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Histological Effects of Chronic Administration of Aqueous Extract of *Phyllanthus amarus* on the Medial Geniculate Body of Adult Wistar Rats.

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ABSTRACT

Effects of chronic administration of *Phyllanthus amarus* commonly used for the treatment of jaundice, diarrhea, dysentery, urogenital disease and wound on the medial geniculate body of adult wistar rats was carefully studied. Rats of both sexes (n = 24), with average weight of 200g were randomly assigned into two treatment groups (A and B) and control group (C) of 8 rats each. The rats in the treatment groups (A and B) received 400mg and 800mg of aqueous extract of *Phyllanthus amarus* per kg body weight respectively through orogastric tube administration daily for thirty days. The control group received equal volume of distilled water daily for thirty days through the same route. The rats were fed with growers mash obtained from Edo Feeds and Flour mill Limited, Ewu, Edo State, Nigeria and given water liberally. The rats were sacrificed by cervical dislocation on the thirty-one days of the experiment. The medial geniculate body was carefully dissected out and quickly fixed in 10% formal saline for further routine histological study. The findings indicated that rats in the treated groups (A&B) showed some necrotic and cellular degenerative changes such as sparse cellular population, hypertrophy, and vacuolations in the stroma of the medial geniculate body as compared to the control group with that of group B more marked. Chronic administration of *Phyllanthus amarus* may therefore have an adverse effect on the auditory sensibilities by affecting the microanatomy of the medial geniculate body of adult wistar rats.

Keywords: **Histological Effects, *Phyllanthus amarus*, Medial Geniculate Body, Wistar rats.**

Most of the population of the underdeveloped and developing countries depend on some form of traditional and herbal medicines since ancient times. One of the plants widely used traditionally for the treatment of many diseases in many countries is the Phyllanthus amarus (Calixto et al., 1998; Muhamad bin Zakaria and Mustafa Ali Mohd, 1994). Phyllantus amarus has bitter, astringent, cooling, diuretic, stomachic, antiseptic, antiviral, antidiabetic, hypotensive, antinociceptive, febrfuge properties and is traditionally used in the treatment of jaundice, diarrhea, dysentery, diabetes, fevers, urogenital diseases, ulcers and wounds (Santos et al., 1995; Calixto et al., 1998). Herbal medicines are widely perceived by the public as being natural, healthful and free from side effects. Plants contain hundreds of constituents and some of them may elicit toxic side effects. Toxic effects of some herbal medicines have been reported (Shaw et al., 1997; Kaplowitz, 1997; Calixto, 2000).

The medial geniculate body is the target of ascending projection from the inferior colliculus and descending input from the auditory cortex this is the obligatory synaptic target in the thalamus for hearing (Fall, 1999). It contains interleaved and overlapping tonotopic and aural bands, the most beautiful structure in the brain (Fall, 1999). The cerebral cortex strongly affects the medial geniculate body through descending projections. These projections were thought to consist primarily of small areas with slow conduction velocities (Winer et al., 1996). It has been demonstrated that neurons of auditory cortex showed great physiological plasticity when rats were exposed to specific stimuli coupled with concurrent stimulation of a forebrain subcortical structure in the nucleus basalis (Winer et al., 1999). Changes include massive expansion of frequency-specific representation (Winer et al., 1999). Cortical structures such as the medial and lateral geniculate bodies, inferior and superior colliculi have higher glucose utilization than other structures (Siesjo, 1978). There is a correlation between functional activity and metabolic rate such as in the visual and auditory system (Siesjo, 1978).

This present study is to investigate the histological effects of chronic administration of phyllanthus amarus on the medial geniculate body of adult wistar rats.

MATERIALS AND METHODS

Animals: Twenty-four (24) adult wistar rats of both sexes with average weight of 200g were randomly assigned into three groups: A, B and C of (n = 8) in each group. Group A and B of (n = 16) served as treatment groups while group C (n = 8) was the control. The rats were obtained and maintained in the Animal Holdings of the Department of Anatomy, School of Basic Medical Sciences, University of Benin, Benin city, Edo State, Nigeria. The animals were fed with grower's mash obtained from Edo Feeds and Flour Mill Limited, Ewu, Edo State, Nigeria and given water liberally. The phyllanthus amarus leaves were obtained in Benin City, dried and processed into aqueous extract at the Department of Pharmacognosy, Faculty of Pharmacy, University of Benin, Benin City, Edo State, Nigeria.

Preparation And Administration of *Phyllanthus amarus*: The plant leaves were obtained in Benin City, cleaned and oven dried at 50°C, and were macerated into dry powder. The *Phyllanthus amarus* powder was extracted with distilled water using Soxhlet apparatus and concentrated by rotary evaporator at 65°C. It was then transferred into a suitable container and freeze dried ready for the experiment.

Animals in group A were given the aqueous extract of *Phyllanthus amarus* at a single dose of 400mg/kg body weight daily for thirty days through the orogastric tube, while animals in group B received 800mg/kg body weight daily via the same route and the same period. Animals in group C received equal volume of distilled water, for the same period and through the same route of administration. The rats were sacrificed by cervical dislocation on the thirty-one day of the experiment. The skulls were opened using bone forceps to expose the brain of the rats and the medial geniculate body was quickly dissected out and fixed in 10% formal saline for routine histological techniques.

Histological Study:

The tissues were dehydrated in an ascending grade of alcohol (ethanol), cleared in xylene and embedded in paraffin wax. Serial sections of 7 microns thick were obtained using a rotatory microtome. The deparafused sections were stained routinely with haematoxyline and eosin (Drury et al., 1967). Photomicrographs of the desired results were obtained using research photographic microscope in the Department of Anatomy, School of Basic Medical Sciences, University of Benin, Benin city, Edo State, Nigeria.

RESULTS

The photomicrograph of the desired sections of the medial geniculate body from the control animals showed normal histological features with the neurons appearing distinct and of various sizes. The neuron and glial cells appeared normal and no distinct vacuolations in the stroma of the sections (fig.1 & 2).

The medial geniculate body of the treated groups revealed some necrotic and cellular degenerative changes such as sparse cellular population, hypertrophy, and vacuolations in the stroma of the medial geniculate body as compared to the control group with that of group B more marked (Fig.3, 4, 5 & 6).

DISCUSSION

The results (H&E) of this experiment revealed some necrotic and cellular degenerative changes such as sparse cellular population, hypertrophy, and vacuolations in the stroma of the medial geniculate body as compared to the control group with that of group B more marked.

Neuronal degeneration has been reported to result in cell death, which is of two types, namely apoptotic and necrotic cell death. These two types differ morphologically and biochemically (Wyllie, 1980). Pathological or accidental cell death is regarded as necrotic and could result from extrinsic insults to the cell such as osmotic, thermal, toxic and traumatic effects (Farber et al., 1981). It was reported that cell death in response to neurotoxins might trigger an apoptotic death pathway within brain cells (Waters, 1994). Cell death in response to neurotoxins occurs as a controlled event involving a genetic programmed in which caspase enzymes are activated (Waters, 1994).

The process of cellular necrosis involves disruption of the membranes structural and functional integrity. Cellular necrosis is not induced by stimuli intrinsic to the cells as in programmed cell death (PCD), but by an abrupt environmental perturbation and departure from the normal physiological conditions (Martins et al., 1978). There is the need to further investigate the actual mechanism by which phyllanthus amarus induced neuronal degeneration in the medial geniculate body of adult Wistar rats in this study.

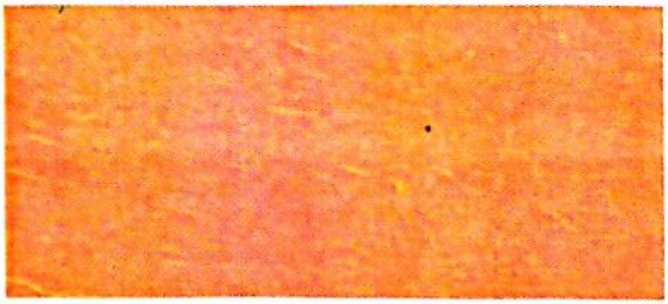

Fig 1: Control section of MGB (H & E Method x100)

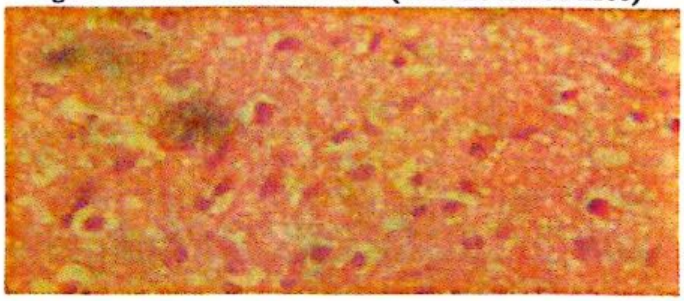

Fig 2: Control section of MGB (H & E Method x400)

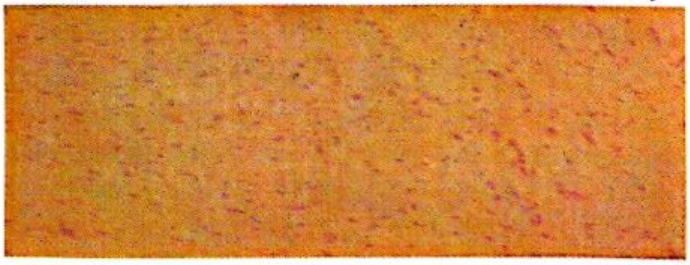

Fig 3: Treated Group A section of MGB (H & E Method x100)

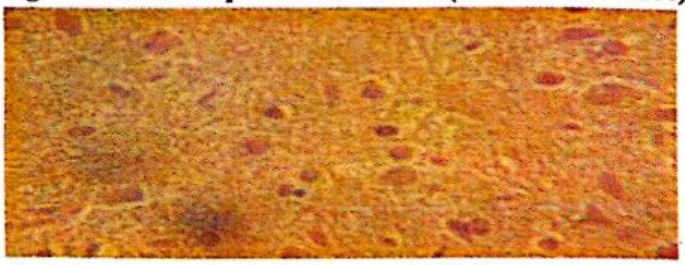

Fig 4: Treated Group A section of MGB (H & E Method x400)

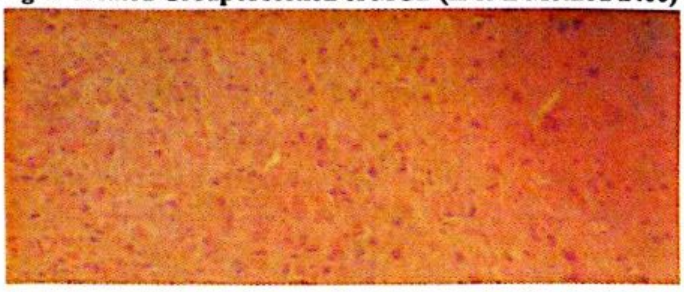

Fig 5: Treated Group B section of MGB (H & E Method x100)

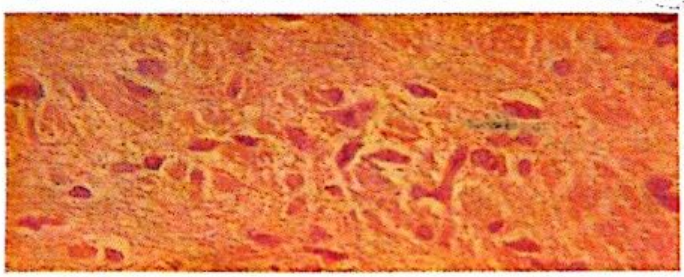

Fig 6: Treated Group B section of MGB (H & E Method x400)

Extensive cell death in the central nervous system is present in all neurodegenerative diseases (Waters, 1994). The type of nerve cell loss and the particular part of the brain affected dictate the symptoms associated with an individual disease (Waters, 1994). In this study phyllanthus amarus may have acted as toxin to the cells of the medial geniculate body, affecting their cellular integrity and causing defect in membrane permeability and cell volume homeostasis.

In cellular necrosis, the rate of progression depends on the severity of the environmental insults. The greater the severity of the insults, the more rapid the progression of neuronal injury (Ito et al., 1975). The principle holds true for toxicological insult to the brain and other organs (Martins et al., 1978). The prime candidates for inducing the massive cell destruction observed in neurodegeneration are neurotoxins (Waters, 1994). These may be substances present in small amounts in the environment, or even naturally occurring chemicals such as glutamate used by the brain as transmitter's substances (Waters, 1994). The latter when present at a critical level can be toxic to the brain cells they normally excite (Waters, 1994). It could be inferred from this results that chronic administration of phyllanthus amarus resulted in increased toxic effects on the medial geniculate body of adult wistar rats. The decrease in cellular population observed in this study may have been as a result of cell death caused by the toxic effects of the phyllanthus amarus. In the same way, it has been reported that chronic administration of chloroquine resulted in the cellular degenerative changes, sparse cellular population and vacuolation appearing in the stroma with some autophagic vacuoles in the inferior colliculus and medial geniculate body of adult Wistar rats (Adjene and Adenowo,2005; Adjene and Caxton-Martins, 2006).

The vacuolations observed in this experiment may be due to phyllanthus amarus interference with the stroma of the medial geniculate body. The cellular hypertrophy observed in this experiment may be due to the adverse effects of phyllanthus amarus on the medial geniculate body of adult wistar rats. It is probable that the results obtain in this experiment may have been due to the neurotoxic effects of phyllanthus amarus on the neuronal cells of the medial geniculate body of adult wistar rats.

CONCLUSION

This experiment revealed that chronic administration of phyllanthus amarus resulted in some necrotic and cellular degenerative changes such as sparse cellular population, hypertrophy, and vacuolations in the stroma of the medial geniculate body as compared to the control group with that of group B more marked. These results may probably affect the auditory sensibility functions of the medial geniculate body of the adult wistar rats. It is recommended that further studies aimed at corroborating these observations be carried out.

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