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Solanum macrocarpon Leaf Extract Effects on Cerebral Cortex Microanatomy in Isoproterenol Induced Myocardial Infarction

J. O. Owolabi[1*], S. Y. Olatunji[1] and A. J. Olanrewaju[1]

[1]Department of Anatomy, Ben Carson [Snr.] School of Medicine, Babcock University, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Authors JOO and SYO designed the study, wrote the protocol, managed the experimental process and wrote the first draft of the manuscript. Author AJO managed the literature searches. All the authors carried out the histomorphological analysis. All authors read and approved the final manuscript.

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ABSTRACT

Solanum macrocarpon is a plant with edible fruit and its potentials as a medicinal herb have also been investigated. Its leaf extract had been suggested to have effects that could ameliorate myocardial infarction. In the current investigation, *S. macrocarpon* leaf aqueous extract effects on the brain tissue was observed when it is being used to ameliorate induced myocardial infarction; because its effects on the brain was also considered to be very important so as to investigate the safety of its use on brain health. Thirty adult male Wistar rats were divided into five groups of six rats each; Group A served as control and were only fed *ad libitum* and administered placebo. Group B rats were animals that suffered induced myocardial infarction but did not receive any therapeutic intervention. Group C received 100 mg/kg of *S. macrocarpon* aqueous leaf extract; Group D received 200 mg/kg body weight of *S. macrocarpon* leaf extract while Group E received 400 mg/kg body weight. The regimen was also to assess the effects of variations in dosages. Experiment lasted for 28 days and the animals were sacrificed by cervical dislocation. Brain tissues were excised and fixed in formal saline; then processed using the Haematoxylin and Eosin method. Specific effects of *S. macrocarpon* include alterations of cell morphologies and loss of cells at the higher doses. There were also evidences of alterations of the cerebral histoarchitecture and the neuropil. Results showed that the extract at all dosages had deleterious effects on the brain tissue and the gravity of effects increased with the dosage.

**Corresponding author: E-mail: olaowolabi001@yahoo.com, owolabijo@babcock.edu.ng;*

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1. INTRODUCTION

Solanum macrocarpon is also known as eggplant and its fruit is edible and popularly consumed especially in West Africa. A number of reports exist on the phytomedicinal potentials of its parts, especially the fruits [1]. The fruit is majorly consumed as vegetable. It has also been found to have weight reducing effects on experimental animals [2]. Another study found it potentially useful in treating hypercholesterolemia [3]. It was also reported to have antioxidant properties, though reportedly weak [4]; this property was also reported to have potentials to ameliorate type 2 diabetes [5]. However, the safety of the other parts of the plant has been questioned by some reports that suggest that they may be toxic, especially at certain doses [6]. Onasanya et al. [7] suggested that the antioxidant properties of the leaf of *S. macrocarpon* could serve protective functions in the brain as well as the liver. However, such a claim would require further *in vivo* validation as scavenging properties might not be enough to validate safety and phytomedicinal potentials considering the possibility of the availability of some other phytochemicals in the plant parts. This may account for why certain literatures have reported the potential toxicity of the extracts of this plant's parts [6]. Interestingly, literatures on the effects of *S. macrocarpon* on the brain are quite scarce or relatively unavailable.

The fruit of S. macrocarpon is believed traditionally to be useful for managing certain heart diseases [8]. Its ability to effectively suppress experimental hypercholesterolemia in Wistar rats was also observed as an indication of a protective role in cardiovascular diseases [9]. This specific role in ameliorating myocardial infarction was experimented using the leaf extract to ameliorate isoproterenol [10] induced myocardial infarction. However, no available report has addressed its effect on the brain tissue *in vivo.* Since previous investigation had considered the potentials of the aqueous extract of *S. macrocarpon* leaf in ameliorating myocardial infarction. It is suggested that this plant might be a potential natural product for treating myocardial infarction. However, little or none has been done to investigate the effects of *S. macrocarpon* on the brain in this context. This is considered crucial to ensuring the usefulness of the plant for treating myocardial infarction. The aim of the current investigation was to observe the effects of *S. macrocarpon* on the brain in an induced myocardial infarction condition; in an attempt to validate the general safety of the leaf extract on the brain *in vivo*. The method employed is therefore patterned based on the context and scope of the investigation primary objectives. Also, the scope of the results presented in this reports includes only the studied effects on the brain tissue.

2. MATERIALS AND METHODS

The research design was to observe the effects of *S. macrocarpon* on the brain in the context of using the plant extract to ameliorate myocardial infarction (MI) as previously reported.

Table 1. Table showing the grouping of the animals, treatment and rationale

Group	Treatment	Rationale
Group A	Normal rats (No induction of MI. No drug and extract administration)	The control group that served as the control and standard reference for the other treated groups of animals.
Group B	ISO (MI Induced) rats. (No drug or extract)	The animal group that suffered untreated myocardial infarction to observe the possible consequence of the condition on cerebrum and to serve as a reference for the other groups with the same condition but treated with *Solanum macrocarpon* extract.
Group C	ISO (MI Induced) rats + *S. macrocarpon* extract (100 mg/kg)	To observe the effects of low dose of *S. macrocarpon* on the cerebral cortex of the animals; thus examining neuro toxicity or otherwise safety at this dosage.
Group D	ISO (MI Induced) rats + *S. macrocarpon* extract (200 mg/kg)	To observe the effects of moderate dose of *S. macrocarpon* on the cerebral cortex of the animals; thus examining neuro toxicity or otherwise safety at this dosage.
Group E	ISO (MI Induced) rats + *S. macrocarpon* extract (400 mg/kg)	To observe the effects of relatively high dose *S. macrocarpon* on the cerebral cortex of the animals; thus examining neuro toxicity or otherwise safety at this dosage.

The drug isoproterenol (ISO) was used to induce myocardial infarction in Groups B-D and it was established by observing biomarkers and examining histological sections of the heart. This had been previously done and reported.

Aqueous extract of *Solanum macrocarpon* was prepared from air dried leaves of the plant and administered using oral gavages. Thirty adult male Wistar rats were procured from the animal holding facility of Babcock University, Nigeria. They were housed under standard laboratory conditions and treated with adequate consideration for ethics. Animals' average weight was 202 g. The administration lasted 28 days after which the animals were sacrificed by cervical dislocation. The brain was excised in each animals and the tissue was processed using the routine haematoxylin and eosin staining technique [11]. Photomicrographs of the tissue samples were taken and analysed using basic principles of qualitative histological analysis [12]. Results were presented at two magnifications of X160[lower] and X640[higher] to illustrate the cerebrum cross-section and histological elements of interest across the cortical layers respectively.

3. RESULTS AND DISCUSSION

3.1 General Cortical Histoarchitecture

The cortical histoarchitecture of the Control Group A represents a healthy cerebral cortex in cross section cortical layers are observable and cells are morphologically distinguished into their various types. Granular cells as well as the pyramidal neurons and glia are prominently demonstrated in the Control group. The neuropil is also observably intact. This group therefore could serve as a reliable reference for the other groups. The cerebral cortex histoarchitecture is largely preserved in the Group B animals that only suffered myocardial infarction. Hence, this condition on its own would not have caused extensive histological disruption of the cerebral cortex in the animals. The cortex is also largely preserved in Group C when the lowest dose of *S. macrocarpon* was administered to the animals; higher magnifications [X640] however suggest that the pattern of cell spatial distribution might be altered.

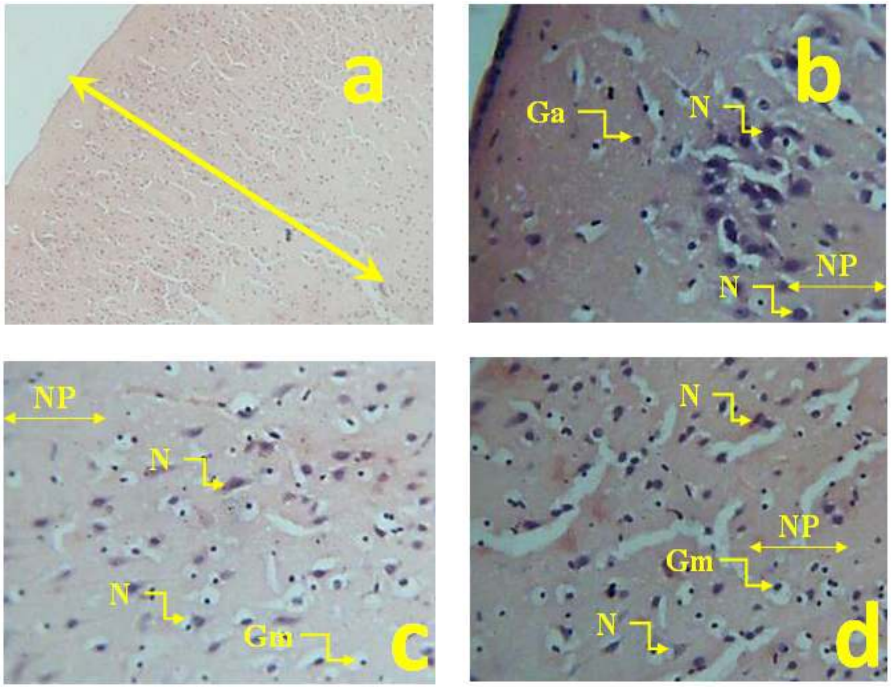

Fig. 1. Photomicrographs of the control group A animals at X160[a, cerebral cortex cross-section], 640[b, superficial cerebral cortex layers], 640[c, deep cerebral cortex layers] and 640[d, deep cerebral cortex layers]. The cerebral cortex histoarchitecture is normal

[N= Neuron; Ga= Glia- Astrocyte; Gm= Glia- Microglia; NP= Neuropil; Double-headed arrow illustrates cortical layers in cross-section]

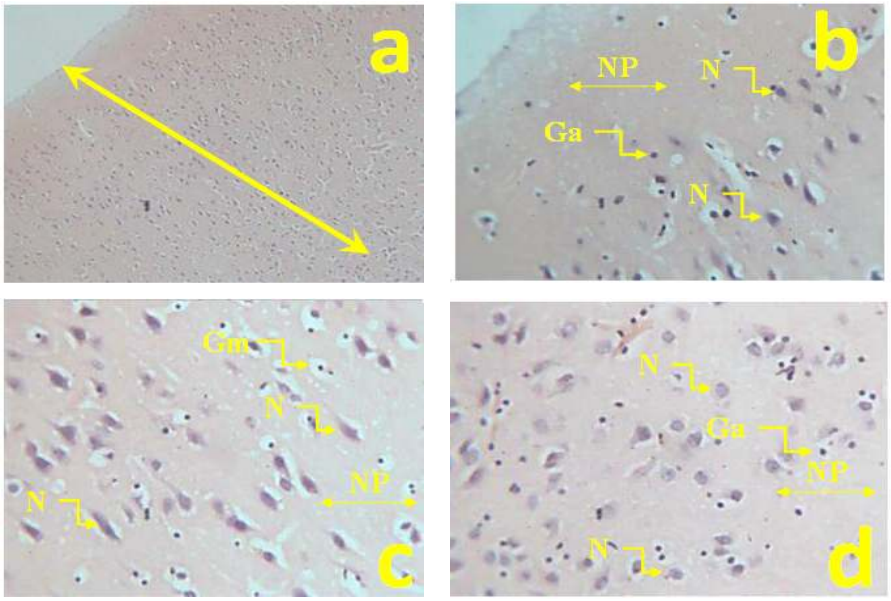

Fig. 2. Photomicrographs of the group B animals that had myocardial infarction at X160[a, cerebral cortex cross-section], 640[b, superficial cerebral cortex layers], 640[c, deep cerebral cortex layers] and 640[d, deep cerebral cortex layers]. The cerebral cortex histoarchitecture is relatively preserved

[N= Neuron; Ga= Glia- Astrocyte; Gm= Glia- Microglia; NP= Neuropil; Double-headed arrow illustrates cortical layers in cross-section]

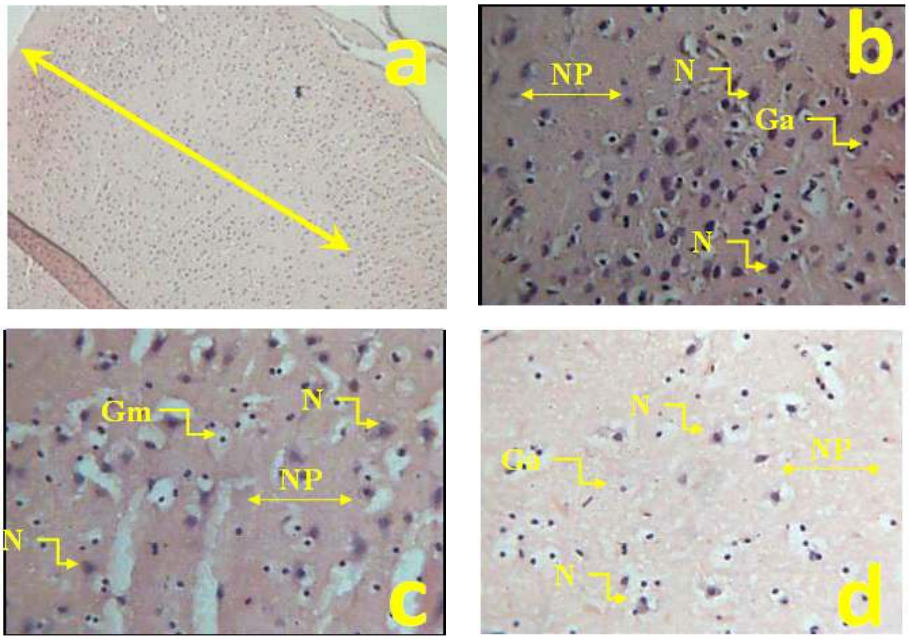

Fig. 3. Photomicrographs of the Group C animals that had myocardial infarction and received 100 mg/kg body weight of *S. macrocarpon* extract; at X160[a, cerebral cortex cross-section], 640[b, superficial cerebral cortex layers], 640[c, deep cerebral cortex layers] and 640[d, deep cerebral cortex layers]. The cerebral cortex has heterogeneous cell morphologies and unusual spatial distribution

[N= Neuron; Ga= Glia- Astrocyte; Gm= Glia- Microglia; NP= Neuropil; Double-headed arrow illustrates cortical layers in cross-section]

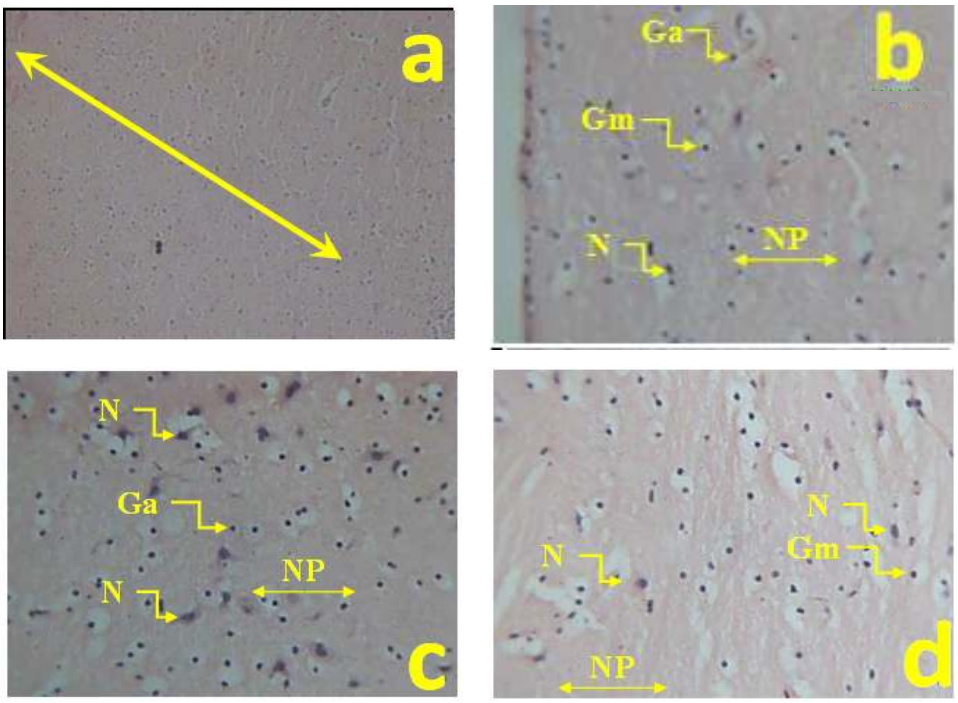

Fig. 4. Photomicrographs of the Group D animals that had myocardial infarction and received 200 mg/kg body weight of *S. macrocarpon* extract; at X160[a, cerebral cortex cross-section], 640[b, superficial cerebral cortex layers], 640[c, deep cerebral cortex layers] and 640[d, deep cerebral cortex layers]. The cerebral cortex has heterogeneous cell morphologies and unusual spatial distribution

[N= Neuron; Ga= Glia- Astrocyte; Gm= Glia- Microglia; NP= Neuropil; Double-headed arrow illustrates cortical layers in cross-section]

There are evidences of abnormalities in the histoarchitectural organisation of the cortex in the Group D that were administered the medium dose of *S. macrocarpon*. The typical cortical layers are poorly defined and the constituent cells are poorly demonstrated. This indicates that the administered substance produced effects that altered the histoarchitecture. This, by implication might also alter the neuronal connections as well as the cellular communications that are responsible for specific mental functions. In additional to such histoarchitectural pattern disruption already noted in the Group that was administered the medium dose; the highest dose group [Group E] presents a more advanced tissue disruption. There are areas that appear relatively acellular with accompanying neuropil alterations (Fig. 5D). This suggests that the deleterious effects of *S. macrocarpon* leaf extract on the brain as observed is dose dependent. As such, emphasis should be laid on the doses of administration or use. These observations confirm the concern raised by Oboh [6] on the potential toxicity of this plant.

3.2 Neuronal and Glia Morphology

Neurons and glia are demonstrated in the Control Group A animals- the neurons [pyramidal and granular] as well as the glia [astrocytes, oligodendrocytes and microglia] are observable as well. Most cells are mildly less prominently demonstrated in the Group B relative to the Control Group A. However, there is no evidence of extensive cell morphological distortions or death. This might suggest a functional consequence on the cells that is not severe enough to have caused a serious structural damage. This might also mean that such effects might be reversible. The low dose might not have produced observable cell death; a number of cells, especially the granular cells however show signs of morphological heterogeneity. Cells in the deeper cortical region are relatively sparsely distributed and the neuropil is less intact. These observations would only point to negative effects of the administered extract on the cortex.

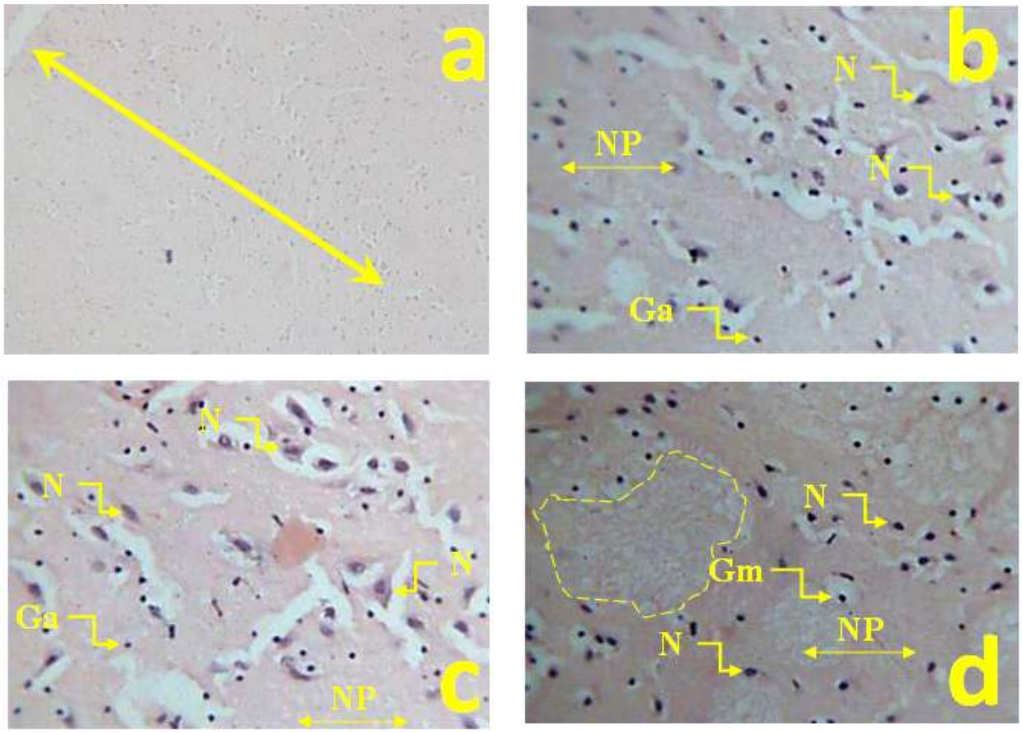

Fig. 5. Photomicrographs of the Group E animals that had myocardial infarction and received 400 mg/kg body weight of *S. macrocarpon* extract; at X160[a, cerebral cortex cross-section], 640[b, superficial cerebral cortex layers], 640[c, deep cerebral cortex layers] and 640[d, deep cerebral cortex layers]. The cerebral cortex has heterogeneous cell morphologies and unusual spatial distribution

[N= Neuron; Ga= Glia- Astrocyte; Gm= Glia- Microglia; NP= Neuropil; Double-headed arrow illustrates cortical layers in cross-section; dotted-line circle indicate area of emphasis]

The medium dose produced observable effects on neuronal and glial morphologies. Cells are generally poorly demonstrated across the cerebral cortex. Individual granular cells are quite small; pyramidal cells in the deeper layers are also poorly demonstrated. Neuropil on the other hand is also less intact. It is observable that the extract administered caused significant morphological distortions to the cells and this would consequently affect the elaboration of their processes and the integrity of neuronal connections and communication. The high dose of the extract caused, in addition to cellular deformation, localised tissue damage. There are areas that appear relatively acellular with distorted neuropil. The characteristic layered cortical pattern can hardly be observed.

3.3 Cell Population Density and Spatial Distribution

The extract affected the pattern of cells distribution relative to one another. The gravity of these effects is observably dose dependent. The highest dose has relatively few neurons which are distorted in spatial arrangement. The areas that have no cells are evident of the fact that cells are not distributed in the characteristic layering pattern; hence the tissue layers are not normally populated. Even the lowest dose still produced observable, though mildly appearing alterations in the spatial distribution of the cells as well as their densities.

Though the fruit extract was recommended as a potential nutraceutical [13] and a natural product with phytomedicinal benefits [14]; the effects of some of the phytochemicals, especially in the leaf would require vital screening and studies based on its potential toxicity as observed on the brain.

3.4 Specific Histological Aberrations of Pathological Importance

There are observable histological aberrations attributable to the effects of the administered

extract of *S. macrocarpon*. These effects observably increased with increases in the doses of the extract; this implies that the effects were dose dependent. The toxicity of *S.macrocarpon* has been attributed to its high glycoalkaloids content [15]. Also Dougnon et al. [16] cautioned against its excessive consumption.

4. CONCLUSION AND RECOMMENDATION

S. macrocarpon leaf extract has deleterious effects on the brain tissue as used in the current investigation. The effects are dose dependent, as such higher doses would cause more severe damages. Specific effects include alterations of cell morphologies and loss of cells at the higher doses as well as alterations of the cerebral histoarchitecture as well as the neuropil.

It is recommended that further investigations be carried on this extract on the brain and other tissues before recommending its use for certain medicinal purposes that have been suggested in certain reports. Furthermore, dosage should be considered of great importance in determining its use as safe and lower doses might be found to ensure efficacy and safety of use.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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