The effect of ethanolic extract of *Annona muricata* leaf on the basal ganglia

Nweke Elizabeth Obioma 1, * and Akpuaka Frank Chinedu 1, 2

1 Department of Anatomy, Faculty of Basic Medical Sciences, Chukwuemeka Odumegwu Ojukwu University, Anambra State, Nigeria.
2 Department of Anatomy, Faculty of Basic Medical Sciences, Abia State University, Uturu, Abia State, Nigeria.

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Abstract

*Annona muricata* (Linn.) is an evergreen tropical tree of the Annonaceae family that possesses phytotherapeutic bioactive compounds known as annonaceous acetogenins effective for the treatment of cancers and several diseases. This study investigated the effect of ethanolic extract of *Annona muricata* leaf on the basal ganglia. Twenty four (24) adult wistar rats were randomly divided into four groups (A, B, C & D) of six animals each. Group A served as the control and received 2 ml/kg of distilled water; the experimental groups B, C & D were orally administered 100 mg/kg, 200 mg/kg and 300 mg/kg body weight of ethanolic extract of *Annona muricata* leaf respectively for thirty days. At the end of administration, the animals were anaesthetized under the influence of chloroform vapour, dissected and their brain harvested for histological examination. The histological result revealed mild increase in the number of basal ganglia nuclei cell body (BGNCB) and fibres (F) with mild necrosis of neurons when compared to their control group. In conclusion, high consumption of ethanolic extract of *Annona muricata* could result in extrapyramidal side effects. Thus, it should be taken at lower doses.

Keywords: *Annona muricata*; Basal ganglia; Wistar rats; Histology

1. Introduction

Medicinal plants have contributed so much in the treatment and management of various diseases and its use has expanded rapidly in both developed and developing countries [1]. This has been attributed to its affordability, accessibility and efficacy. However, the toxic effects of these medicinal plants are sometimes overlooked [2]. An example of medicinal plant considered useful is *Annona muricata*.

*A. muricata* commonly known as graviola or soursop, belongs to the member of *Annonaceae* family. It is widely distributed throughout the tropical and subtropical parts of the world, including India, Malaysia and Nigeria [3]. *A. muricata* is an evergreen, terrestrial, erect tree of about 5–8 m in height with large, glossy, dark green leaves. The edible fruits are heart-shaped and green in colour with a diameter between 15 and 20 cm [4]. The leaf, bark, root, stem, and fruit seed extracts of *A. muricata* have been reported to have anti-bacterial [5, 6], antifungal [7] and anti-malarial [8, 9] properties. Among the chemical constituents found in the leaf of *A. muricata* are alkaloids [10], essential oils [11] and acetogenins [12]. Acetogenins were found to be a promising new anti-tumor and anticancer agent [13] and demonstrated the ability to be selectively toxic against various types of cancerous cells without harming healthy cells [14]. However, many acetogenins are characterised by neurotoxicity of which an example is annonacin. Annonacin has been reported to be a potent neurotoxin that is associated with neurodegenerative disease [15].
Previous research has suggested that a connection between soursop consumption and atypical forms of Parkinson's disease is conceivable due to high concentrations of annonacin [16, 17]. This research therefore aims to ascertain that fact.

2. Material and methods

2.1. Breeding of animals

Twenty four (24) male Wistar rats weighing between 180-200 g were procured from the animal house of the Department of Anatomy, Nnamdi Azikiwe University. The rats were kept in standard cages under normal temperature (27-30 °C), with each cage having wire gauze for cross ventilation. The ethical committee of the College for animal care and use approved the study design in compliance with the National regulation for animal research. The animals were acclimatized for a period of two weeks before commencement of treatment. They were fed with normal rat chow and water ad libitum.

2.2. Preparation of the extract

Fresh leaves of A. muricata were procured from Uturu, Abia State. They were identified at the herbarium units of the Department of Botany, Abia State University Uturu, Abia State. The leaves were washed in a basin of water to remove dirt and dried under ambient temperature. The dried leaves were ground using laboratory blender to a coarse powdery form. 600 g of the powder was macerated in four (4) litres of ethanol, sealed and allowed for 48 hrs. After 48 hours, the mixture was sieved using a porcelain cloth and filtered using filter paper into a clean glass beaker. The filtrate was further dried using rotary evaporator into a jelly-like/paste-like form and stored in refrigerator for future use.

2.3. Experimental design

The twenty four (24) rats were weighed and randomly allocated into four (4) groups of six (6) animals. The groups were designated as group A, B, C, and D. Group A served as the control group and was administered 2 ml/kg body weight of distilled water. The experimental groups B, C, and D were administered with 100 mg/kg, 200 mg/kg and 300 mg/kg body weight of the extract of A. muricata respectively.

The administration was given orally between the hours of 10-11 am daily and lasted for thirty (30) days. Twenty four (24) hours after the last dose, the animals were anaesthetized by chloroform inhalation and dissected. The brain tissues were harvested and fixed in 10% formal saline for histological examination.

2.4. Histopathological examination

The brain tissues from the animals were fixed in 10% formal saline and were processed by passing them through ascending grades of alcohol. The tissues were then cleared in xylene after which embedding in paraffin wax was carried out. Rotatory microtome was used to obtain tissue sections of 3-5 μm thick. The sections were deparaffinised, hydrated and stained using haematoxylin and eosin (H&E) dye. The sections were then mounted using neutral dibutylphthalate xylene (DPX) medium for microscopic examination at x150 magnification.

3. Results and discussion

3.1. Histopathological analysis

Photomicrograph sections of the basal ganglia of animals in group A (Figure 1) showed normal sub-cortical basal ganglia cell body (BGCB) and fibers (F). Group B (Figure 2) showed a mild increase in the number of basal ganglia nuclei cell body (BGNCB) and fibers (F). Group C (Figure 3) showed mild to moderate increase in the number of basal ganglia nuclei cell body (BGNCB) and fibers (F) while Group D (Figure 4) showed moderate increase in the number of basal ganglia nuclei cell body (BGNCB) and fibers (F)
Medicinal plants contain several phytochemical substances that are known to have healing properties. People without access to modern medicine rely mostly on these medicinal plants for treatment of diseases, as they are similar in terms of active compound. *Annona muricata* is evidently one of these beneficial medicinal plants known for its diverse...
biological activities [18] which also have its toxic effect. The basal ganglia control voluntary motor movement, eye movement, cognition and learning. Its dysfunction results in a wide range of neurological conditions.

The result of this study revealed an increase in the number of basal ganglia nuclei cell body (BGNCB), nerve fibres (F), cytoplasmic vacuolization of neurons and necrosis of neurons in the treated groups when compared to the control. These changes show that high doses of *A. muricata* extract is likely to damage the basal ganglia which could result in extrapyramidal Parkinsonism-like side effects. Necrosis in the substantia nigra was also evident and reached the stage of degeneration. This effect is understandable given the strength of acetogenin compounds in soursop plants. This acetogenin can passively diffuse into the cell and is fifty times more toxic to dopaminergic neurons and two thousand times more toxic to non-dopaminergic neurons, when compared with 1-methyl-4- phenylpyridinium (MPP) [19, 20]. Substantia nigra is rich in dopaminergic neuronal cell bodies and there is a possibility that the acetogenins in ethanolic extract of soursop leaf could preferentially affect non-dopaminergic neurons as compared to dopaminergic neurons. These results are consistent with that of Champy *et al* [20]. Previous research has suggested that a connection between soursop consumption and atypical forms of Parkinson’s disease is conceivable due to high concentrations of annonacin [16, 17]. This is in agreement with the outcome of this research.

4. Conclusion

Findings from this research reveal that high consumption of ethanolic extract of *A. muricata* could result in atypical forms of Parkinsonism. Therefore, its consumption should be regulated and taken at low doses.

Compliance with ethical standards

Disclosure of conflict of interest

There was no conflict of interest in the research of this work.

Statement of ethical approval

The experiment was carried out at Abia State University, Uturu with approval by the local ethics committee for animal care and use.

References


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