. It is a small shrub and grows in cultivated field, waste lands and it is highly competitive. Phytochemical result reveals the present of alkaloids such as vasicine, ephedrine and cryptolepine as the main alkaloids [5]. The plant is used for the treatment of various diseases in different parts of the world. It is used to treat diseases such as fever, headache, skin diseases, diarrhea and dysentery [6].

Rauvolfia vomitoria is of the Apocynaceae family. It is commonly found in forest where fallow period is prolonged [7]. It is reported to contain reserpine, ajmaline, yohimbine, rescinnamine, raucaffricine, sarpagine etc. These alkaloids exhibit antimalarial, antitumor and antidiabetes potentials [8]. It is effective in the treatment of malaria and mental disease [9]. The two plants (*Sida acuta* and *Rauvolfia vomitoria*) are used to treat closely related diseases, thus there is need to sufficiently document their interactive influence as this could lead to the discovery of a safer and effective polyherbal drug.

2. MATERIALS AND METHODS

2.1 Plant Material and Authentication

Fresh leaves of both *Sida acuta* and *Rauvolfia vomitoria* were obtained from the city of Uyo. They were identified and authenticated by Mrs. E. G. Udoma of the Faculty of Botany, University of Uyo herbarium with voucher number UUPH 6(c) for *Sida acuta* and UUPH 46(e) for *Rauvolfia vomitoria*.

2.2 Experimental Animals

Thirty- five adult female albino Wistar rats, weighing between 180 and 200 g were used for this study. The Wistar rats were obtained from the Faculty of Basic medical sciences animal house University of Uyo. They were transferred to the Faculty of Pharmacy animal house University of Uyo, where they were acclimatized for one week before administration. They were housed in wooden cages with adequate space to enhance free movement and good ventilation. Saw dust was used as bedding and were replaced with clean ones every two days. They were allowed twelve-hour light and twelve hour dark cycle at the normal room temperature obtainable in the test environment. The animals were fed with standard rat pelletized diet (Vital Feed Growers, Green Cereals Nigeria Ltd) and water ad libitum.

All animals were treated in accordance with the "guide for the care and use of laboratory animals" prepared by the national academy of sciences and published by the national institute of health [10].

2.3 Extracts Preparation

The leaves were separately cleaned to remove adhering dirt, air-dried and grinded separately into powder using a manual blender. Extraction was carried out by separately macerating and sucking in commercial ethanol for extraction for about 48hours with intermittent agitation and were then filtered and left separately in the water bath to concentrate. The doses and protocols for *R. vomitoria* and *Sida acuta* extracts were as previously described by [11,12] respectively.

2.4 Experimental Design

The animals were grouped into seven groups of matured female albino rats labelled 1-7.

Group 1: Animals in this group were the control; they were given food and water only.
Group 2: Animals in this group were given oral gavage of 200 mg/kg body weight of *Sida acuta* only for 14 days.
Group 3: Animals in this group were given oral gavage of 212.5 mg/kg body weight of *Rauvolfia vomitoria* only for 14 days.
Group 4: Animals in this group were given oral gavage of 200 mg/kg body weight of *Sida acuta* and 212.5 mg/kg body weight of *Rauvolfia vomitoria* for 14 days.
Group 5: Animals in this group were given 200 mg/kg body weight of *Sida acuta* for 14 days and from the 15th day, 212.5 mg/kg body weight of *Rauvolfia vomitoria* was then administered till the 28th day.
Group 6: Animals in this group were given 400 mg/kg body weight of *Sida acuta* for 14 days and from the 15th day, 425 mg/kg body weight of *Rauvolfia vomitoria* was then administered till the 28th day.
Group 7: Animals in this group were given 600 mg/kg body weight of *Sida acuta* for 14days from the 15th day, 850 mg/kg of *Rauvolfia vomitoria* was then administered till the 28th day.

3. RESULTS AND DISCUSSION

3.1 Histomorphology

The result of the section of the hippocampus of rats treated with ethanolic leaf extracts of *Sida acuta* and *Rauvolfia vomitoria* on the hippocampus of rats are shown in Figures 1-7.

3.2 Discussion

The hippocampus is a major brain part and a component of the limbic system responsible for the consolidation of information from short-term memory to long-term memory and in spatial memory that enables navigation [13]. The major input to the hippocampus is through the entorhinal cortex while the major output is through the Cornu Ammonis1 (CA1) to the subiculum [14]. The pyramidal cells are the major excitatory cells of the hippocampus. This study reveals degeneration of the pyramidal cells of the hippocampus in group 2 (Figure 2) administered with 200 mg/kg body weight of *Sida acuta* compared with that of the control (Figure 1) that showed the normal cytoarchitecture of the hippocampus. This finding agrees with that reported by Eluwa et al. that *Sida acuta* has a degenerative effect on the cells of the central nervous system [12]. This micro-anatomical alteration observed in the pyramidal layer of the CA3 of the hippocampus has the ability to tamper with the normal functioning of the CA3 relative to the memory function of the hippocampus. The CA3 is known to receive impulse from the mossy fibres from the granule cells of the dentate gyrus which is part of the hippocampal formation [15]. This alteration may also have a negative implication on the flow of information within the hippocampus as the CA3 is part of the indirect trisynaptic pathway of the hippocampus. Therefore, the disruption of the pyramidal cells of the hippocampus may hinder the flow of information and hence memory. This study also reveals the near normal cytoarchitecture of the pyramidal cells in group 3 (Figure 3) administered with 212.5 mg/kg body weight of ethanolic leaf extract of *Rauvolfia vomitoria*. This finding is in agreement with that reported by [16], that *Rauvolfia vomitoria* has a neuroproctective effect due to the present of high antioxidant such as reserpine and ajmaline. In group 4 (Figure 4) co-treated with *Sida acuta* at 200 mg/kg body weight and *Rauvolfia vomitoria* at 212.5 mg/kg body weight presented only with mild degeneration of pyramidal cells compared to group 2 (Figure 2). This may be due to the interaction between the active biological constituents of *Sida acuta* and *Rauvolfia vomitoria*. This result agrees with that reported by [17]. That herbal medicine derived from two or more herbal plants have pharmacological constituents which may exert synergistic, potentiative, agonistic and antagonistic action by virtue of the active different constituents. It is also in harmony with another study which reported that biologically active constituents have pharmacological principles that work in a dynamic way to produce maximal therapeutic effect and eliminate undesirable side effects [18].

The study also reveals progressive improvement in groups administered with *Sida acuta* and later *Rauvolfia vomitoria* with increasing dosage of the two leaf extracts (group 5 with 200 mg/kg body weight of *Sida acuta* and then 212.5 mg/kg body weight of *Rauvolfia vomitoria*, group 6 with 400 mg/kg body weight of *Sida acuta* and then 425 mg/kg body weight of *Rauvolfia vomitoria* and group 7 with 600 mg/kg body weight of *Sida acuta* and the 850 mg/kg body weight of *Rauvolfia vomitoria*). This is in accordance with a report which revealed that *Rauvolfia vomitoria* has an ameliorating effect on the pyramidal cells of the CA3 region of the hippocampus and that there exists a direct relationship between the concentration of the degenerating agent, ameliorating agent and the proportion of neurodegeneration [19]. The results also showed cellular vacoulation. Cytoplasmic vacuolization or vacuolation develops spontaneously or after exposure to bacterial or viral pathogens as well as to various natural and artificial low-molecular-weight compounds [20].

Cytoplasmic vacuolization of mammalian cells can be transient or irreversible. Transient vacuolization is observed only during the exposure to an inducer and reversibly affects the

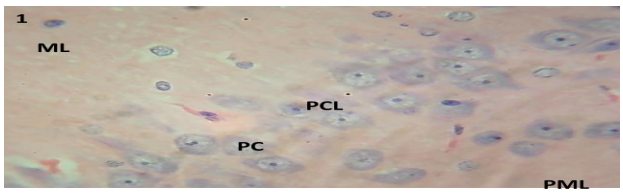

Figure 1. Section of the hippocampus of control rat given distilled water, showing pyramidal cell layer-PCL, molecular layer-ML, Polymorphic layer-PML. (H&E x400)F

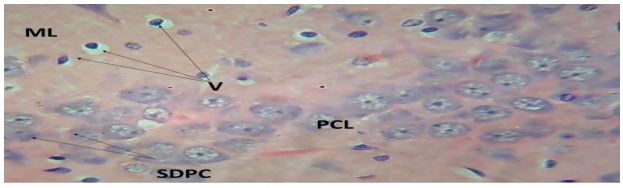

Figure 2. Section of the hippocampus treated with 200 mg/kg body weight of *Sida acuta* showing severe degeneration of pyramidal cell –SDPC in the pyramidal cell layer-PCL and vacoulation-V in the molecular layer (H&E x400)

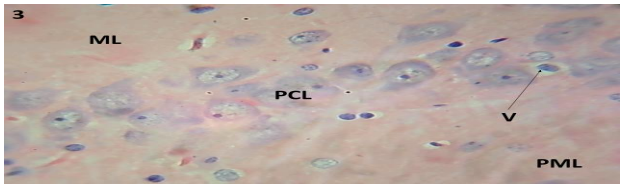

Figure 3. Section of the hippocampus treated with 212.5 mg/kg body weight of *Rauvolfia vomitoria* showing a normal pyramidal cell layer - PCL, Molecular layer-ML and polymorphic layer-PML (H&E x400)

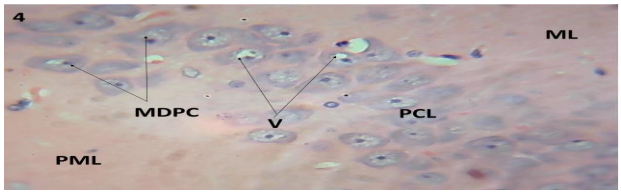

Figure 4. Section of the hippocampus treated with 200 mg/kg body weight of *Sida acuta* and 212.5 mg/kg body weight of *Rauvolfia vomitoria* for 14 days showing Mild degeneration of pyramidal cells -MDPC and vacoulation in the molecular layer-V (H&E x400)

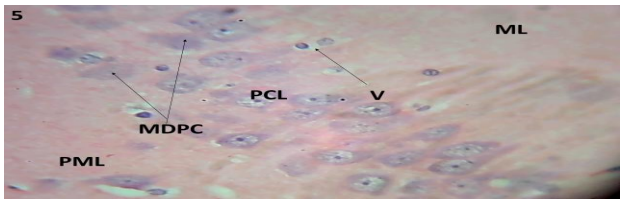

Figure 5. Section of the hippocampus treated with 200 mg/kg body weight of *Sida acuta* for 14 days and 212.5 mg/kg body weight of *Rauvolfia vomitoria* for 14 days showing mild degeneration of pyramidal cells- MDPC and Mild vacoulation in the molecular layer V (H&E x400)

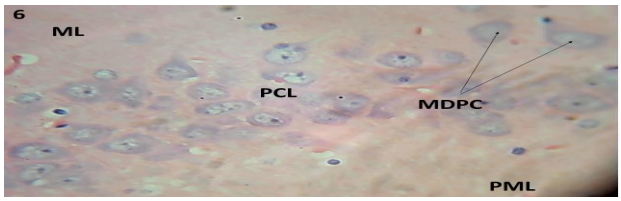

Figure 6. Section of the hippocampus treated with 400 mg/kg body weight *Sida acuta* for 14 days and 425 mg/kg *Rauvolfia vomitoria* for another 14 days showing mild degeneration of pyramidal cells-MDPC (H&E x400).

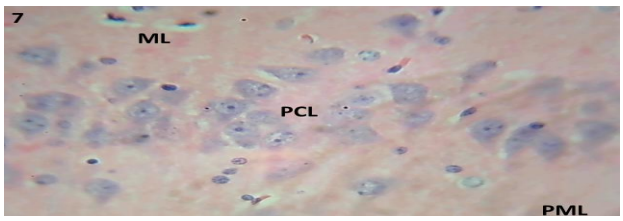

Figure 7. Section of the hippocampus treated 600 mg/kg body weight *Sida acuta* for 14 days and 850 mg/kg of *Rauvolfia vomitoria* for another 14 days showing normal molecular layer-ML, pyramidal cell layer- PCL and polymorphic layer- PML. (H&E x400)

cell cycle and migration [21]. The vacoulation evident in Figs. 2, 4 and 5 are the onset of cellular degeneration. This finding agrees with that reported by Chen et al. that irreversible vacoulation accompanies cell death [20].

4. CONCLUSION

From the results of the experiment, this study therefore suggests that the ethanolic leaf extract of *Rauvolfia vomitoria* contains alkaloid that have the potential of ameliorating the neurodegenerative effect caused by the *Sida acuta* leaf extract. This ameliorating effect could be attributed to high antioxidant activity of *Rauvolfia vomitoria* leaf extract.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hu X, Sato J, Oshida Y, Yu M, Bajotto G, Sato Y. Effect of Gosha-jinki-gan (Chinese herbal medicine): Niu-che-sen-qi-wan on insulin resistance in STZ induced diabetic rats. Diabetes Research and Clinical Practice. 2003;59:103–111.
2. Kazemipoor M, Radzi C, Cordell G, Yaze I. Safety, efficacy and metabolism of traditional medicinal plants in the management of obesity: A review. International Journal of Chemical Engineering. 2012;3(4):288–92.
3. DaSilva J, Hoareau L. Medicinal plants: A re-emerging health aid. Electronic Journal of Biotechnology. 2005;2:61-69.
4. Herbal Medicine Research Centre, Institute for Medical Research, Kuala Lumpur.

Compendium of Medicinal Plants used in Malaysia. 2002;2:341-342.
5. Karou S, Savadogo A, Canini A, Yameogo S, Montesano C. Antibacterial activity of alkaloids from *Sida acuta.* African Journal of Biotechnology. 2005;4:1452-1457.
6. Ignacimuthu S, Ayyanar M, Sankara-Sivaramann K. Ethnobotanical investigations among tribes in Madurai District of Tamil Nadu (India). Journal of Ethnobiological and Ethnomedicine. 2006;2:25-31.
7. Etukudo I. Conventional and traditional uses of plants. Forestry. 2003;1(22):13-16.
8. Katič M, Kušan E, Prošek M, Bano M. Quantitative densitometric determination of reserpine and ajmaline in *Rauwolfia vomitoria* by High-Performance Thin Layer Chromatography (HPTLC). Journal of High Resources and Chromatography. 2011;3: 149–150.
9. Pesewu G, Cutler R, Humber D. Antibacterial activity of plants used in traditional medicines of Ghana with particular reference to Methicillin-resistant Staphylococcus aureus (MRSA). Journal of Ethnopharmacology. 2008;116:102–111.
10. American Physiological Society. Guiding principles for research involving animals and human beings. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2002;283:281-283.
11. Hunt M, Auriemma J, Ashara C. Self-report bias and underreporting of depression on the BDI-II (Beck Depression Inventory- II). Journal of Personality Assessment. 2003;80(1):26–30.
12. Eluwa A, Ubah O, Akpantah O, Asuquo R, Ekanem B, Akpan P, Isamoh E. Neurohistological study of the effect of ethanolic leaf extract of *Sida acuta* on cerebral astrocytes of adult Wistar rats. International Journal of Pharmaceutical Science Invention. 2013;2:1907-10.
13. Aboitiz F, Morales D, Montiel J. The evolutionary origin of the mammalian isocortex: Toward an integrated developmental and functional approach. The Behavioral and Brain Sciences. 2003;26(5):535-52.
14. Cho R, Gilbert A, Lewis D. The neurobiology of schizophrenia. In Charney DS, Nestler EJ (Eds). Neurobiology of Mental Illness. Oxford University Press US; 2005. ISBN: 978-0-19-518980-3.
15. Snell R. Clinical neuroanatomy. 6th Edition. Lippincott Williams & Wilkins. 2006;4:69-497.
16. Erasto P, Grierson D, Afolayan J. Evaluation of antioxidant activity and the fatty acid profile of the leaves of *Vernonia amygdalina* growing in South Africa. Food Chemistry. 2007;104:636–642.
17. Karou S, Tchacondo T, Ilboudo D, Simpore J. Sub-saharan rubiaceae: A review of their traditional uses, phytochemistry and biological activities. Journal of Biological Science. 2011;14: 149-169.
18. Sarwar M, Attitalla I, Abdollahi M. A review on the recent advances in pharmacological studies on medicinal plants: Animal studies are done but clinical studies needs completing. Asian Journal of Animal and Veterinary Advances. 2011;6:867-883.
19. Oguche E, Ibegbu A, Hamman W. The effect of *Rauvolfia vomitoria* on mercury-induced changes on the histology of the hippocampus of adult Wistar rats. African Journal of Cellular Pathology. 2016;6:54-59.
20. Chen R, Duan C, Chen S, Zhang C, He T, Li H, Liu Y, Dai R. The suppressive role of p38 MAPK in cellular vacuole formation. Journal of Cell Biochemistry. 2013;114: 1789–1799.
21. Morissette G, Lodge R, Marceau F. Intense pseudotransport of a cationic drug mediated by vacuolar ATPase: Procainamide-induced autophagic cell vacuolization. Toxicology and Applied Pharmacology. 2008;228:364–377.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/58438