

### ABSTRACT

The neuro-behavioural responses to luffa aergyptiaca mill on mefloquine-induced seizure was investigated in rats. Thirty (30) Albino Wistar rats Weighing (190-250g) were randomly assigned into 5 groups with five rats in each group. Group one was control. Group two was induced with mefloquine only (4.28mg/kg). Group three were Induced with mefloquine (4.28mg/kg) & treated with diazepam (5ml/kg). Group four were Induced (4.28kg/kg) with mefloquine & treated with low dose luffa aergyptiaca mill (400mg/kg). Group five were Induced with mefloquine (4.28mg/kg) & treated with high dose luffa aergyptiaca mill (1200mg/kg). Doses of mefloquine and aqueous luffa aergyptiaca mill leaf extract were administered to the adult Wistar rats according to their individual body weight. After thirty (30) minutes of administration, the rat was placed subsequently in the center platform of the maze then observed for five (5) minutes. Open arm entries, closed arm entries, time spent in open arm, time spent in closed arm, grooming and frequency of rearing were recorded with a video camera. Precaution was taken to ensure that no external stimulus evokes anxiety in the rat. From the experiment, it was observed that control only has a steady task performance, mefloquine only has low entry into open arm indicating high level of anxiety, while mefloquine plus high dose luffa aergyptiaca mill has high entry into open arm indicating decreased in anxiety 0.05 is significant for open arm entry. It is observed that there was no significant difference activity, hence P across the groups in time spent in closed. There was significant difference for time spent in open arm. Mefloquine plus high dose luffa aergyptiaca mill has the highest time spent in open arm indicating decreased anxiety while mefloquine only has the lowest indicating increase in anxiety, hence P 0.05 is significant. Grooming was high in mefloquine only compared to control and treated groups. There was significant different between control and mefloquine plus high dose luffa aergyptiaca mill for frequency of rearing. The results suggest that aqueous extract of leaf of luffa aergyptiaca mill causes neurobehavioral responses in rats.

Keywords: Nuero-behavioural, Luffa Aergyptiaca Mill, Aqueous Extract, Mefloquine, Seizure, Elevated Plus Maze

### **INTRODUCTION**

There are millions of Africans who have preference for traditional methods of treating diseases<sup>1</sup>. Increased usage, less or no toxic effect of some plant makes them more valuable than others<sup>2</sup>. Even though, the use of medicinal plants is sometimes associated with superstition, and consequently rejected by some people in favour of western medicine<sup>1</sup>. The increasing dependence on the use of medicinal plants in the industrialized societies has been traced to the extraction and developments of several drugs and chemotherapeutics from plants as well as from traditionally used herbal remedies. This practice has gained more grounds because of the ready availability of plants, the insignificant cost of preparation and the new crave to avoid the side effects of chemotherapy<sup>2</sup>. Anxiety is an unpleasant state of inner turmoil, often

accompanied by nervous behavior<sup>3</sup>. Anxiety is not the same as fear <sup>4</sup>. It is often accompanied by muscular lesion, restlessness, fatigue, and problems in concentration<sup>5</sup>. Anxiety related disorders such as panic, phobias, obsessive-compulsion and post-traumatic stress are the most common mental illness and major cause of disability in the world<sup>6</sup>.

Synthetic anxiolytic drugs such as benzodiazepines (BDZ), barbiturates, buspirone(BUSP) and tricyclic antidepressants(TCA's) are considered as the main category of compounds prescribed for treatment of anxiety disorder. Unfortunately, they have several side effects such as rebound insomnia, tolerance, amnesia, weakness, loss of sexual drive, gastrointestinal effects and changes in body weight, sedation, muscle relaxation and physical dependence, which lead

patients to seek alternative therapies. In an attempt to resolve these issues, an interest has increased in alternative plant –related drugs. Many of the traditional plant secondary metabolites are being used for the treatment of psychotic disorders especially for anxiety, most of which directly or indirectly affects the central nervous system, noradrenaline, serotonin, GABA and BDZ<sup>7</sup>.

Defensive behaviours are innate and unconditioned reactions of an organism towards actual or potential threats<sup>8</sup>. Anxiety, fear and stress are behavioural outcome of the activation of CNS defensive system<sup>9</sup>. Rodent becomes defensive when placed in a strange place<sup>10</sup>.

Antimalarial drug mefloquine disrupts central autonomic and respiratory control in the working heart brainstem preparation of wistar rat<sup>11,12,13</sup>.

Elevated plus maze is an apparatus used to student exporatory and locomotive activity in rodent<sup>14</sup>. Total number of arm entries and number of closed-arm entries were used as measures of general activity<sup>15</sup>.

*Luffa aergyptiaca mill* commonly known as sponge guard has several medicinal values. The fruit, seed, leaves and root have all been used to treat several diseases. The plant belong to the family curcubitaceae, genus; Luffa and species; aegyptiaca mill.

It is an annual climbing crop which produces fruit containing fibrous vascular system. It is a summer season vegetable.

The leaf of Luffa Aergyptiaca mill has been used traditionally in Ogoni, Rivers State, Nigeria to treat anxiety and convulsion. There have been claims that luffa aegyptiaca leaf extract influences behavioural patterns, but this has not been fully evaluated. However this research and experiment is centered on investigating, analyzing and evaluating the effects of this plant on neuro-behavioural patterns in albino Wistar rat.

### **MATERIALS AND METHODS**

**Plant Material-** The leaves of *Luffa aergypltica mill* was collected from several plants in Khana Local Government Area of Rivers State in the month of June 2014. This plant *Luffa aergyptica mill* was identified by a Herbarium in the department of Plant Science, University of Port Harcourt, Choba Nigeria.

**Ethical Clearance**-Ethical clearance was obtained from the School of Post Graduate Studies, University of Port Harcourt, Choba, Rivers State, Nigeria. All procedures involving the use of animals in this study were done in accordance with the guiding principles for research involving animals as recommended by The Research Ethics Committee of the University of Port Harcourt.

#### **Extraction and Photochemical Streaming**

The aqueous crude extract (1g) was completely dissolved in 100 ml of distilled water. It was prepared with the stock solution. The obtained stock solution was used for the phytochemical screening following stardard qualitative methodology of Sofora<sup>16,</sup> and Harborne<sup>17</sup>.

#### **Elevated Plus Maze**

The elevated plus maze (EPM) is a rodent model of anxiety that is used as a screening test for putative anxiolytic or anxiogenic compounds and as a general research tool in neuro-behavioural anxiety research. The elevated plus maze(EPM) apparatus consist of wood and brownishly painted 2 open arm (40 x 10 cm) and 2 closed arms (40 x 10 x 20 cm). They were arranged perpendicularly to each other with a small central square  $(10 \times 10 \text{ cm})$  between arms. Both arms have open roof which was raised up to 50cm from the ground. The model is based on rodents' aversion of open spaces. This aversion leads to the behavior termed thigmotaxis, which involves avoidance of open areas by confining movements to enclosed spaces or to the edges of a bounded space. In EPM this translates into a restriction of movement to the enclosed arms. Anxiety reduction in the plus-maze is indicated by an increase in the proportion of time spent in the open arms (time in open arms/total time in open or closed arms), and an increase in the proportion of entries into the open arms (entries into open arms/total entries into open or closed arms). Total number of arm entries and number of closed-arm entries were used as measures of general activity<sup>15</sup>.

#### Procedure

After administration of drugs and extracts, rats were placed into the central space of the maze and allowed to explore the apparatus facing either side of the arms indiscriminately then observed for five minutes. An entry into an arm was noted when the rat with its four paws crosses the demarcation of respective arm. The time spent in open and enclosed arms and numbers of open and enclosed arms entries, grooming rearing were recorded with a video camera; and every precaution were taken to ensure that no external stimulus evokes anxiety in the rat. After each test, the maze was carefully cleaned up with a wet tissue paper (70% ethanol solution) to eliminate the interference of the olfactory cues on the next rat.

### RESULTS

The charts below show the neuro-behavioural response of animals (wistar rats) to luffa aegyptiaca mill extract using elevated plus maze method.

From the experiment, it was observed that the group administered with mefloquine only, has low entry into open arm indicating high level of anxiety, while M+DHL has high entry into open arm indicating decreased in anxiety activity, hence P 0.05 is significant for open arm entry. From the above chart, it is seen that there was no significant difference across the groups in time spent in closed arm. There was significant difference for time spent in open arm. M+HDL has the highest time spent in open arm indicating decreased anxiety while mefloquine only has the lowest indicating increase in



anxiety; hence P 0.05 is significant.

Grooming was high in mefloquine only compared to control and treated groups. There was significant different between control and M+HDL for frequency of rearing.



Figure.1. Showing open arm entries, closed arm entries, time spent in open arm, time spent in closed arm, grooming, frequency of rearing.

Group

KEY M+D-1

M+D= Mefloquine + Diazapam M+LDL= Mefloquine + Low Dose of Luffa aergyptiaca mill M+HDL= Mefloquine + High Dose of Luffa aergyptiaca mill.

# DISCUSSION

Several studies have shown that traditional medicinal plants have been recognized for the treatment of central nervous system(CNS), these plants such as *luffa aergyptiacamill* which this study is focused could serve as source of effective medication that maybe more readily accessible and inexpensive and hence would be helpful in improving anxiety.

A research was conducted on anxiolytic and anticonvulsant activity of methanol extract of leaves of alternantherabrasiliana (L.) kuntze (Amaranthaceae) in laboratory animals and the result obtained is similar to our resuts<sup>18</sup>.

Another research carried out showed the anxiolytic effect of Equisetum arvense Linn. extract in mice<sup>19</sup>. Their findings show that the extract has anxioytic effect which is in line with our findings. Remington<sup>20</sup> also carried out work on epileptogenic potential of mefloquine chemoprophylaxis: a pathogenic hypothesis.

Investigation by Edvaldo Rodriques de Almeida et al.<sup>21</sup> came up with a report on the evaluation of the anticonvulsant and anxiolytic effect of *Artemisia vulgaris* through the methanol extract of its leaves using Swiss albino mice. The anxiolytic activity was also observed using the EPM.

Sampath et. al.<sup>22</sup> carried out a research on the anxiolytic effect of ethanolic extract of oxalis corniculata L in mice.

Geoffrey et. al.,<sup>23</sup> studies have demonstrated that gerbils exhibit an anxiety–like profile on an elevated plus-maze, and that the gerbil elevated plus-maze may have predictive validity for anxiolytic, and antidepressants with potential anxiolytic-like effects.

Lin et al.,<sup>24</sup> investigated the anxiogenic-like and anxiolytic-like effects of MDMA (3,4methylenedioxymethamphetamine) on mice in the elevated plus maze, in comparison with amphetamine; They were able to report the drug's action by using an animal model of anxiety, the elevated plus maze test in male mice.

Increments in the number of entries or in the time spent by albino wistar rats in the plus-maze open arms commonly indicate the presence of decreased levels of anxiety<sup>14</sup>.

Defensive behaviours are innate and unconditioned reactions of an organism towards actual or potential threats<sup>8.</sup>

Anxiety, fear and stress are behavioural outcome of the activation of CNS defensive system<sup>9</sup>.

Rodent becomes defensive when placed in a strange place<sup>10</sup>.

However, from the analysis and study above, it is

clearly understood that mefloquine, diazepam and aqueous luffa extract has neurological effects in their respective mechanism of action as regards to anxiolytic like responses.

# CONCLUSION

From the analysis, it is clear that mefloquine, diazepam and aqueous luffa extract has neurological effects, resulting in neuro-behavioural responses in rat. It also shows that aqueous leaf extract of luffa aergyptiaca mill have anxiolytic properties at theraupeutically acceptable doses. This effect may be due to the interaction of the extract with chemical mediators in the brain e.g Gamma Aminobutyric Acid (GABA) which are responsible for the anxiety-like behavior. The extract has proven to be a good anxiolytic agent in treating anxiety. Further pharmacological researchs are ongoing to identify and isolate the active constituents of the aqueous leaf extract of *Luffa aegyptiaca mill* plant responsive for this anxiolytic activities.

## ACKNOWLEDGEMENT

We would like to express our gratitude to the International Society for Neurochemistry (ISN) for funding Lekpa Kingdom David on a Research visit to the University of the Witwatersrand, Johannesburg, South Africa and to Prof. Amadi Ihunwo for hosting him. We also thank the Faculty of Pharmaceutical Sciences, University of Port Harcourt, for their technical assistance and for the welfare of the animals.

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