histology. There were four groups of mice (n = 6) treated intraperitoneally with - distilled water; insulin (10 I.U./kg/day); insulin (10 I.U./kg/day) + $N^{\omega}$-nitro-L-arginine methyl ester hydrochloride (L-NAME) (50 mg/kg); and L-NAME (50 mg/kg). Learning and memory were assessed using novel object recognition test at the end of the seven-day treatment. Concentrations of NO, MDA, as well as GPx activity were determined in brain homogenates using assay kits. Histological examination of cerebellar cortex was also conducted. Numerical values were compared using ANOVA or r-ANOVA on IBM SPSS Statistics version 20.0. Ethical approval for the study was provided by the Animals Research Ethics Committee of Ahmadu Bello University, Zaria, Nigeria.Insulin treatment resulted in higher levels of NO compared to controls ($p < 0.05$). The increased NO level was associated with increased MDA concentration, decreased GPx activity and impaired memory in the treated animals. The increased oxidative stress was reversed by L-NAME treatment. Brain slides appeared normal and showed no indication of histopathological changes. The insulin-induced increase in NO level observed inthis study was associated with memory impairmentwhich corroborates the findings of other studies thatdemonstrated impairment in spatial learning andmemory using Morris water maze. As shown by previous studies, the effect of exogenous insulin on memory variesaccording to the duration of the treatment, withimprovement observed during acute exposure, andimpairment reported during chronic exposure. This study has demonstrated memory impairment following a sub-acuteexposure. The findings of this study show that insulin maypotentially damage the brain by inducing oxidativestress. As reported previously in other studies, exposure of the brainto high doses of insulin may negatively affectcognitive signalling pathways. NO-dependent oxidative stress is hereby proposed as themechanism of insulin-induced memory impairment. The increase in NO levels was reversed by L-NAME,a non-selective nitric oxide synthase (NOS)inhibitor, which was used in this study to create NOdeficiency. With the increase in NO concentration, there was also an increase in oxidative stress in thebrain of the animals as evidenced by depletion ofMDA and reduced activity of GPx.Even though previous studies have reported insulin-induced increase in brain MDA levels and decreased GPx activity in animals, the present study has provided evidence, in addition to the findings in these studies, that there is a concurrent insulin-induced increase in the brain NO in the animals. Normal histology of the cortex was observed in the control and all the treated animals. Thisfinding indicates that insulin did not causesignificant damage to the cortex detectable byhistological examination. The finding disagree with thesignificant changes reported in this study at themolecular (NO, MDA and GPx) as well as thesystemic (learning and memory) levels. The absence of histological changes (which could be due to relatively short duration of treatment), however, does not exclude changes at thecellular levels such as apoptosis (not investigated in this study), which could bedetectable using the appropriate laboratory methods. Our data has led to the conclusion that insulin treatment causes an NO-dependent increase in oxidative stress in the brain; and that insulin impairs non-spatial working memory but does not affect brain histology in the treated mice. Insulin treatment may have negative consequences on the brain through increased NO levels.

Keywords: Nitric oxide, Oxidative stress, Learning and Memory, Brain histology, Malondialdehyde, Glutathione peroxidase.

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**E2**

## The antidepressant effects of *albizia zygia* root extract in mice are mediated via catecholaminergic mechanisms

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There is a pressing need for novel medicines to better manage neuropsychiatric disorders such as depression since current options are limited by suboptimal efficacy, disabling side effects and low availability in certain regions. The roots of *Albizia zygia* (DC.) J.F. Macbr. (Leguminosae) are used to treat mental disorders in traditional African medicine. Nonetheless, there is limited scientific evidence to justify its use at present. Therefore, this study was designed to evaluate the antidepressant-like properties of the hydroethanolic root extract of *Albizia zygia* (AZE) in murine models for antidepressants. The extract was prepared from freshly harvested roots of *Albizia zygia* collected in Kumasi, Ghana (6°40′31.8″N 1°34′44.1″W). After authentication, the roots were cleaned, air-dried and milled into a coarse powder which was extracted by maceration (27-28 °C) in 70% (v/v) ethanol for 5 days. The supernatant was filtered, concentrated in a rotary evaporator (60 °C) and dried to yield a brown-coloured extract (9.03% w/w yield) which was stored at 2-8 °C until use. In order to assess the antidepressant activity of AZE, several tests were carried out. First, the antidepressant activity of AZE was evaluated in acute depression models: the forced swim test and tail suspension test, and a chronic model, the open space swim test. Next, the mechanisms involved in the observed antidepressant actions of AZE were investigated by selective depletion of various neurotransmitters using $\alpha$-methyl-*para*-tyrosine (an inhibitor of catecholamine synthesis), *para*-chlorophenylalanine (an inhibitor of serotonin synthesis) and reserpine (an inhibitor of vesicular monoamine storage). Lastly, the effect of AZE on spontaneous locomotion was assessed in the open field test. Ethical approval for this study was obtained from the Department of Pharmacology Ethics Committee, Kwame Nkrumah University of Science and Technology.AZE (100-1000 mg $kg^{-1}$, *p.o.*) reduced immobility in the forced swim and tail suspension tests (at least $P < 0.05$) similar to the control antidepressants, imipramine and fluoxetine. Alsoin the open space swim test, AZE (100-1000 mg $kg^{-1}$, *p.o.*) reduced immobility (at least $P < 0.05$) while concomitantly increasing distance swum ($P < 0.01$). This suggests a significant antidepressant effect of AZE since a reduction in immobility is predictive of antidepressant activity. Furthermore, no significant increase in spontaneous locomotion was detected in AZE-treated mice, thus ruling out a psychostimulatory effect which could yield false positive results. Similar to imipramine, the antidepressant effects of AZE were abolished by $\alpha$-methyl-*para*-tyrosine and reserpine pretreatment. However, unlike fluoxetine, the antidepressant effects of AZE persisted after *para*-chlorophenylalanine pretreatment. This finding supports the involvement of catecholaminergic rather than serotonergic mechanisms in the antidepressant actions of AZE.In summary, the results obtained indicate that the hydroethanolic root extract of *Albizia zygia* possesses antidepressant-like properties which are likely mediated via catecholaminergic mechanisms and support its traditional use in the treatment of depression.

Keywords: Forced swim, Tail suspension, Open space swim, Reserpinea-methyl-para-tyrosine

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**E3**

## Assessment of anxiolytic potential and acute toxicity study of combretum micranthum g. don. leaves (combretaceae) in mice

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The use of herbs has evolved as the most common form of traditional, complementary and/or alternative medicine therapies included in the management of anxiety disorders. This could possibly be due to their relative safety, widespread availability, cost effectiveness, ease of administration, cultural acceptability, systemic tolerability, and compliance. Anxiety disorders are the most widely recognized type of mental disorders worldwide and affect nearly 30 percent of adults at some point in their lives. *Combretum micranthum* is an ethnomedicinally valuable, undomesticated, and indigenous shrub to West Africa. It is commonly called 'kinkileba' with local names as; *ògàn bul?* (Yoruba), and *farar geézaà* in Hausa. Anxiolytic potentials of the ethanolic leaf extract of *Combretum micranthum* (*Cm*EE) has not been reported, despite its being used traditionally to treat anxiety disorders, hence this study. The leaves of *Combretum micranthum*were collected around Idofian town in Kwara state. It was authenticated at the Department of Plant biology, University of Ilorin, Ilorin and a sample was deposited at the herbarium. Ethical approval was obtained from the University of Ilorin Ethical Review Committee (UERC/ASN/2019/1604). *Combretum micranthum* Ethanolic Extract (*Cm*EE) was prepared and the $LD_{50}$ was determined using Organization for Economic Cooperation and Development (OECD) guideline. Mice (18 - 25 g, n = 5) were randomly selected into groups and treated as follows: Group I-III orally received CmEE (500, 1000, and 2000 mg/kg) respectively while Group IV and V were respectively administered diazepam 1 mg/kg and normal saline 0.5 ml intraperitoneally and thereafter subjected to Open Field Test. The treatment pattern was repeated for mice used in the elevated plus maze (EPM) procedure. Data were expressed as ± Standard Error of Mean (S.E.M) and statistically analyzed using Students-t test, and one way analysis of variance (ANOVA) followed by Student-Newman Keuls (SNK) test with $P < 0.05$ considered significant. The percentage yield of the ethanolic leaf extract of *Bryophyllum pinnatum* was 14.28% w/w.*Cm*EE displayed very low toxicity for oral administration in mice at $LD_{50} \geq 2000$ mg/kg. *Cm*EE at 500, 1000, and 2000 mg/kg exhibited decreased locomotion $P < 0.05$ in mice when compared to the saline group. Significant decrease in rearing but nonetheless, increase in grooming indices (though not significant) was observed in mice administered2000 mg/kg when compared to the saline group. There was a noticeable decrease in the index of open arm avoidance though not significant, suggestive of an aversion that can be interpreted as an anxiolytic effect. Assessment of the behavioural and anxiolytic effects of *Cm*EE showed that it is a non-toxic herbal preparation and preliminary information about CNS activity wereprovided. However, it is recommended that specific models of anxiety should be employed while considering other methods of extraction such as aqueous or aqueous ethanol.

**Keywords**: *Combretum micranthum*, Elevated plus maze, Open field test, Open arm avoidance index.

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**E4**

## Effects of acetone extract of *cola nitida* on memory and metabotropic glutamate receptor1a (mGlutR1a) in female wistar rats

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*Cola nitida* is the seed of the Kola tree commonly grown in the tropical rainforest of Africa. It is popularly known for its adopted sociocultural use and active contents which include caffeine and theobromine. It is also consumed for its beneficial use such as enhancing metabolism, increasing heart rate and improving cognition. The aim of this study is to investigate the effects of Acetone extract of *Cola nitida* on memory, plasma aspartate aminotransferase activity, mGlutR1a and body weight in female Wistar rats.

Fifteen (15) female Wistar rats were used and grouped into three (3). Control group (1.2 ml normal saline (po)), low dose group (50 mg/kg extract (po)) and high dose group (100 mg/kg extract (po)).

Body weight of animals was monitored throughout the experiment. Memory was evaluated using Morris water maze and Y-maze. Time spent probing the new object was also evaluated for cognition by novel object recognition test. Plasma aspartate aminotransferase activity and lactate dehydrogenase activity was also estimated. Immunohistochemistry was finally conducted for mGlutR1a.

There was significant ($p < 0.05$) decrease in body weight of animals administered the extract compared to control. There was also significant ($p < 0.05$) decrease in time spent to locate the hidden platform in Morris water test of animals administered high dose extract when compared to control. There was no significant difference in percent alternation between the groups in Y-maze test. There was a significant ($p < 0.05$) increase in time spent with novel object recognition test in animals administered low dose extract compared to control. Plasma aspartate aminotransferase activity was significantly increased in low dose extract group compared to control and no change was observed for lactate dehydrogenase activity. Enhanced stimulation of mGlutR1a was observed from immunohistochemical analysis of the rat brain compared to control.

This study revealed that *Cola nitida* enhanced memory and stimulates glutamate receptors in hippocampus and amygdala.

**Keywords**: Acetone, *Cola nitida*, Memory, Receptors, Hippocampus.

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