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In vivo Modulatory Effect of *Clerodendrum Splendens* (Glory Blossom) in Aluminum Induced Alzheimer Diseases and *Lonchocarpus Sericeus* in Rotenone Induced Parkinson's Disease on Na^+/K^+ Atpase (Sodium Pump) in the Cerebral Tissues of Male Albino Wister Rats

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Abstract

Elegant research has shown that plants are useful for both curative and preventive purpose on the humans populous. Prevalent among diseases associated with humans are neurological diseases which affect a large sector of the population especially the elderly. The most common neurological diseases are Parkinson and Alzheimer disease which affect a large sector of the brain and also cause an imbalance in brain electrolyte. Among such electrolytic mechanisms of the brain are those which regulate the inflow an out flow of sodium and potassium levels in the cerebral tissue and the system responsible for such is the sodium pump. This is a p type ATPase which controls the influx and out flux of sodium and potassium ions in the brain and whose damage can trigger a lot of neurological problems. Due to the important of this "pump", this research was aimed at examining the modulatory effect of two plants species (Clerodendrum Splendens and Lonchocarpus sericeus) on sodium potassium ATPase in the cerebral tissue of mammals. Methodologies employed in this research are the Na^+/K^+ ATPase by Svoboda and Mosinger, 1981. All results were estimated at $P<0.05$. It is interesting to know that result obtained from this research shows that there was no significant different in the sodium potassium ATPase level in group three and four of both groups. However, as compared to the positive control, the sodium potassium ATPase level was higher and to the negative and standard, it almost obtained 100% efficiency. This implies that Clerodendrum Splendens and Lonchocarpus sericeus have great impact on restoring the sodium potassium ATPase activity in the cerebral tissue of Alzheimer and Parkinson disease patients and may also serves as a medicament in treating other neurological disorders.

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INTRODUCTION

Our brain is one of the largest and most specialized organ in the body and also the seat of intelligent. Physiologically, it is a soft of tissue, with about 1.4 kg in weight and containing 86 billion nerve cells. This specialized organ (brain), has three main parts which are; the cerebrum, the brainstem, and the cerebellum each with their own

unique function. Furthermore, the brain coordinate the intellectual activities of the body, which include processing, integrating, and coordinating the information or signals received from the sensory organs and interpreting such information for the body to fully understand and swing into actions [4]. The largest component of the brain is the cerebrum and is divided into two halves which are called cerebral hemispheres (right and left respectively). The cerebral hemispheres makes up two third of the total weight of the brain tissue. One hemisphere is functionally dominant and controls language and speech, while the other hemisphere interprets visual and spatial information. The two hemispheres of the human brain, the left and right, are connected together by a group of nerve fibers called the corpus callosum. Each of the hemispheres is divided into four lobes, which are: the frontal lobe, temporal lobe, parietal lobe, and occipital lobe [6]. The neurons which are the never cells in the brain are basically, made up of three parts: the cell body or soma, branching dendrites, and the axon. These nerves cells are the building blocks of the brain and they send informations to other neurons, muscles and tissues throughout the body. The neurons or nerves cells also help to think, feel, move, and comprehend the world around us [7].

Conversely, there are divers' diseases which affect the brain cells, causing either partial or total damages to the cells. Chief among these diseases are the Alzheimer's disease (AD) and the Parkinson's Diseases PD. The Alzheimer's disease (AD) which is the most prevalent, affects the population of above 60 years (the elderly). This disease was first described in 1906 by German Physician Alois Alzheimer on the basis of a medical case of Auguste D, a patient who showed symptoms of memory loss and some psychological changes such as mood swing and unresponsive behavior. AD was named after German Doctor Alois Alzheimer by Emil Kraepelin, who was the colleague of Dr. Alzheimer. In 1910, he mentioned for the first time this disease as "Alzheimer's disease" in his medical book named 'Psychiatrie' [3]. Also, Parkinson's disease (PD) which happens to be the second most common neurodegenerative disease after AD is an advance central nervous (CNS) disorder that affects mainly the locomotion of the body. It affects both motor as well as non-motor functions in the body. Its causes are still puzzled researches and medical practitioner, but it can be inferred that the involvement of both genetic and environmental factors may be responsible for the progression of the disease. It was described by Dr. James Parkinson (1817) in his monograph entitled "An Essay on the Shaking Palsy" [5].

Apparently, neurological damage don't only brain cells but also causes imbalance in some chemicals in the brain such as the sodium potassium ATPase (Na^{2+}/K^{2+} ATPase) and other electrolyte and non-electrolytes in the brain tissue. Furthermore, Na^{+}/K^{+}-ATPase is an integral membrane protein present in all mammalian cells. It moves Na^{+} and K^{+} ions across the plasma membrane, and is essentials for creating an equilibrium in the electrochemical gradient which is important in the processes of electrical excitation and the transport of other ions. Na^{+}/K^{+}-ATPase is a heterodimer composed of two subunits which are the alpha and beta subunits. The alpha subunit, which is a catalytic in nature and it has a 10 trans-membrane segments, which act in coupling ATP hydrolysis with ion transport. The beta subunit on the other hand, is involved in the processes of the structural and functional maturation of the enzyme and in movement to the plasma membrane [3]. This enzyme plays an essential role in maintain the level of sodium and potassium ion in the brain and other organs in the body. Meticulous studies from renowned researchers have shown that this signaling pathway, and its alterations, is involved with a number of clinical disorders, including cancer, chronic kidney disease, and cardiovascular diseases, such as uremic cardiomyopathy [12, 8].

Over time, plants have been harnessed for their numerous therapeutic qualities such as their antimicrobial, antifungal, anti-inflammation nuro protective among others. Peculiar to these medicinal plants are the *Clerodendrum Splendens, Lonchocarpus sericeus* which has been widely studied and observed their usefulness in treating many diseases damages. Conversely, Clerodendrum splendens plant which belongs to the Lamiaceae family is a shrub of about 3.7 m high. It has a simple and opposite dark green leaves [10], which are used in folklore medicine by local people to treat shingles,

spleen in children, asthma, rheumatism, ulcers and malaria [9]. Results obtained from *In vivo* and *In vitro* studies conducted by many researchers have shown that Clerodendrum splendens has anti-inflammatory [10], antioxidant [2], properties which further illuminate its medical properties. Previous chemical studies performed on Clerodendrum splendens have leads to the isolation and characterization of some secondary metabolites among which, Carbohydrates, Steroids, Terpenoids and Flavonoids [11]. Also, Lonchocarpus sericeus Poir. (Papilionaceae) a leguminous plant commonly known as Senegal lilac or Cube root is a dry deciduous tree that grows up to 16 meters high, has a dense hanging racemes of purple flowers which makes it perfect for display purposes. The flowers have a unique aroma which is similar to vanilla [1]. These plant has been used in folklore medicine due to their vast medicinal properties in view of this, this research was aimed at studying the *Invivo* modulatory Effect of Clerodendrum Splendens (Glory Blossom) In Aluminum Induced Alzheimer Diseases and Lonchocarpus sericeus in rotenone-induced Parkinson's Disease On Na+/K+ ATPase (sodium pump) In the cerebral tissues of Male Albino Wister Rats.

MATERIALS AND METHODS

Chemicals and Reagents

Potassium chloride, sodium chloride, Distilled water, ATP, TCA, Ammonium molybdate, ANSA, Tris HCl mallic acid Na EDTA Rotenone carboxymethyl cellulose chloroform Ubiquinone were all of analytical grade.

Sample Collection

Fresh samples of *clerodendrum splendens* (glory blossom) leaves were obtained from-king's market Akure. The plant was Authenticated by Dr. O. P. Aiyelari, Department of Crop Soil and Pest Management, Federal University of Technology, Akure, Nigeria. The samples were washed, air-dried, ground into fine powder using a blender, the powdered sample was macerated in 80% methanol for 72 h and then filtered using filter paper. The filtrate was concentrated to a small volume using rotary evaporator and thereafter lyophilized in order to obtain the methanol extract of *C. splendens*. This was kept in an amber bottle to prevent light from damaging the active ingredients in the sample and refrigerated at -20^0c to preserve freshness and subsequently kept for further experiments. The yield of the extract was calculated.

Animals

50 adult male Wister albino rats which weighed about 100-245g were gotten from a private animals holding facility in Ogbomoso, and was used for the research. The rats were fed on standard laboratory diet, given water *ad libitum* and maintained under laboratory conditions.

Animal Care and Handling

All of the animals received human care according to the criteria outlined in the Guide for the Care and the Use of Laboratory Animals prepared by the National Academy of Science and published by the National Institute of Health (USA). The ethic regulations were followed in accordance with national and institutional guidelines for the protection of animals' welfare during experiments (PHS, 1996). The experiment was carried out at the Applied Clinical Laboratory, Department of Biochemistry, Federal University of Technology, Akure, Nigeria.
The animals were group into two major group with five sub groups as shown below

Group A (Aluminum induced Alzheimer Disease)

Animals were grouped into five groups as shown below:

- Group I (control): animal were administered normal-saline (0.9% NaCl) intraperitonally for one week, giving an interval of a day each.
- Group II: Animals were administered 500µl of 50mg/kg $AlCl_3$ solution i.p. / no treatment
- Group III: Animals were administered 500µl of 50mg/kg $AlCl_3$ solution i.p./ 100mg/kg BWT of Methanolic leaf extracts of *Clerodendrum splendens*

- Group IV: Animals were administered 500µl of 50mg/kg $AlCl_3$ solution i.p./ 200mg/kg BWTof Methanolic leaf extracts of *Clerodendrum splendens*
- Group V: Animals were administered 500µl of 50mg/kg $AlCl_3$ solution i.p./ standard only (malic acid)

Group B (Rotenone induced Parkinson 's disease).

Animals were grouped into five groups as shown below:

- Group 1: Sham-operated with oral administration of vehicle (4% carboxymethylcellulose and 1.25% chloroform)
- Group 2: Rotenone–induction (5mg/kg BWT i.p) with oral administration of vehicle (4% carboxymethyl cellulose and 1.25% chloroform)
- Group 3: Rotenone–induction (5mg/kg BWT i.p) and 1000mg/kg BWT of LILS extract
- Group 4: Rotenone –induction (5mg/kg BWT i.p) and 1600mg/kg BWT of LILS extract
- Group 5: Rotenone –induction (5mg/kg BWT i.p) with Ubiquinone 5mg/kg BWT i.p

Preparation of Tissue Homogenates

The rats were decapitated under mild diethyl ether anesthetic conditions and the whole brain tissue was quickly isolated and placed on ice and weighed. The tissues were subsequently homogenized in cold saline (1/5 w/v) with about 10-up-and-down strokes at approximately 1200 rev/min in a Teflon glass homogenizer. The homogenates were centrifuged for 10 min at 3000 rpm to yield pellets that were discarded, and a low-speed supernatant (SI) fractions were kept for lipid peroxidation assay (Belle *et al.*, 2004).

Na^+/K^+ ATPase Activity

Na^+/K^+ ATPase activity was measured by the method of Svoboda and Mosinger, 1981, and described by Sunil *et al.*,2011.

Principle

This is a trans membrane protein belonging to the p-type ATPase family, it maintain a vectoral transport of cation, and to establish a proper ion gradient inside and outside of cells, where the intensity of the blue colour was assessed spectrophotometrically at 640nm.

Procedure

The reaction mixture contains 250µl of Tris HCl buffer, 50µl of NaCl, 50µl of KCl, Na EDTA and 50µl of ATP. The reaction mixture was pre-incubated at 37°C for 10min. then 25µl of supernatant was added to the reaction mixture and incubated at 37°C for 1h. the reaction mixture was immediately arrested by the addition of TCA. The precipitate was removed by centrifugation at 3500rpm for 10min. to 50µl of supernatant, 925µl of distilled water, 125µl of ammonium molybdate and 50µl of ANSA were added and incubated for 10min at 370c. The intensity of the blue colour was read at 640nm against a reagent blank containing all the reaction mixture apart from the sample. The control reaction was prepared by adding the sample after the addition of TCA. The result is expressed as nanomole of inorganic phosphorus liberated /min/mg protein.

$$(Abs_{sample} - Abs_{control}) \times 1.15 \times 10)/(0.556 \times 0.05 \times 10)$$

DISCUSSION AND CONCLUSION

Na/K ATpase (NKA) is found in the membranes of most eukaryotic cells and acts as ion pump. NKA can be modulated by hormones and neurotransmitters, thus allowing them to regulate NKA's diverse important effects, which includes the control of neurotransmission and other cerebral functions. Apart from Parkinson disease (PD) and Alzheimer Disease, changes in NKA activity, also occurs in aging. When it arise from mutations, it will play a role in a host of CNS diseases, partly via deficits in energy and glutamatergic control. Central energy deficiency has been/

Proposed to be a major factor in many, currently poorly managed, neurodegenerative diseases, which are linked to changes in brain metabolism and increased levels of apoptosis (programmed cell death). Given that NKA is pivotal for optimizing central synaptic functioning, as well as energy regulation, its further study, including its environmental, epigenetic and genetic regulation, are likely to be important in the development of new pharmacological and non-pharmaceutical treatments for a host of medical conditions that are currently poorly managed such as AD and PD. Results are presented in graphical form in Figures 1 and 2.

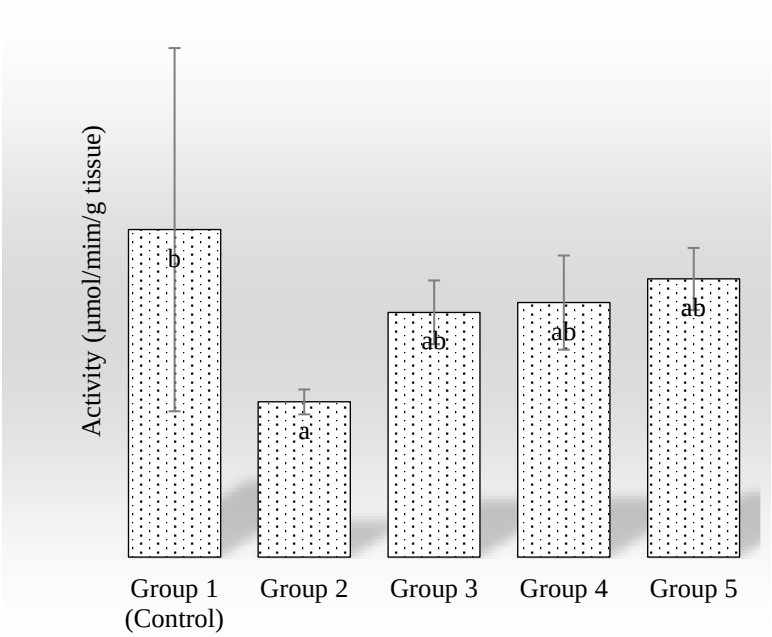

Figure 1. Effects of methanolic leaf extracts of *C. splendens* on Na^+/K^+ATPase activity in Alzhiemer's diseased albino rats (µmol/min/g tissue). Values are expressed as mean (n=5), Values with different superscripts are significantly different ($p<0.05$). *Keys:* Group 1- negative control; Group 2 – positive control; Group 3 – treated with 100mg/kg bwt; Group 4 - treated with 200mg/kg bwt; Group 5 – treated with standard.

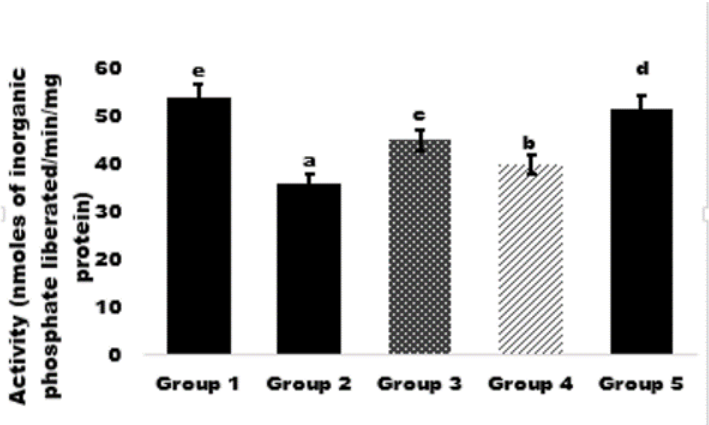

Figure 2. Effects of *L. sericeus* leaf extracts on the activity of Na^+/K^+ ATPase in the brain of rotenone-induced **Parkinson's Disease** albino rats. Bars are expressed as mean (n=5), bars with different superscripts are significantly different ($p<0.05$). *Keys:* Group 1- Negative control; Group 2 – Positive control (Rotenone-induced but not treated); Group 3 – Rotenone-induced, treated with 1000mg/kg bwt LILS; Group 4 - Rotenone-induced, treated with 1600mg/kg bwt LILS; Group 5 – Rotenone-induced, treated with 0.2mg/kg Ubiquinone.

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