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Moringa oleifera (Lam) Root Extracts Elevate Catecholamine Levels in Experimental Rats: Potential Role of Ethnopharmacology in Combating Depressive Conditions

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Abstract

Rising cases of neurodegenerative disorders negatively impact human and economic resources of the globe, hence the need to search for safe, affordable, and effective psychotherapeutic interventions. In the present study, the effect of extracts from roots of *Moringa oleifera* (*M. oleifera*) on norepinephrine and epinephrine levels in brain and serum of seemingly healthy rats was investigated.

Fresh roots of *M. oleifera* were collected, dried, ground and subjected to aqueous, methanol and diethyl-ether extractions. Median lethal dose (LD_{50}) of *M. oleifera* aqueous root extract was determined. Animal experimental groups received 100- and -200 mg/kg body weights of the different root extracts of *M. oleifera*. The animals were sacrificed after anesthesia on the eleventh day, ~~and~~ blood and brain samples were taken and tested for total proteins and catecholamines. All data were analysed using one-way-analysis of variance and Tukey tests. Value less than 0.05 was considered for statistical significance.

High doses of aqueous, methanol, and diethyl ether root extracts of *M. oleifera* significantly ($p<0.05$) reduced brain total protein concentration. Level of serum epinephrine was not significantly ($p>0.05$) altered by the aqueous, methanol and diethyl-ether root extracts, whilst brain epinephrine concentration was significantly ($p<0.05$) raised by the diethyl-ether root extract. Norepinephrine levels in the brains and serum of rats that appeared to be in good condition were only marginally elevated by high and low dosages of the plant's aqueous and methanol root extracts, but they were markedly elevated ($p<0.05$) by both doses of the di-ethyl-ether extract.

The present study reveals that di-ethyl-ether root extract of *M. oleifera* can dose dependently alter norepinephrine and epinephrine levels in brain and serum of apparently healthy rats. Consequently, it is crucial to investigate the mechanism by which the administration of di-ethyl-ether root extract of the plant to animals modulate catecholamine production.

KeyWords: Root-extracts, *M. oleifera*, Brain, Epinephrine and Norepinephrine

1. Introduction

Neurodegenerative diseases (NDs) and depressive disorders (DDs) are heterogeneous groups of disorders characterized by progressive deterioration of structures and functions of central and peripheral nervous systems (Harris *et al*., 2014; Dawson *et al*., 2018). NDs and DDs are life threatening clinical conditions affecting humans worldwide (Solomon, 2019). Cases of depression are alarmingly rising because of pandemic and insecurity challenges bedeviling the globe (Dadi *et al.*, 2020). Recent reports have shown that DDs manifest in patients with other underlying medical conditions (Almeida *et al*., 2017; Alexopoulos, 2019). A number of medical conditions, such as Parkinson's disease, seizures, and Alzheimer's disease, have been linked to depressive symptoms (Solomon, 2019; Hussain *et al*., 2020). The unpleasant symptoms of the diseases reveal a complex pathological state that develops in later life, when chronic inflammation and oxidative stress cause proteins to change, leading to eventual malfunction (Crocco *et al*., 2010).

In the central nervous system (CNS), NDs and DDs are frequently restricted to particular cells, such as dopaminergic neurons in Parkinson's disease or hippocampal neurons in Alzheimer's disease (Leonelli *et al*., 2009; Cassano *et al*., 2017). Reports have shown that DDs linked to NDs can conveniently be studied by targeting active structures within the CNS (Cai *et al*., 2016; Pinto-almazán *et al*., 2022). The pathophysiology of DDs and NDs is not clearly understood, but some studies have associated malfunctioning of adrenergic neurotransmitters to increased incidence of the diseases. DDs and NDs have been shown to involve mechanisms of neuro-inflammation and aggregation/deposition of misfolded proteins, which are presumably the cause of progressive CNS diseases (Sweeney *et al*., 2017; Hussain *et al.*, 2020).

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Catecholamines are a class of biogenic amines that are produced from the precursor L-tyrosine. Norepinephrine (also called noradrenalin), epinephrine (also called adrenalin), dopamine, and L-dopa serve as neurotransmitters in the brain and as hormones in the muscles, respectively. It has been reported that catecholamine levels are dysregulated in illnesses such as Parkinson's disease, bronchial asthma, hypertension, and some conditions leading to heart surgery (Qureshi, 2019). L-tyrosine is primarily converted to L-noradrenaline in the sympathetic nervous system and some parts of the brain. Changes in serum catecholamine levels have recently been utilized to diagnose a number of medical problems (Goldstein *et al*., 2018).

For ages, several Asian and African nations have used the edible plant *Moringa oleifera*, a member of the *Moringaceae* family, for both food and medicinal purpose. Potassium, calcium, phosphorus, iron, vitamins A and D, vital amino acids, antioxidants including beta-carotene, vitamin C, and flavonoids have all been shown to be abundant in this plant's leaves (Abd-alwahab, 2018). Alkaloids, tannins, phenolics, saponins, and steroids are additional antinutrients that were found (Bisong *et al*., 2019). Zeatin, quercetin, β- sitosterol, caffeoylquinic acid, and kaempferol are abundantly and commonly found in the Moringa plant (Milla *et al*., 2021). As cardiac and circulatory stimulants, they also have antitumor, antipyretic, antiepileptic, anti-inflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol-lowering, antidiabetic, hepatoprotective, antibacterial, and antifungal properties. Various parts of this plant, including the leaves, roots, seed, bark, fruit, flowers, and immature pods, are used for the treatment of various illnesses (Hodas *et al*., 2021). It has been shown in previous studies that several parts of plants possess neuroprotective and antidepressant activities (Es-Safi *et al.*, 2021). The antidepressant activity of *M. oleifera* leaf extract was recently reported in experimental animals (Yunusa and Musa, 2018). In an effort to search for potential neuroprotective properties of *M. oleifera* root extracts, the levels of norepinephrine and epinephrine in the brain and serum of apparently healthy rats were currently examined.

2. Materials and methods

2.1. Chemicals and reagents

Every chemical and reagent utilized in this study was of the analytical grade. The following items were obtained from Sigma Aldrich: Bovine serum albumin (BSA), Copper sulphate (CuSO4), Potassium iodide (KI), Sodium potassium tartarate (NaK-tartarate), Silver nitrate (AgNO3), Polyvinylpyrrolidone (PVP), Sodium hydroxide (NaOH), Epinephrine, and Norepinephrine.

2.2. Collection of plant

M. oleifera's fresh roots were harvested from its native environment in Nigeria's Chikaji, Sabon-Gari, Zaria, and Kaduna. Mr. Namadi Sunusi of the Department of Biological Science at Ahmadu Bello University (A.B.U), Zaria, certified the plant's authenticity, and a voucher specimen was added to the department's herbarium (number 571). Immediately after being chopped into small pieces, the fresh roots were cleaned and dried in the shade at room temperature (25°C). Using a mortar, the dried root was pounded into powder.

2.3. Preparation of root extracts

Exactly one hundred and fifty grams (150 g) of the fine powdered root of *M. oleifera* was weighed and transferred into a sample bottle and about 750 ml of each of the extracting solvent (water, diethyl-ether and methanol) was added separately and then allowed to stand for 48 hours. After 48 hours, the soaked *M. oleifera* powder was filtered and filtrate transferred into an evaporating dish. The filtrate on the dish was then put on a water bath at 60°C for about 35 hours until a solid extract was obtained.

2.4. Experimental animals

Forty-eight adult albino Wistar rats of either sex weighing 100-150 g were obtained from Nigeria Institute for Trypanosomiasis and Onchocerciasis Research, Kaduna, Nigeria. They were divided into 2 main groups: thirteen and thirty-five rats for the conduct of acute toxicity study and experimental study, respectively. The rats were kept at room temperature (25 °C) with 5 per cage and 12-hour light/dark cycles, as well as open access to food and water. Prior to the experiment, the rats were given three weeks to acclimatize in the animal home of the Biochemistry Department of Ahmadu Bello University Zaria.

2.5. Acute toxicity study

To assess the acute toxicity of *M. oleifera's* aqueous root extract, Lorke's method (1983) was employed. In accordance with this, for phases one and two, thirteen rats of either sex were split into three groups of three rats each and three groups of one rat each. The last rat served as normal control. Each group in the phase one was administered different doses of 10 mg/kg body weight (b.w.), 100 mg/kg b.w., and 1000 mg/kg b.w., respectively, of *M. oleifera* aqueous root extract, but in the second phase, each group was differently administered 1600 mg/kg b.w., 2900 mg/kg b.w., and 5000 mg/kg b.w. of the of the plant aqueous root extract, respectively. The behavior and potential for mortality were tracked and observed for 24 hours in each phase. The formula below was used to calculate median lethal dose (LD_{50}) of the aqueous root extract of *M. oleifera*.

$$LD_{50} = \sqrt{(D_0 \times D_{100})}$$

Where D_0 represents the highest dosage from phase one that didn't cause mortality,

D_{100} represents the lowest dose from phase two that caused mortality.

Accordingly, safety margin of the aqueous, methanol and diethyl-ether root extracts of *M. oleifera* was decided to be any value close or equal to 0.1 of their LD_{50s}.

2.6. Animal groupings

Thirty-five Wistar rats that appeared to be in good health were split into seven subgroups of five rats each. For ten days, the first subgroup—which acted as the normal control (NC)—received food and distilled water at their leisure. Two subgroups separately received low and high doses from *M. oleifera's* aqueous root extract (AL and AH) as 100 and 200 mg/kg rat b.w., while two further subgroups separately received low and high doses from *M. oleifera's* methanol root extract (ML and MH) as 100 and

200 mg/kg rat b.w. The last two subgroups separately received low and high doses from *M. oleifera*'s diethyl-ether root extract (DL and DH) as 100 and 200 mg/kg rat b.w. The extracts were administered orally to animals in all groups for an experimental period of ten days using syringe and cannula.

2.7. Sample collection

Animals of all groups were sacrificed by anaesthetizing them with chloroform on the eleventh day of the experiment. Separate blood samples were taken from rats' tail veins, transferred into clean, dry and plain tubes, allowed to clot for around 30 minutes, then spun at 3000 rpm for 10 minutes to separate sera. After excision of whole brain samples from rats, exactly 0.08 g of each brain tissue was homogenized in 5ml HCl-butanol, spun at 3000 rpm for 10 minutes. 1 ml of resulting supernatant was transferred into a centrifuge containing 2 ml of heptane and 0.3 ml of 0.1 M HCl. Following vigorous shaking for 10 minutes, each tube was spun at 3000 rpm for 10 minutes, giving rise to two phases (organic and aqueous phases), the organic phase was thrown off while the aqueous phase served as sample for catecholamine assay.

2.8. Spectrophotometric determination of total protein

The Biuret method, created by Gornall *et al.* (1949) was used to measure the amount of total protein in serum and brain homogenate. The working standard, 5 mg/ml BSA, was transferred in exactly 0.0, 0.2, 0.4, 0.6, 0.8, and 1 ml increments into five test tubes with labels. A test tube was filled with one milliliter (1 ml) of the serum or brain homogenate (unknown). Each test tube's capacity was adjusted to 1 ml, and a 1 ml tube filled with distilled water served as the blank. The test tubes, including the blank and unknown, received four milliliters (4 ml) of Biuret reagent. Shaking and 30 minutes of heat at 37°C were used to combine the contents of the tubes. The resultant mixes were cooled to room temperature and their absorbance was measured at 540 nm in comparison to a blank. Standard curve was plotted, and concentrations of total protein in either the serum or brain homogenates were calculated from the curves.

2.9. Spectrophotometric determination of norepinephrine and epinephrine

Hormozi-Nezhad *et al.* (2010) approach was used to determine the levels of norepinephrine and epinephrine. One milliliter of each of the epinephrine and norepinephrine solutions with concentrations of 0.1, 0.01, 0.001, and 0.0001 mg/ml, as well as one milliliter each of water, serum, or brain homogenate, were placed individually into two sets of five test tubes with the labels blank and unknown. 1 ml, 0.7 ml, and 1 ml of 0.01 M $AgNO_3$, 9.09 x 10-6 M PVP, and 0.001 M NaOH, respectively, were added to each of these tubes, slowly mixed, and incubated at 37°C for 7 minutes.

After reaching room temperature, the resultant mixes were tested for absorbance at 440 nm in comparison to a blank. The concentration of epinephrine and norepinephrine in the solution was determined using standard curves for both substances.

2.10. Statistical analysis

GraphPad-Instat (v3) was used to analyze all of the data. For the purpose of comparing group means and performing statistical comparisons between groups, Tukey's test and one-way analysis of variance were used. A p-value of less than 0.05 was used to establish the statistical significance of the data, which were presented as Mean ± Standard Deviation (SD).

3. Results

3.1. Acute toxicity result of aqueous root extract of M. oleifera

The acute toxicity result of the aqueous root extract of *M. oleifera* is shown in Table 1. There was no record of animal mortality in the first phase, but in the second phase, all the animals of the first group "13 rats" died after acute exposure to 1600 and 5000 -mg/kg b.w. of the aqueous root extract of *M. oleifera*. The LD_{50} was calculated as 1264.91 mg/kg b.w.

Table 1. The acute toxicity result of aqueous root extract of *M. oleifera* base on Lorke method (1983).

Phase	Group	No. of animals	Dose of extract (mg/kg)	Number of mortality recorded
One	1	3	10	0/3
	2	3	100	0/3
	3	3	1000	0/3
Two	1	1	1600	1/1
	2	1	2900	1/1
	3	1	5000	1/1

3.2. Serum and brain total protein levels

Table 2 depicts the effects of *M. oleifera* root extracts on serum and brain total protein levels. Rats that had received a high dose of *M. oleifera's* aqueous root extract had their brain total protein levels significantly ($p<0.05$) lowered, whereas rats which had received a low dose had their serum total protein levels significantly ($p<0.05$) increased. The serum total protein level was not substantially affected by the two dosages of *M. oleifera's* methanol root extract ($p>0.05$), but the high dose significantly ($p<0.05$) decreased the total protein level in the brains of apparently healthy Wistar rats. While the two doses of di-ethyl-ether extract of *M. oleifera* had significantly lessened serum total protein level, only high dose of the di-ethyl-ether extract was observed to cause significant ($p<0.05$) reduction in the animals' brain total protein level.

Table 2. Effect of *M. oleifera* root extracts on serum and brain total protein levels of apparently healthy rats.

Animal Groups	Serum Total Protein (mg/ml)	Brain Total Protein (mg/ml/g)
NC	34.86 ± 3.95[a]	4.22 ± 1.26[a]
AH	39.00 ± 0.71[a]	2.78 ± 0.23[b]
AL	118.17 ± 3.53[c]	3.15 ± 0.54[a]
MH	32.90 ± 7.91[a]	2.64 ± 0.59[b]
ML	41.52 ± 5.02[a]	3.33 ± 0.18[a]
DH	26.82 ± 5.63[b]	2.28 ± 0.49[b]
DL	24.24 ± 1.83[b]	3.52 ± 1.18[a]

Data are expressed as mean ± SD of 5 rats. Values bearing different superscript alphabets (a – c) along the respective vertical columns are significantly different (Tukey's HSD multiple range post hoc test, P < 0.05). NC represents normal control group; AH represents group of rats administered 200 mg/kg b.w. *M. oleifera* aqueous root extract; AL represents group of rats administered 100 mg/kg b.w. *M. oleifera* aqueous root extract; MH represents group of rats administered 200 mg/kg b.w. *M. oleifera* methanol root extract; ML represents group of rats administered 100 mg/kg b.w. *M. oleifera* methanol root extract; DH represents group of rats administered 200 mg/kg b.w. *M. oleifera* diethyl-ether root extract, and DL represents group of rats administered 100 mg/kg b.w. *M. oleifera* diethyl-ether root extract.

3.3. Serum and brain epinephrine levels

The effects of several *M. oleifera* root extracts on epinephrine levels in the serum and brain are shown in Table 3. Rats' serum levels of epinephrine were significantly ($p<0.05$) raised by the high dose of *M. oleifera* aqueous root extract, while their brain levels were not significantly ($p>0.05$) affected. Both the high and low doses of *M. oleifera* methanol root extract that were given to rats which appeared to be in good health did not significantly ($p>0.05$) change the levels of epinephrine in their serum and brains. Similar to this, both high and low doses of *M. oleifera's* diethyl-ether root extract did not significantly ($p>0.05$) change the amount of epinephrine in the rats' serum, but they did significantly ($p<0.05$) raise it in their brains.

Table 3. Effect of *M. oleifera* root extracts on serum and brain epinephrine levels of apparently healthy rats.

Animal Groups	Serum Epinephrine (mg/ml)	Brain Epinephrine (mg/ml/g)
NC	1.13 ± 0.05[a]	0.89 ± 0.14[a]
AH	2.02 ± 0.17[b]	1.18 ± 0.23[a]
AL	1.47 ± 0.25[a]	1.12 ± 0.08[a]
MH	1.74 ± 0.48[a]	1.13 ± 0.08[a]
ML	1.89 ± 0.56[a]	1.01 ± 0.14[a]
DH	1.43 ± 0.23[a]	2.30 ± 0.48[b]
DL	1.79 ± 0.79[a]	2.34 ± 0.18[b]

Data are expressed as mean ± SD of 5 rats. Values bearing different superscript alphabets (a – b) along the respective vertical columns are significantly different (Tukey's HSD multiple range post hoc test, P < 0.05). NC represents normal control group; AH represents group of rats administered 200 mg/kg b.w. *M. oleifera* aqueous root extract; AL represents group of rats administered 100 mg/kg b.w. *M. oleifera* aqueous root extract; MH represents group of rats administered 200 mg/kg b.w. *M. oleifera* methanol root extract; ML represents group of rats administered 100 mg/kg b.w. *M. oleifera* methanol root extract; DH represents group of rats administered 200 mg/kg b.w. *M. oleifera* diethyl-ether root extract, and DL represents group of rats administered 100 mg/kg b.w. *M. oleifera* diethyl-ether root extract.

3.4. Serum and brain norepinephrine levels

Table 4 depicts how various *M. oleifera* root extracts affected the levels of norepinephrine in the serum and the brain. Norepinephrine levels in serum and brain of apparently healthy Wistar rats were not significantly ($p>0.05$) changed by the issuance of aqueous and methanol root extracts of *M. oleifera*. Similar to this, the two doses of *M. oleifera* diethyl-ether root extract did not significantly ($p>0.05$) modify the serum norepinephrine level, but they did significantly ($p<0.05$) increase the norepinephrine level in the rats' brains.

Table 4. Effect of *M. oleifera* root extracts on serum and brain norepinephrine levels of apparently healthy rats.

Animal Groups	Serum Norepinephrine (mg/ml)	Brain Norepinephrine (mg/ml/g)
NC	0.049 ± 0.002[a]	0.039±0.010[a]
AH	0.075 ± 0.027[a]	0.051±0.010[a]
AL	0.053 ± 0.038[a]	0.049±0.003[a]
MH	0.076 ± 0.021[a]	0.049±0.004[a]
ML	0.072 ± 0.030[a]	0.044±0.005[a]
DH	0.062 ± 0.010[a]	0.100±0.021[b]
DL	0.078 ± 0.019[a]	0.102±0.010[b]

Data are expressed as mean ± SD of 5 rats. Values bearing different superscript alphabets (a – b) along the respective vertical columns are significantly different (Tukey's HSD multiple range post hoc test, P < 0.05). NC represents normal control group; AH represents group of rats administered 200 mg/kg b.w. *M. oleifera* aqueous root extract; AL represents group of rats administered 100 mg/kg b.w. *M. oleifera* aqueous root extract; MH represents group of rats administered 200 mg/kg b.w. *M. oleifera* methanol root extract; ML represents group of rats administered 100 mg/kg b.w. *M. oleifera* methanol root extract; DH represents group of rats administered 200 mg/kg b.w. *M. oleifera* diethyl-ether root extract, and DL represents group of rats administered 100 mg/kg b.w. *M. oleifera* diethyl-ether root extract.

4. Discussion

Mental disorders including depression and anxiety have been partly associated with loneliness, social media use, and insecurity challenges (Escobar-Viera *et al.*, 2018; Okruszek *et al.*, 2020). Hence, these disorders are not only common amongst diseased subjects but can be observed in some apparently healthy individuals. Recent reports have revealed rising cases of depression and other mental disabilities around the globe (Lim *et al.*, 2018; Dadi *et al.*, 2020); there is therefore an urgent need to search for safe, effective, and affordable psychotherapies. Several studies have examined the tissue-protection and psychotherapeutic potentials of plants preparations (Cai *et al.*, 2016; Es-Safi *et al.*, 2021). In fact, Hegazy *et al.* (2020) have recently reported the nephro-protective ability of *M. oleifera* seed preparation. Thus, in a bid to extend the search for plant-based remedy against mental disorders, the ability of *M. oleifera* root extracts to alter catecholamines levels in apparently heathy rats was investigated where different root extracts of *M. oleifera* dose dependently lessened brain total protein level while diethyl-ether root extract of the plant elevated norepinephrine and epinephrine levels. The findings from the present study inform the need to replicate same study in an established animal depressed model. Since the present study was not gender specific, the

impact of reproductive hormones on the changes in catecholamine levels was not investigated. In this context, Hegazy *et al.* (2018) have reported the potential influence of sex hormones in vitamin E protection of hepatic injury.

The safeness of different plant parts must be established prior to consumption by experimental animals. This is in view of the reports that certain herbs possess the ability to cause toxicity *in vivo* (Vengal Rao *et al*., 2018). In the present study, only LD_{50} of aqueous root extract of *M. oleifera* was determined, and the result was suggestive of a high toxicity at 1264.91 mg/kg b.w. Previously, Bisong *et al*. (2019) and Kadam and Gaykar (2017) reported the LD_{50s} of methanol- and -diethyl-ether root extracts of *M. oleifera* to be greater than 5000 mg/kg and 2000 mg/kg, respectively.

The activities of dopamine-β-hydroxylase, monoamine oxidase, phenylalanine hydroxylase, catalase, tryptophan hydroxylase-2, xanthine oxidase, L-amino acid decarboxylase, and some RNA binding proteins have been reported to change during depression and other neurodegenerative disorders (Berguig *et al.*, 2019; Ding *et al.*, 2020; Sun *et al.*, 2021). Moreover, *in vivo* administrations of excess phenylalanine and phytochemicals including chalcones, coumarins, alkaloids, and isothiocyanates were shown to competitively block L-amino decarboxylase and monoamine oxidase, respectively (Engelbrecht *et al*., 2018; Kamal *et al.*, 2022). Thus, the observed reduction in brain total protein concentration may be attributed to down-regulation of some genes and inhibition of some enzymes by the plant-borne metabolites.

The primary neurotransmitters involved in neuro-motor control, cognition, emotion, memory processing, and endocrine regulation are catecholamines (Ranjbar-Slamloo *et al*., 2020; Cai *et al*., 2021). Although adrenaline is crucial to metabolic processes, especially fat and glucose metabolisms, noradrenaline is largely involved in the sympathetic control of blood pressure and flow in peripheral tissues, while both can be released in response to stress and arousal induced-stimuli (Chen *et al.*, 2019). Reports have linked reduced synthesis of neurotransmitters, oxidative stress, and abnormal ubiquitination to severity of DDs and NDs (Karim *et al.*, 2018; Menghani *et al.*, 2021). The increase in brain noradrenalin and adrenalin levels caused by the di-ethyl-ether root extract of *M. oleifera* could be linked to the presence of β-sitosterol which possibly served as an allosteric modulator of phenylalanine hydroxylase, the enzyme catalyzing the committed step in catecholamines biosynthetic pathway. Contrastingly, the aqueous and methanol root extracts of the plant could not elevate the levels of adrenalin and noradrenalin, possibly due to absence of activators for phenylalanine hydroxylase. The work of Mokler *et al.* (2019) had associated prenatal protein malnutrition to reduction in noradrenalin and dopamine levels in ventral prelimbic and infralimbic cortices of rats brains. Thus, the observed increase in noradrenalin level may have occurred following a steady concentration of phenylalanine in rats' brain after administration of the di-ethyl-ether root extract. Berguig *et al*. (2019) reported that elevated level of phenylalanine could impair transportation of tyrosine via large amino transporter 1 of the brain, competitively inhibit the activity of L-amino acid decarboxylase, and increase the biosynthesis of phenethylamine as well as cause a decrease in the synthesis of noradrenalin. It can thus be suggested that the diethyl-ether extract of the plant raised brain noradrenalin level of apparently healthy rats because of the absence of inhibition of L-amino acid decarboxylase by phenylalanine.

Furthermore, DDs and NDs have been reported to be managed with plants possessing antioxidant activities (Asif *et al.*, 2019; Cai *et al.*, 2021). Given the established phytochemical contents of *M. oleifera* (Hodas *et al.*, 2019), it could be possible to link the neurotransmitter-enhancement function of the plant via antioxidative mechanism. Bioactive compounds such as alkaloids and flavonoids have been recently reported to confer neuroprotective effect, and these compounds were hugely traced to the extracts of the plant (Abdel-Rahman *et al.*, 2019), suggesting that the root extracts could truly be neuroprotective by raising catecholamine levels in brain.

5. Conclusion

The present study reveals that di-ethyl-ether root extract of *M. oleifera* can dose dependently alter norepinephrine and epinephrine levels in brain and serum of apparently healthy rats, which suggests a possibility of the extract to confer protection against depressive and neurodegenerative symptoms in animals.

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Ethical consent

The consent of Ahmadu Bello University Zaria Ethics Committee on Animal Use and Care was sought before commencement of the study. Approval was granted with the following number: ABUCAUC/2022/066.

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