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AMELIORATIVE EFFECTS OF THE AQU0EOUS ROOT EXTRACTS OF *CURCUMA LONGA* (TURMERIC) ON LEAD ACETATE-INDUCED PREFRONTAL CORTEX TOXICITY IN ADULT FEMALE WISTAR RATS

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Abstract: **Background: The prefrontal cortex is an area of the brain in the frontal lobe of both cerebral hemispheres that is responsible for decision making, behavior and emotional control (Miller and Cohen, 2001). Exposure to Lead has been linked to neurotoxicity leading to diverse neurological disorders. There are increasing literatures showing medicinal use of *Curcuma longa* (turmeric), especially in neurological disorders. Aim: This study aims at exploring the ameliorative potency of the aqueous root extract of *Curcuma longa* (ARECL) on the histology of the prefrontal cortex following lead-acetate induced neurotoxicity. Methodology: Thirty (30) non-pregnant adult female wistar rats (150-200g) were divided into 6 groups of 5 rats each. Group A received only normal saline. Group B received 30mg/kg of lead acetate daily. Each of Groups C-E was all exposed to simultaneous administration of 30mg/kg of lead acetate and 100mg/kg, 300mg/kg and 500mg/kg of ARECL respectively daily. Group F received simultaneous administration of 30mg/kg of lead acetate and 100mg/kg of Vitamin E daily. All administrations were oral and the experiment lasted 24 days. The animals were sacrificed 24 hours after their last treatment via ketamin (100mg/ml) as anaesthesia. The brain was carefully harvested, washed in normal saline and fixed for 24 hours after which the prefrontal cortex was further harvested, fixed accordingly and processed for routine H&E staining. Results: Group B administered with only 30mg/kg of lead-acetate displayed pathologies such as vacuolated cytoplasm, widespread tissue edema and loss of neurons. Similar characteristics were noticed in animal groups C-D. Animal groups E-F displayed the normal histoarchitecture of the prefrontal cortex with no pathologies. Conclusion: The Aqueous root extract of *Curcuma longa* has ameliorative potency in the management of lead-induced neurotoxicity.**

Keywords: ***Curcuma longa*, lead acetate-induced toxicity, prefrontal cortex, wistar rats.**

1. INTRODUCTION

Neurotoxicity occurs when exposure to a substance; specifically a neurotoxin or neurotoxicant, alters the normal activity of the nervous system in such a way as to cause permanent or reversible damage to nervous tissue (Cunha-Oliveira, *et al*. 2008). Lead has the ability to pass through the blood-brain barrier and thus, has been linked to neurotoxicity. This action is largely due to its ability to substitute for calcium ions. Within the brain, lead can induce harm to the pre-frontal cerebral cortex, hippocampus and cerebellum leading to diverse neurological disorders such as behavioral problems, nerve damage, mental retardation (Lanphear, 2005).

Lead is one of the environmental pollutants that can threaten the lives of living creatures in various ways (Missoun *et al.*, 2010). Lead toxicity is probably the most common form of heavy metal intoxication. It is well documented as one of the most dangerous and insidious poisons (Mervat, 2012). The damage done by lead toxicity is dose and duration dependent (Landrigan, 1989).

Due to its wide range of use, children are more prone to getting this toxicity which affects the brain causing convulsions, coma and death (Kumar and Scott Clark, 2009; Lanphear, 2005). Small amount of lead is excreted in urine and the rest accumulates in various body tissues, mainly the Central Nervous System which may result in structural changes that can persist even after lowering of its blood level (Sidhu and Nehru, 2004; Taib *et al*., 2004; Flora *et al*., 2006; Ibrahim *et al*., 2012).

Diseases such as Alzheimer's disease, Parkinson's disease and schizophrenia are also linked to lead toxicity (Sanders, *et al.*, 2009). Those who survive the acute toxicity will have low IQ level, neuropathy, retarded neonatal growth, behavioral and mental problems (Lanphear, 2005; Nigg, 2008; Iavicoli, 2006).

Medicinal plants are globally considered to be a rich source of bioactive phytochemicals or bionutrients which can be used in drug development (Arvigo and Balick, 1993). This is why human beings have relied on natural products as a resource of drugs for thousands of years, (Pradeep and Sudipta 2013). *Curcuma longa* (turmeric) is a flowering plant of the ginger family; Zingiberaceae that is used in cooking. The record of use of turmeric in Indian traditional ayurvedic medicine for hundreds of years supports its possible therapeutic efficacy and its likely low toxicity (Huang, *et al*., 2016). It is a well-known indigenous herbal medicine and its major constituents, the yellow coloring matter curcumins and other curucinoids and essential oils major bioactive ingredients exhibited a wide range of biological activities (Sabale *et al*., 2013; Shiyou *et al.*, 2020). Aqueous extract of Tumeric is also found to possess antitumor (Deshpande *et al*., 1998), antidiabetic (Mohankumar *et al*., 2011), antimicrobial (Sunilson *et al*., 2009), hepatoprotective (Subramanian and Selvam, 1999), fertility enhancing (Mishra and Singh, 2009), antidepressant (Yu *et al*., 2002), antioxidant (Selvam *et al.*, 1995), antibacterial, and immunomodulatory activities (Yue *et al.*, 2010).

There is increasing literature showing medicinal activities of turmeric, especially in neurological disorders (Kulkarni and Dhir, 2010; Kim *et al*., 2012). It has been indicated by previous studies to soothe the activity of C6 glial cells monoamine oxidize (MAO), which plays a central role in numerous psychiatric and age-related neurological disorders, including clinical depression and Parkinson's disease (Madiha *et al*., 2018). Abdallah *et al.*, (2020), also suggested that Tumeric should be exploited as an adjuvant in the phytotherapeutic management of some substance-induced toxicity.

However, in its popularity and wide usage, there is paucity of information on its effects on the histology of the brain to back up claims of its use in neurological disorders. Also, its efficacy on neurotoxicity is minimally explored. Thus, this study aimed at exploring the ameliorative potency of the aqueous root extract of *Curcuma longa* (ARECL) on the histology of the prefrontal cortex after lead-acetate induced neurotoxicity.

2. MATERIALS AND METHODS

Plant Materials

Fresh roots of *Curcuma longa* were obtained from a reputable vendor at Ogbete main market Enugu. The roots were authenticated at the Faculty of Agricultural Science, Enugu State University of Science and Technology, Enugu.

Processing of Plant Materials

Newly procured roots were thoroughly washed under a running tap water, cut into smaller pieces and air dried under shade at room temperature for 14 days the dried roots were pulverized to fine powder and properly sieved. Aqueous extraction of the plant material was done according to the methods of Sengupta *et al.*, (2011). The extract was kept in airtight containers and stored in a refrigerator at 4°C until ready to use.

Experimental animals

30 healthy and non-pregnant adult female wistar rats with an average weight of 150g were procured from animal house facility of the University of Nigeria, Enugu campus. However, this study was carried out in the Animal facility of the Enugu State University of Science and Technology College of Medicine, Parklane, Enugu. The animals were kept in well ventilated breeding rooms and housed in netted iron cages. There were provided easy access to food (standard poultry mesh) and water and were also allowed to acclimatize for 2 weeks. The animals were maintained under standard laboratory conditions and handling was done following the guidelines of the college committee for purpose of control and supervision of experiments on animals.

Experimental design

The rats were grouped into 6 groups of 5 rats each, placed in separate cages within the Animal facility. All administrations were done orally with the use on oral gavages and the experiment lasted 24 days. Group A was the control group and was given normal saline till the end of the experiment. Group B served as the untreated positive control group and was administered 30mg/kg of lead acetate daily for 24 days. This dose was adopted from Saleh and Meligy, (2018). Group C-E were all exposed to 30mg/kg of lead acetate daily for 12 days and then received simultaneous administration of 10mg/kg of lead acetate and 100mg/kg, 300mg/kg and 500mg/kg of ARECL respectively daily for another 12 days. Group F received 30mg/kg of lead acetate daily for 12 days and then received simultaneous administration of 30mg/kg of lead acetate and 100mg/kg of Vitamin E daily for another 12 days. This dose of Vitamin E was also adopted from Saleh and Meligy, (2018).

Histological Study

The animals were sacrificed 24 hours after their last administration via cervical dislocation. The whole brain tissue was carefully harvested, washed in normal saline and fixed in labeled containers for 24 hours after which the prefrontal cortex of the cerebrum were further harvested and fixed accordingly in plastic containers for 72 hours prior to processing. The fixed tissues were processed using the standard protocols for histological tissue processing and stained accordingly with hematoxylin and eosin for histological studies. Photomicrographs of the organized slides were taken using Amscope 14MP USB 3.0 digital microscope camera at x100 magnification

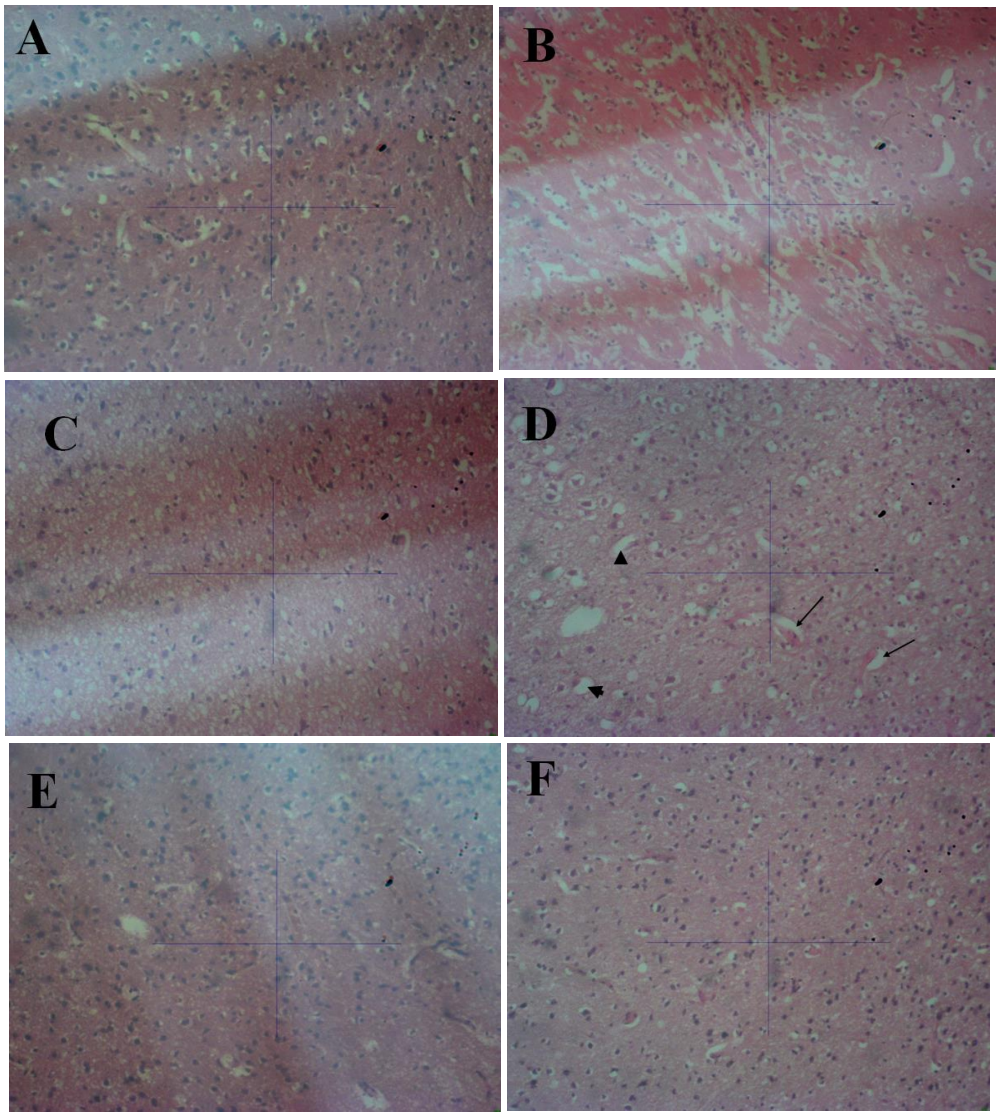

Fig 1: Photomicrograph of a section of the prefrontal cortex of the different animals ssgroups

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3. RESULTS

Histological Analysis

Group A: Photomicrograph of a section of the prefrontal cortex of the control animal group **fed with only food and water** showing the normal histoarchitecture of the prefrontal cortex of the cerebrum. Neurofibrilary network appears condensed and normal. Neurons of different categories and neuroglia appear normal. H&E.X100. **Group B:** Untreated animal group **administered only 30mg/kg of lead acetate** showing neurons with mild vacuolated cytoplasm, widespread tissue edema and loss of neurons. H&E. X100. **Group C:** Treatment with 100mg/kg of ARECL showing decreased cell population and widespread mild vacuolated cytoplasm. H&E. X100. **Group D:** Treatment with 300mg/kg of ARECL showing neurons with well developed vacuolated cytoplasm (Arrow heads) and shrinkage of neurons (Arrows). Neurofibrilary network appears normal. H&E. X100. **Group E:** Treatment with 500mg/kg of ARECL showing the normal histoarchitecture of the prefrontal cortex of the cerebrum. Neurofibrilary network appears condensed and normal. H&E. X100. **Group F:** Treatment with 100mg/kg of Vitamin E showing the normal histoarchitecture of the prefrontal cortex of the cerebrum. Neurofibrilary network appears condensed and normal. H&E. X100.

4. DISCUSSION

Detrimental effects of lead exposure on the nervous system of both animals and humans have been documented (Brenet, 2006). Sidhu and Nehru (2004), indicated that factors such as the integrity of the blood-brain barrier, lead-binding proteins and interactions with other micro-nutrients accounts for the neurotoxic effects of lead

From the observations of this study, the histology prefrontal cortex of the untreated animal group administered only 30mg/kg of lead acetate displayed pathologic changes such as the presence of mild vacuolated cytoplasm, widespread tissue edema and loss of neurons. These histological findings are similar to those reported by Saleh and Meligy, (2018), who reported that 30 mg/kg of lead acetate dissolved in distilled water and orally administered daily for two months led to shrinkage of cerebellar neurons with distorted shapes and their nuclei appearing irregular. These findings are in harmony with Engin (2006), who also testified that degeneration in the neurons was evident when rats consumed lead acetate in their drinking water for 60 days. Similarities in this histological finding were also reported by Amal and Mona (2009), Musa *et al.* (2012) and Fakunle *et al.* (2013). The pathologic changes in neurons reported in this study could be linked with the depletion of antioxidant reserves and generation of reactive oxygen species which is a common characteristic of lead exposure as it inactivates endogenous antioxidants by directly binding of its sulfhydryl group (Pajović *et al.*, 2003; Sanders *et al.*, 2009).

According to Saleh and Meligy (2018), vitamin E is the most essential lipophilic antioxidant which stays mainly in the mitochondria thus helping to sustain membrane stability. It decreases cell death which is due to free radicals. The ingestion of vitamin E gives a fortification against lipid peroxidation through its anti-oxidant activity (Serbecic and Beutelspacher, 2005).

The normal histological appearance of the prefrontal cortex of rats treated with vitamin E as observed in this study when weighed against the striking pathological alteration in the untreated group that received lead acetate alone is a potent indication of the anti-oxidant and the neuro-protective effects of vitamin E. Our findings agree with the findings of Saleh and Meligy, (2018), who recorded that animals treated with vitamin E after lead intoxication revealed marked improvement in the altered histological architecture of cerebellar cortex as the purkinje, molecular and the granular cell layers appeared almost normal. Our findings also correspond with Crouzin et al. (2010) who indicated that the pretreatment of hippocampal neurons of rats by vitamin E gave a lasting protection against oxidative damage.

From our findings, ARECL displayed a strong neuroprotective potential on the prefrontal cortex in lead-acetate induced neurotoxicity and had is similar healing effects as Vitamin E. This protective capacity was dose dependant as the animals treated with 500mg/kg displayed no pathologies present within the histology of the prefrontal cortex while animals treated with 300mg/kg and 100mg/kg respectively of ARECL still displayed pathological changes similar to the untreated group. This protective capacity could be attributed to the strong antioxidant activities of ARECL as it has been recorded to possess both antidepressant (Yu et al., 2002) and antioxidant activities (Selvam *et al.*, 1995).

Our findings corresponds with similar findings of Manal *et al.*, (2019), where Ethyl acetate extract of *Curcuma longa* rhizomes yielded high concentration of curcuminoids and exhibited anti-neurodegenerative, anti-oxidant, anti-inflammatory

and anti-apoptotic properties in rats' models Parkinson's Disease. They attributed their results to the role of curcuminoids as antioxidants, anti-inflammatory and anti-proliferative agents that inhibit the neurodegeneration features in Parkinson's disease. Similar findings were also recorded by *Zahra et al.*, (2012), where she reported that 50 mg/kg of Curcumin was injected intraperitoneally once daily for a period of 10 days was considered as a therapeutic agent prevention and treatment of homocysteine rat model of Parkinson's disease.

5. CONCLUSION

This study aimed at exploring the ameliorative potency of the aqueous root extract of *Curcuma longa* (ARECL) on the histology of the prefrontal cortex after lead-acetate induced neurotoxicity. ARECL displayed a strong dose dependant neuroprotective potential on the prefrontal cortex in lead-acetate induced neurotoxicity and had similar healing effects as Vitamin E. Thus, this study supports the claims of the use of *Curcuma longa* in the management of neurological disorders. Therefore, ARECL could be considered as a promising agent against the management neurological disorders that may arise as a result of lead exposure.

CONSENT

It is not applicable

ETHICAL APPROVAL

Ethical clearance was obtained from the Research and Ethical Clearance Committee, Faculty of Basic Medical Sciences, College of Medicine, Enugu State University of Science and Technology with ethical clearance code; ESUCOM/FBMS/ ETR/2021/018.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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