ISSN No:-2456-2165

# Effect of Carica Papaya Leaf Extract Against Aluminum Neurotoxicity in the Frontal Cortex of Female Albino Wistar Rats

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**Abstract:- $AlCl_3$ is commonly administered to simulate neurotoxic effects and cognitive disorders that affect the central nervous system (brain and spinal cord) such as Alzheimer's and Parkinson's disease. This study assessed the effects of Carica Papaya leaf extract on $AlCl_3$ induced animals to see the neurotoxic effect of $AlCl_3$is greater than the ameliorative or antioxidative function of Carica Papaya leaf extract. 30 adult female wistar rats were split into 5 groups and housed six rats per group. Group 1 was designated as the control group by which other groups would be measured against, hence received nothing with regard to administration. Group 2 rats were administered 250g/1250mls of Carica Papaya leaf extract. Group 3 rats were administered 0.1g of $AlCl_3$. Group 4 rats were administered 0.1g of $AlCl_3$ first then 250g/1250mls of Carica Papaya leaf extract second. Group 5 rats were administered 250g/1250mls of Carica Papaya leaf extract first then 0.1g of $AlCl_3$ second. The general administration time was 14 days. After administration, the cognitive parameters of the rats were then accessed through a variety of behavioural tests. The concentration of MDA and the activities of GSH, LDH and AchE in the prefrontal cortex of the mice were evaluated. There was a decrease in the brain weight of the group exposed to aluminium chloride only (group 2) as opposed to the control group. The study also showed significant increase in the AChE levels of group 2 rats which were given just $AlCl_3$ as opposed to the control group. Group 3 rats that were given only Carica Papaya leaf extract had the highest MDA levels out of all the groups. The LDH levels for all the groups were the same except rats that were given CP whichhad more elevated levels of LDH. GSH increase in rats that were administered $AlCl_3$ was observed. The results gotten suggest that Carica Papaya may effectively prevent neurotoxic effects induced by $AlCl_3$ and could also be ameliorative for already existing $AlCl_3$ conditions.**

***Keywords:-*** *Aluminium Chloride; Carica papaya; Prefrontal Cortex; Melondialdehyde; Gluthiatone.*

## I. INTRODUCTION

Aluminium induced neurotoxicity has been a steady cause for concern and has been a topic at the table of a lot of researchers due to the abundance of the element in nature. It is the most common neurotoxic agent present in nature (1).

Aluminium (Al) is the third most abundant element and the most common metal in the earth's crust and aluminium toxicity only happens when there is exposure to an extreme level of Aluminium content (2). In the brain, aluminium accumulates in sensitive areas such as hippocampus and frontal cortex and is considered a potential contributing factor of neurodegenerative disorders like Alzheimer's disease (AD) and Parkinson's disease (PD) (3). Aluminium exists in one oxidation state (+3), and doesn't go through oxidation reduction reactions and it can react with other metals in the environment to create different complexes. Exposure to this light weight and toxic metal is through air, food and water (3).

Aluminium toxicity is proportional to its bioavailability and has been observed to accumulate in specific regions of the brain such as the brain, bone, liver and kidney (1).

Aluminium has been shown to accumulate in all the regions of rat brain following chronic exposure, maximum being in hippocampus, which is the site of memory and learning (2). Further evidence was added (4) for Aluminium distribution in rat brain regions and found that Aluminium accumulation was more significant in the group receiving Aluminium via intraperitoneal than oral route, suggesting that its distribution is dependent on the route of administration (5). Aluminium uptake in the brain is much slower as compared to other organs but once gained access into the brain, Aluminium distributes into the various regions(6). It is also known that the brain consists of low levels of Aluminium burden when compared to other organs and Al content of human brain increases with ageing (7).

*Carica papaya* (family Caricaceae) originated in Central America. Papaya is a rapid-growing, semi-woody plant with a single stem and broad green leaves that are limited and can be found in tropical regions. The means of reproduction of pawpaw is quite complex. The plants are male, hermaphrodite, or female (8). Pawpaw fruits are rich in antioxidant nutrients like carotene, vitamin C, vitamin B, flavonoids, folate, panthotenic acids and minerals such as potassium and magnesium, the fruit is also a good

source of fibre. The extract of *Carica papaya* is also known to have antioxidant properties (9).

Currently, fresh papaya leaf extract is taken orally in 2 tablespoons every 12 hours by most of the people in dengue- epidemic localities in the Philippines. This practiced herbal remedy is supported by the significant results in increasing blood platelet in dengue fever patients in current studies performed in Malaysia, Pakistan, Indonesia and Sri Lanka (10). In addition to the natural usage in treating dengue fever, *Carica Papaya* also helps in a lot of other conditions in the body and it also boosts the overall function and improves general health and well-being of the human body system, both internally and externally (11).

The largest cortical area in the brain is the prefrontal cortex which makes up about 29% of the whole cerebral cortex and it is located in the frontal lobe and is anterior to the primary motor cortex and premotor cortex (12). The major function is to define personality and behaviour but also maintains attention, planning complex movements, controlling emotions, discriminating between good and bad, speech, memory, temporal perception and working memory (13).

Consumption of Aluminium is almost unavoidable. Al enters into the human body through drinking water, food, use of utensils, deodorants, and drugs. It is estimated that the dietary intake of Aluminium can be from 3 to 30 mg/day (7). It causes damage to the frontal cortex which is in charge of planning complex cognitive behaviour, personality expression and decision making. Aluminium Chloride has an oxidative and inflammatory effect on the frontal cortex making it necessary to find out if *Carica Papaya* leaf extract which has an anti-oxidant and anti-inflammatory effect can be used to prevent damage caused by Aluminium Chloride on the frontal cortex of the brain.

The aim of this study is to evaluate the effect of *Carica Papaya* on the morphological,behavioural, biochemical and histological components against Aluminium Chloride insult in the frontal cortex of adult female albino Wistar rats.

## II. MATEIALS AND METHODS

### *A. Materials Used*

Aluminium Chloride ($AlC_3$), absolute alcohol, brooms, beaker, dustpan, cotton wool, cover slips, dissecting sets, distilled water, handkerchiefs, dropping pipettes, Eosin stain, feeds, feeding and drinking troughs, syringe (calibrated), female wistar rats, weighing scale (sensitive & non-sensitive), flash drive, forceps, formalin, latex examination gloves, Wattman's filter paper, methylated spirit, Morris water maze, open field boxes, oral cannulas, paper tapes, rat cages, sample bottles, surgical blades, tap water, video camera, plastic funnels, markers, soaps, sponges, large bowl, disposable bags.

### *B. Animal care and Ethical Approval*

Wistar rats were procured from Ogbomoso and arrived around 10am at the animal holding facility of the faculty of basic medical sciences, college of health sciences, University of Ilorin, Nigeria. The animals were fed with Ogo-Oluwa feeds and proper care was given to the animals and they were all in good condition. They were fed daily and their cages were constantly cleaned in order to keep them clean and prevent diseases that may stem from lack of proper hygiene. The environment they were placed in was also constantly taken care of in order to make sure no external predators or organisms would affect the rats and also to reduce the smell to the barest minimum. Their cages were placed in a properly ventilated area to ensure that the rats weren't affected by heat or lack of oxygen.

Ethical approval was given on the aim of the project which was to test for the neuroprotective and ameliorative effects of Carica papaya against AlCl3 induced neurotoxicity on the frontal cortex of female wistar rats by the departmental research and ethics committee in the Department of Anatomy, Faculty of Basic Medical Sciences, University of Ilorin.

## III. EXPERIMENTAL DESIGN

The female wistar rats were grouped into five groups with each group comprising of six animals. The table below further displays how they were grouped:

| S/N | *Groups* | *Number of Mice* | *Administered Drugs* |
|---|---|---|---|
| 1 | Control | 6 | no dosage given |
| 2 | Aluminium Chloride (AlCl3) | 6 | AlCl3 (0.1mg/kg) |
| 3 | *Carica papaya* (CP) | 6 | CP (250g/1250mls) |
| 4 | AlCL3 + CP | 6 | AlCl3 + CP (0.1mg/kg + 250g/1250mls) |
| 5 | CP + AlCL3 | 6 | CP + AlCl3 (250g/1250mls + 0.1mg/kg) |

Table 1: experimental design

[a]Mice were randomly divided into 6 groups.

## IV. CHEMICAAL PREPARATIONS

### *A. Aluminium Chloride Preparation (AlCl3)*

The dose/animal weight was 100mg/kg which is calculated per average weight of rat for each group of rats labelled with Aluminium Chloride (AlCl3). 1g of AlCl3 crystal was dissolved in 50mls and calculated with the average weight of each group labelled with AlCl3 to determine the amount of Aluminium Chloride solution to be given to the rats for 14days. 5.6g of AlCl3 dissolved in 280mls was calculated as the total amount of AlCl3 needed for administration.

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## V. CARICA PAPAYA EXTRACTION

*Carica papaya* being an antioxidant was plucked and confirmed from the department of plant biology. It was air-dried and grinded into powder; it was weighed and found to be 590g. 250g of it was dissolved in 1250ml of distilled water for 48hours and first filtered with white handkerchief. The volume extracted was 850mls. The extract was further filtered with filter papers. 0.5ml was calculated to be the volume of extract to be administered per animal. 140mls was eventually calculated as the total volume of extract required for the groups labelled with *Carica papaya* for administration.

## VI. METHODS OF ADMINISTRATION AND DOSAGES

The administration was done orally with the aid of the cannulas. In this method, extreme caution was taken, because it involved a lot of struggles by the animal especially during the first administration. So, in order to avoid injuries to the animals or even death, a lot of caution was taken during the handling, ensuring that administration goes smoothly and the health of the animal intact while simultaneously preventing the various things being administered from wasting as a result of the struggle and spillage. Each female wistar rat was carried gently from its cage with the bulk of its back lying of the palm using the thumb and the fingers next to it to hold the two forelimb ensuring that the animal wasn't being choked. That's also done to avoid infuriating it and getting injured from its bite while maintaining a firm, steady nonlethal grip on the animal. The other hand is used to hold the cannula which contains the solution you want to administer to the animal which was carefully inserted into its oesophagus through its mouth to make sure it all goes in and the animal doesn't spit it out.

## VII. BEHAVIOURAL TESTS

*A. Open Field Test (OFT)*

The open field apparatus was a 100cm x 100cm wooden box with 38cm high walls (opened at the top) which was placed in an isolated room with normal lighting and temperature. The floor of the maze was divided by straight lines into squares of 10cm each using permanent marker. A video recording system was stationed at an angle where the movement of the animals within the box could be captured the movement of the animals within the box, preferably above the box. Each group was taken to the open field arena in separate cages while making sure there was no agitation to avoid making the animals uncomfortable. Subsequently, each rat was placed in the open field arena, away from the others and also restricting human movements around the area to ensure there were no external inputs on the data to be gathered. Their explorative movement activities were measured for 5 minutes each using the video recorder. This was repeated for rats across all the groups. The apparatus was wiped thoroughly with methylated spirit in order to remove traces of whatever odour (urine and faeces) left by the previously tested animal before introducing the next animal so that whatever action carried out by the animal wasn't influenced by any factor but itself. The observer stayed away from the apparatus during each test to avoid agitating the rats which might influence the results. Following the completion of the exercise, the observers analysed the video to make sure the experiment was successful and that enough data can be collated from the experiment before deeming it successful.

The following parameters were taken into consideration:

- Number of lines crossed.
- Centre of square entering
- Rearing frequency.
- Centre of square duration
- Stretch attend posture frequency
- Faeces and urine (14)

This test was done on the 13th day of the treatment to assess locomotive activities.

*B. Morris Water Maze (MWM)*

This was conducted to test spatial learning and memory in the rats. The test was conducted in an isolated environment using a standard maze labelled north (N), south (S), east (E), west (W) and a stage (which was placed in the maze) to avoid distractions (15). The maze was a big circular basin which was filled with water till three-quarter of the maze and made opaque by adding milk and the stage 1cm below the water. A point was chosen as the starting point and the assessment for each animal lasted for a period of 60 seconds in which the time it took the animal to locate the stage was recorded.

## VIII. ANIMAL SACRIFICE AND TISSUE PREPARATION

On the 15$^{th}$ day the animals were sacrificed by the process of cervical dislocation.

Perfusion fixation is done in order to prevent autolysis of the brain tissue collected, and after perfusion the tissue was subjected to manual routine tissue processing procedures:

Fresh tissue specimen obtained from the prefrontal cortex from each animal across the groups was first processed by fixation.

- Fixation: The tissue was fixed in 4% PFA (paraformaldehyde) to prevent autolysis, and bacterial attack.
- Dehydration: The tissue is then dehydrated by passing it through ascending grades of alcohol (50% - 70% - 90% - 95% - absolute 100%) for 30 – 60 minutes in each grade of alcohol. To remove fixative and water from the tissue and replace them with dehydrating fluid.
- Clearing: The tissue is then cleared in xylene to remove the alcohol because the alcohol is immiscible with the wax.
- Infiltration and Embedding: the tissue is then infiltrated with paraffin wax and embedding was done to prepare the tissue for sectioning.
- Sectioning: Once embedded the tissue are then cut into thin sections ready to be placed on the slide.

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## IX. STAINING

- Place the glass slides that hold the paraffin sections in staining racks. Clear the paraffin from the samples in three changes of xylene for 2mins per change
- Hydrate the samples as follows:
  - Transfer the slides through three changes of 100% ethanol for 2 min per change.
  - Transfer to 95% ethanol for 2 min.
  - Transfer to 70% ethanol for 2 min.
  - Rinse the slides in running tap water at room temperature for at least 2 min.
- Stain the samples in hematoxylin solution for 3 min.
- Place the slides under running tap water at room temperature for at least 5 min.
- Stain the samples in working eosin Y solution for 2 min.
- Dehydrate the samples as follows:
  - Dip the slides in 95% ethanol about 20 times.
  - Transfer to 95% ethanol for 2 min.
  - Transfer through two changes of 100% ethanol for 2 min per change.
- Clear the samples in three changes of xylene for 2 min per change.
- Place a drop of Permount over the tissue on each slide and add a coverslip. View the slides using a microscope. (16)

*A. Cresyl Violet (CFV)*

The tissue sections were;

- Deparaffinized and hydrated to distilled water.
- Cresyl violet, two minutes.
- Wash in distilled water.
- Dehydrated, cleared in xylene, coverslip.
  - Cresyl violet Stock solution:
- 0.2 g cresyl violet acetate in 150 ml distilled water. Mix with a stir bar for at least 20 minutes.
- Buffer solution pH 3.5:
  - 282 ml of 0.1 M acetic acid (6 ml of concentrated acetic acid per 1000 ml distilled water) and add to
  - 18 ml of 0.1 M sodium acetate (13.6 g in 1000 ml of distilled water)

Take 30 ml of the cresyl violet stock solution and add 300 ml of buffer. Mix for at least 30 minutes.

## X. RESULTS

*A. Weight Changes*

a) Body Weight Changes

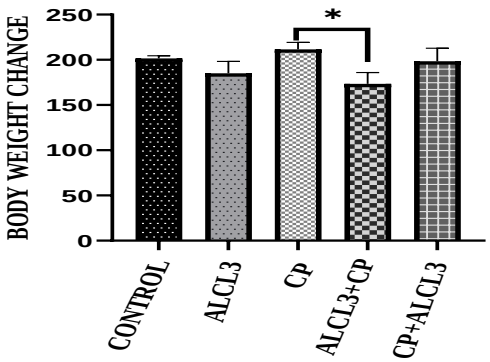


Fig 1: Graph showing Body Weight Changes

There is a significant difference between group 3 and group 4. This graph also shows decrease in the body weight in group 2 compared to the control group.

b) Brain Weight Changes

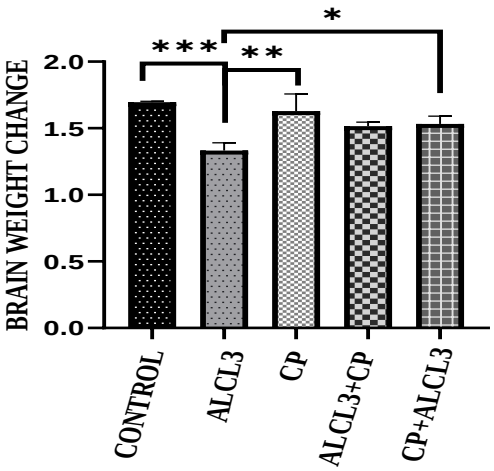


Fig 2: Graph showing Brain Weight Changes

This graph shows a decrease in the brain weight of the group exposed to aluminium chloride only (group 2) as opposed to the control group ($P \leq 0.01$). There were also noticeable differences between groups 2 and 3 and groups 2 and 5.

*B. Behavioural Analysis*

After administration of $AlCl_3$ to some groups, an open field test was carried out and the following parameters were the main focus

- Number of lines crossed
- Rearing frequency
- Stretched attend posture frequency

a) Open Field Test (OFT)

i. Number of lines crossed

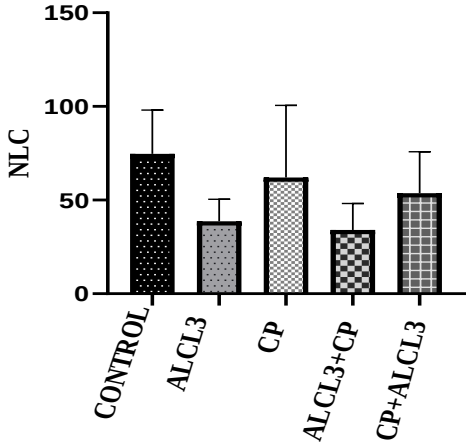


Fig 3: Graph showing Near Line Crossing

The graph shows there is no significant difference between the control group and the group exposed to aluminum.

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b) Rearing Frequency

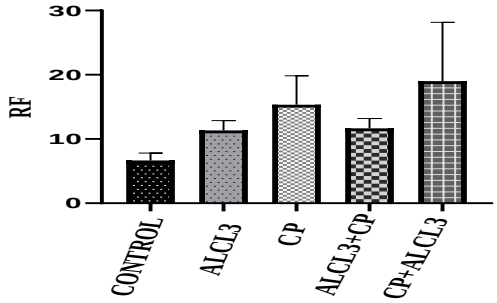


Fig. 4: Graph showing Rearing Frequency

The graph shows there is no significant difference between the control group and the group exposed to aluminum.

c) Stretched attend posture frequency

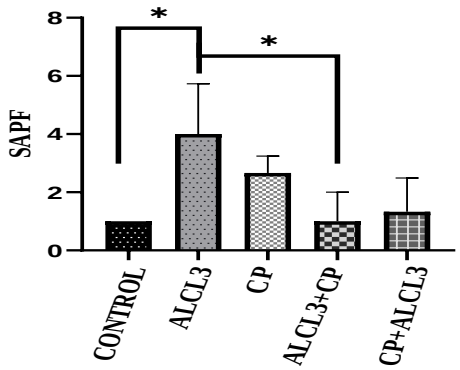


Fig 5: Graph showing Stretch Attend Posture Frequency

The graph shows a significant difference between the control group and aluminum chloride group. There is also a significant difference between group 2 and group 4.

- *Number of lines crossed:* The graph shows there is no significant difference between the control group and the group exposed to aluminum
- *Rearing Frequency:* The graph shows there is no significant difference between the control group and the group exposed to aluminum

d) Morris Water Maze (MWM)

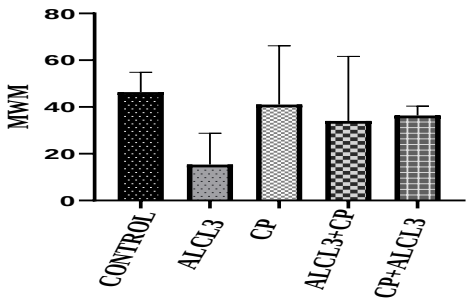


Fig 6: Graph Showing results from the Morris Water Maze test

The graph shows significant difference between the control group and the group exposed to aluminum.

*C. Biochemical Analysis*

a) AcetylCholinesterase (AChE) in PreFrontal Cortex

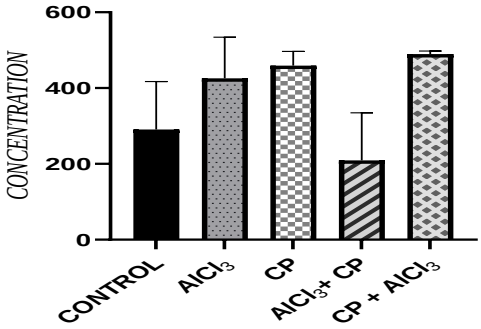


Fig 7: Graph of AcetylCholinesterase (AChE) in PreFrontal Cortex

There is a significant difference between the control group and the group administered with $AlCl_3$. There's also a significant difference between groups 4 and group 5 suggesting that CP is more neuroprotective than ameliorative.

b) Melondialdehyde (MDA) in PreFrontal Cortex

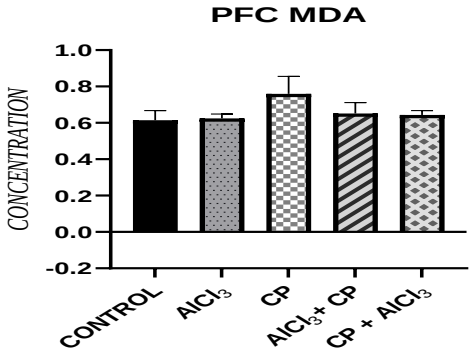


Fig 8: Graph of Melondialdehyde (MDA) in PreFrontal Cortex

MDA levels in the PFC are relatively the same across all the groups with the only difference being in the elevation of MDA levels in group 3.

c) Lactatedehydrogenase (LDH) in PreFrontal Cortex

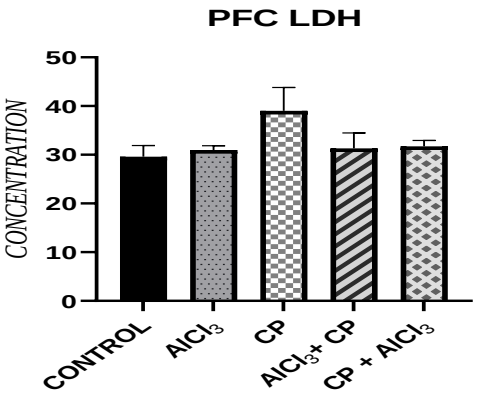


Fig 9: Graph of Lactate dehydrogenase (LDH) in PreFrontal Cortex

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There's slight elevation of LDH levels in the PFC across the board with the highest increase being from group 3 rats.

d) Glutathione (GSH) in PreFrontal Cortex

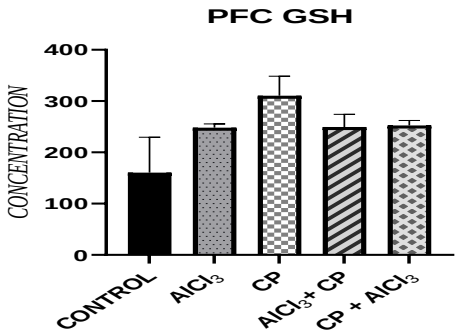


Fig 10: Graph of Glutathione (GH) in PreFrontal Cortex

This graph shows significant elevations in GSH levels across all groups when compared with the control. With group three rats having the highest levels of GSH.

e) Graph of Protein Carbonyl in PreFrontal Cortex

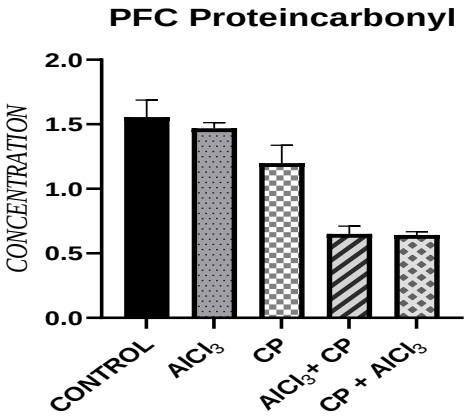


Fig 11: Graph of Proteincarbonyl in PreFrontal Cortex

This graph indicates a progressive decrease in protein carbonyl levels across the rats of all groups. It is highest in the control and the same in the last two groups.

*D. Qualitative Analysis*

a) Cresyl fast violet stain

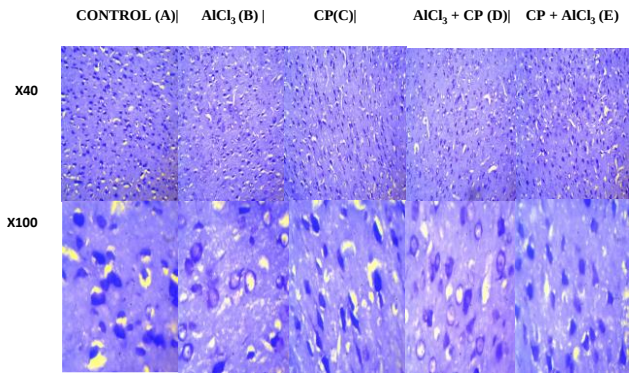


Fig. 12: Representative photomicrograph of a section of the frontal cortex extra pyramidal cell layer stained with Cresyl fast Violet Stain

At Mag. x40 and x100. The control (A) showed Nissl positive neurons without chromatolysis. B, which is the $AlCl_3$ showed the presence of chromatolysis and loss of Nissl substance. Group C (CP) treated group lacks chromatolysis with Nissl substance present. Group D ($AlCl_3$ + CP) showed degradation of Nissl substance made mild by the presence of CP indicating CP repairing damage. Group E (CP + $AlCl_3$) shows little to no chromatolysis showing the neuroprotective effect of CP.

Cresyl fast violet stain was used to demonstrate neuronal morphology and Nissl or Chromatophilic bodies' aggregation use to represent ribosomes of the rough endoplasmic Reticulum in the neuron's cytoplasm (Fig. 12). This histochemical demonstration in our study is used to explain for Nissl bodies as compared to Group B with chromatolysis in the neuropil as compared to group E with some neuron positive to Nissl stain within the neuron's cytoplasm.

b) Haematoxylin and Eosin stain

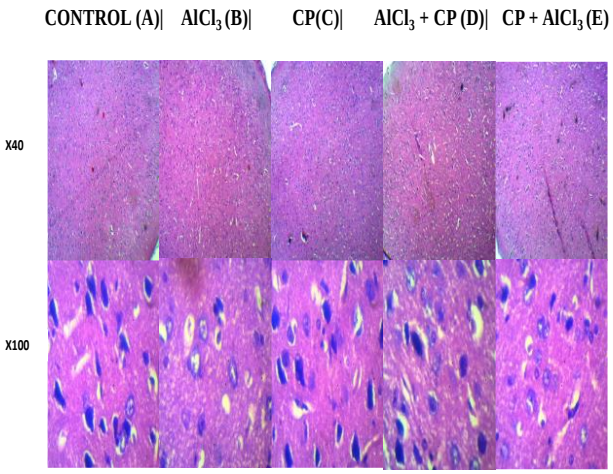


Fig 13: Representative Photomicrograph of the frontal cortex extra pyramidal cell layer showing the pyramidal cells of animal stained with Haematoxylin and EosinStain

Control shows well-pigmented neurons and intact neuropil, Aluminium (B) treated shows severe vacuolations, necrosis and pericellular spaces around the necrotic neurons and pyknotic neurons as compared to Control (A). $AlCl_3$ + CP shows few vacuolations and necrotic neurons in the neuropil with presence of few normal appearing neurons. The CP + $AlCl_3$ (Group E) shows regenerating neurons. The histomorphological appearance of Group A (Control) showed characteristically well-arranged pyramidal cells with apical and basal dendritic extensions. There are no signs of pyknosis or necrosis as compared to $ALCl_3$ treatment displaying necrotic/pyknotic cells. Comparatively, the CP treated group (C) has normal neuron appearance as compared to $ALCl_3$ + CP co-treated group (D) with few degenerated neurons. Group D shows self-repairing neuron, few necrotic cells and absence of vacuolation within the neuropil while Group E shows normal Pyramidal neurons indicating neuroprotection.

ISSN No:-2456-2165

In this present study, we use Haematoxylin and Eosin (H and E) stain to demonstrate histo-architecture of the frontal cortex with specific focus on the extra pyramidal cell layer (Fig. 13). The histological demonstration shows that the Control group (A) frontal cortex has intact neuropil with no vacuolations or pericellular spaces around the neurons. The neurons were well arranged with a central nucleus and its surrounding eosinophilic cytoplasm, as compared with the $ALCl_3$ treated group (B) with a lot of necrotic neurons having homogenous cytoplasmic contents, red neurons, necrotic neurons and pericellular spaces within the neuropil. CP treated group (C) shows normal extra pyramidal neurons and no neuronal disruption as compared to Group B. Group D shows the endogenous mechanism of neuronal restoration following the assault of $AlCl_3$. In the CP+$AlCl_3$ group (E) we observed protection of the neurons displayed by the few necroses, vacuolation in the neuropil and presence of some healthy morphological appearance of some of the pyramidal neurons as compared with Group B.

## XI. DISCUSSION

### A. Body and Brain Weight

Exposure to excess Al can have lethal effects on the brain, bone, liver, spleen, kidney, and ovary in humans and animals (5). Al has been shown to modify calcium (Ca2+) flux and homeostasis, and assist the peroxidation of membrane lipids. Lipid peroxidation is one of the consequences of free radical reactions which leads to cell membrane malfunction and damage (17). Aluminium induces neurodegeneration, through a boost in Fe accumulation and reactive oxygen species manufacture (18).

According to (19), there was about an 8% noticeable decrease in the net brain weight of the animals after oral administration of Al for three weeks. This phenomenon further corresponds with our results as there was weight loss in group 2 as opposed to the control group for both brain and body weight change. There was a body weight loss in group 4 which proved that *C. papaya* is neuroprotective.

### B. Behavioural Changes

Al acts as a powerful cholinotoxin by causing various neurochemical and neuroanatomical changes in the brain. Al contaminated dialysates such as Al phosphate binders can create progressive encephalopathy with severe behavioural deficits, including agitation, confusion, speech disorders, myoclonus, seizures and coma. This study shows no significant difference for OFT in NLC and RF whereas there is a significant difference ($P \leq 0.05$) in SAPF for OFT between groups 2 and the control group and groups 2 and 4. The MWM showed significant differences among the groups and taking a looking at the graph, group 2 showed that when animals are exposed to prolonged Al, it would result in cognitive delay.

### C. Acetylcholinesterase (AChE)

Acetylcholinesterase (AChE) is an enzyme in the brain which breaks down AChE into inactive metabolites choline and acetate, and thus the augmented activity of this enzyme can result in an AChE deficiency. Drugs (AChE inhibitors) were made on the grounds of cholinergic hypothesis of AD to be able to inhibit the actions of AchE and restore the required levels of AchE(20). The study showed that the in group 2 rats which were given aluminium had their AchE levels significantly increased ($P>0.05$) when compared with the control group. This result disagrees with(21) but agrees with (20) and (5).

### D. Melondialdehyde (MDA)

Quite a lot of studies have documented the susceptibility of cerebral tissues to oxidative stress. The current boost in lipid peroxidation confirms an increase in oxidative stress in the cortex, hippocampus, and striatum of $AlCl_3$-intoxicated rats (22).Augmented oxidative stress in the brain resulted in neurotoxic effects produced by Al which wasapparent from a distinctly increased in LPO in terms of MDA levels in the tested rats compared to those of the control group. Oxidative stress plays a vital role in $AlCl_3$ mediated neurotoxicity. Free radical generation has damaging effects on antioxidant enzymes and results in their inhibited actions. Distortion in activities of antioxidant enzymes will lead to brain damage and neurodegeneration through the commencement of peroxidation processes of the phospholipids in brain cells (5). This agrees with our study as Al-exposed rats had increased levels of MDA compared to the control group.

### E. Lactate Dehydrogenase (LDH)

Lactate dehydrogenase (LDH) is a tetrameric enzyme which catalyzes the reversible conversion of pyruvate to lactate, coupled with the oxidation of nicotinamide adenine dinucleotide dehydrogenase (NADH) to NAD+, in the final step of the glycolytic pathway. It is an important enzyme in the glycolytic pathway (23). Heightened LDH is deemed as a negative prognostic biomarker in many cancer cases and is directly associated with increased tumor growth and proliferative index, maintenance, metastasis, and tumor survival (23). In this study, there are no significant differences among the groups with the exception of rats administered with CP alone suggesting that CP increases LDH levels.

### F. Glutathione (GSH)

Glutathione (GSH) is a tri-peptide (γ-glutamylcysteinylglycine) which acts as a xenobiotic detoxifier and an endogenous antioxidant and is involved in metabolic regulation. GSH is the most common antioxidant in aerobic cells and is present in in millimolar (mM) concentrations in tissue and micromolar (µM) concentrations in bodily tissues (24).

The specific GSH content of the brain is dependent on the species investigated and varies between brain regions. Forebrain and cortex seem to have the highest GSH content, followed by cerebellum, hippocampus, striatum, and substantia nigra, whereas low GSH contents in the brain region include the brain stem, spinal cord, and the sciatic nerve (25). This study showed that the level of GSH was

increased in the animals that were given aluminium chloride when compared with the control group.

*G. Protein Carbonyl*

Protein Carbonyl (PC) is the most familiar type of carbonylated protein oxidation and it is composed of different oxidative mechanisms (26). It is a common protein modification mechanism and carbonyl derivatives can show in diverse ways: as a result of direct oxidation of the amino acid residues of lysine, arginine, proline and threonine, or underneath the action of reactive oxygen species, as well as in reactions with carbonyl-containing oxidized lipids (27).In this study the rats showed a decreasing level of protein carbonyl with control group possessing the normal levels of PC in the PFC.

## XII. CONCLUSION

This study, confirmed the morphological, behavioural, histological and biochemical distortion of the prefrontal cortex of $AlCl_3$ and CP treated Wistar rats for a period of 14 days. With consideration to the observed results of $AlCl_3$ oral administration, it can be concluded that $AlCl_3$ has harmful actions on the prefrontal cortex at 0.1g body weight. It can also be concluded that the leaf extract of CP possesses therapeutic potentials against $AlCl_3$ induced neurotoxicity in the PFC of female albino wistar rats. The therapeutic property of the extract, could be attributed to the antioxidant properties of its constituent phytochemicals, such as flavonoid, papain and chemopapain.

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