Antidepressant, antianxiolytic and antiepileptic effects of Mojeaga herbal remedy®in albino mice

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Abstract

The Mojeaga herbal remedy is made up of several herbs, including *Alchornea laxiflora, Pennisetum purpureum,* and *Sorghum bicolour*. It is primarily used to treat anaemia, boost immune system function, and provide antioxidant effects. The aim of this work is to investigate the antidepressant, anti-epileptic, and anxiolytic effects of the Mojeaga herbal remedy®. The forced swim test and the tail suspension test in mice were employed to examine the antidepressant effect. Pentylenetetrazol and strychnine-induced seizure models were used to assess the anti-epileptic activity, while the elevated plus maze was used to evaluate anxiolytic activity. Mojeaga extract at 5 mg/kg, 10 mg/kg, 20 mg/kg, and fluoxetine (20 mg/kg) significantly reduced immobility time when compared to the control ($P < 0.05$) in the forced swim and the tail suspension tests. In the elevated plus maze**,** diazepam (10 mg/kg) significantly increased the time spent in the open arm, the number of open arm entries, and the percentage of open arm entries when compared to control ($P < 0.01$). At doses of 5, 10, and 20 mg/kg, the herbal remedy® did not significantly protect against strychnine- or pentylenetetrazol-induced seizures. Diazepam (10 mg/kg) provided 25% protection against strychnine-induced convulsions and 50% protection against seizures caused by pentylenetetrazol. The study suggests that the herbal remedy Mojeaga has antidepressant-like properties, but it lacks anxiolytic and antiepileptic properties.

Keywords: Antidepressant, Anxiolytic, Antiepileptic, Mojeaga, Fluoxetine

Introduction

Medicinal plants are vital for human survival, acting as a self-sustaining source of healthcare and a diverse resource for

traditional remedies (Abubakar *et al.,* 2014; Evan, 2009; Sofowara, 1993). Over 350 traditional remedies use approximately 456 species to treat various ailments (Abubakar *et al.,* 2014; Evan, 2009; Sofowara, 1993). Plant sources yield around 80% of pharmaceutical drugs, which have historically played a crucial role in regions with limited access to modern healthcare (Abubakar *et al.,* 2014). The biological activities of plant-derived natural compounds have been thoroughly studied, and the results have revealed new therapeutic targets of agents and disease-treating processes (Nasim *et al.,* 2022; Wangchuk*,* 2018). These compounds are valuable in drug development, either as direct agents or leads (Bauer and Bronstrup, 2014). Mojeaga herbal remedy is made up of several herbs, including *Alchornea laxiflora, Pennisetum purpureum,* and *Sorghum bicolor* (Elejee*t al*., 2022; Elejee*t al*., 2018). It is primarily used to treat anemia, boost immune system function, and provide antioxidant effects (Elejee*t al*., 2022). African traditional medicine widely recognizes *Alchornea laxiflora* for its antibacterial, antifungal, antidepressant, and antioxidant properties (Akinpelu *et al.,* 2015). According to Ugbogu and Chukwuma (2019), the stem of *Alchorea laxiflora* is usedas a chewing stick and aids in food preservation, while its leaves combat stress, depression, anxiety, aging, malaria, and inflammation. Traditional practices utilize the roots and bark of *Pennisetum purpureum* to manage conditions such as fibroids, hemorrhoids, menstrual disorders, infections, and detoxification (Oyeyemi *et al.,* 2019). Awika and Rooney (2004) have reported that *Sorghum bicolor* reduces inflammation and neutralizes free radicals. Some of the composition of the remedy possesses antidepressant, anti-anxiety and anticonvulsant properties. The aim of this work is to investigate the antidepressant, anti-epileptic, and anxiolytic

effects of Mojeaga herbal remedy® in mitigating symptoms of depression, anxiety, and epilepsy.

Materials and methods

Procurement of Mojeaga herbal remedy®

Mojeaga herbal remedy was obtained from Mojeaga International Ventures Ltd, located at 2A, Erhuomase Street, Idumwomwina, IkpobaOkha local government area, off Benin-Auchi Road, Benin City, Edo State, Nigeria. Theherbal remedy consisted of *Alchorneacordifolia*, *Sorghum bicolor*, and *Pennisetumglaucum*extracts.

Preparation of Mojeaga herbal remedy®

Mojeaga herbal remedy powder® macerated. Exactly 500 g of the powder was weighed and soaked in a jar with 2 L of distilled water. This was left to stand for 72 hours. The mixture was filtered, and the filtrate freeze-dried (Model FD-10S, China) before storing in an amber bottle at 4°C prior to its use.

Experimental animals

A total of 100 healthy male and female albino mice (20–30 g) were procured from Mr. Niyi's animal facility in Ibadan, Oyo State, Nigeria for the study. The mice were housed in the animal house of the Department of Science Laboratory Technology, University of Benin, Benin City. They were provided with a standard diet and allowed free access to food and water. The animals were allowed to acclimatize for a period of 14 days and handled in accordance with normal protocol for laboratory animals (National Research Council, USA, *Guide for the Care and Use of Laboratory Animals*, 2011). This study was approved by Life Sciences Research Ethical Committee Faculty of Life Sciences, University of Benin with reference number LS20316.

Dose determination

The adult dose of the Mojeaga herbal remedy ® preparation already consumed with NAFDAC registration No: A7-0996L

is 800 mg/day; thus, the dose was calculated as follows:

Dose for adults per day: 800 mg

= 800 mg/day

= 800 mg/70 kg

Dose per kg $= \frac{800}{70}$

= 11.43 mg

Therefore, the calculated dose per kg was rounded up to 10 mg/kg and divided by 2 to get 5 mg/kg and multiplied by 10 mg/kg by 2 to get 20 mg/kg.

Antidepressant study

The antidepressant activity of Mojeaga herbal remedy was evaluated using the forced swim test (FST) and tail suspension test (TST), two widely used models to screen for antidepressant-like effects (Castagné*et al.,* 2011).

Forced Swim Test (FST): Twenty mice weighing 20-30 grams were allotted into five groups with four animals in each.Group 1 received distilled water 10 ml/kg; groups 2, 3 and 4 received 5 mg/kg, 10 mg/kg, and 20 mg/kg of Mojeaga extract respectively, while group 5 received the 20 mg/kg of the standard drug, fluoxetine orally. One hour after administration of Mojeaga and fluoxetine respectively, the mice were placed in an inescapable transparent cylinder (height 40 cm, diameter 20 cm) filled with water (depth 30 cm) at 25˚C. The animals were allowed to swim for 10 minutes, and the time of immobility (a sign of despair-like behavior) was recorded. A reduction in immobility time after treatment is indicative of antidepressant-like activity (Koek*et al.,* 2018; Unal and Canbeyli, 2019).

Tail Suspension Test (TST): Twenty mice weighing 20-30 grams were allotted into five groups with four animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received Mojeaga extract 5, 10 and 20 mg/kg, respectively group 5 received the standard drug fluoxetine (20 mg/kg) orally.

One hour after administration of Mojejaga and fluoxetine, the mice were suspended from the edge of a shelf 60 cm above the tabletop by their tails using adhesive tape, and the time of immobility (immobility being indicative of a depressive state) was recorded for 10 minutes for each animal. The test was conducted in a noise-free room to minimize external stressors(Koek*et al.,* 2018; Unal and Canbeyli, 2019).

Anxiolytic activity

The elevated plus maze (EPM) test was employed to assess the anxiolytic effects of the extract (Mechiel and De Boer, 2003).

Elevated Plus Maze (EPM):

The maze consists of two open arms and two closed arms, elevated 50 cm above the floor. Twenty mice weighing 20-30 grams were randomly divided into five groups with four animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received Mojeaga extract (5, 10 and 20 mg/kg, respectively); and group 5 received the standard drug diazepam (10 mg/kg). One hour after the administration of Mojeaga and diazepam, the animals were placed in the center of the maze and allowed to explore for 10 minutes. The percentage of time spent in the open arms and the number of entries into the open arms were used as indicators of anxiety. Increased exploration of the open arms is considered a sign of anxiolytic-like behavior (Mechiel and De Boer, 2003).

Antiepileptic activity

Pentylenetetrazol (PTZ)- and strychnine-induced convulsion models were used to evaluate the anti-epileptic effects of Mojeaga tea extract(Krishna, *et al*., 2016;Bhat*et al*., 2012;Dhir*et al.,* 2006).

Pentylenetetrazol (PTZ)-induced Seizure Model: Twenty mice weighing 20-30 grams were divided into five groups with four animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received

Mojeaga extract (5, 10 and 20 mg/kg, respectively); and group 5 received the standard drug diazepam (10 mg/kg). All mice received an intraperitoneal injection of PTZ (60 mg/kg/i.p) to induce seizures one hour after the administration of Mojeaga and Diazepam. Mice were then observed for the occurrence of seizures (clonic, tonic, and tonic-clonic) 30 minutes post-injection. Percentage protection of seizures was calculated as $[(\frac{NCA}{TNA}) \times 100]$,

where NCA=number of convulsed animals, TNA=total number of animals

Strychnine-induced Seizure Model: Twenty mice weighing 20-30 grams were randomly divided into five groups with four animals in each. Group 1 received distilled water (10 ml/kg); groups 2–4 received Mojeaga extract (5, 10 and 20 mg/kg, respectively); and group 5 received the standard drug diazepam (10 mg/kg).One hour later, seizures were induced by intraperitoneal injection of strychnine (2.5 mg/kg/i.p) During the next 30 min time period, number of seizures (clonic, tonic, and tonic-clonic) were recorded. Percentage protection of seizure was calculated as $[(\frac{NCA}{TNA}) \times 100]$, where NCA=number of convulsed animals, TNA=total number of animals

Statistical analysis

The data are presented as the mean ± standard error of the mean (SEM), with 'n' showing the number of mice in each experimental group. A one-way analysis of variance (ANOVA) was conducted, followed by the Tukey's test. GraphPad Prism software version 9 from the UK was used for all data analysis. $P < 0.05$ indicated significant differences between compared data.

Results

Forced swimming and tail suspension endurance test

Figures 1 and 2 showed the effect of the Mojeaga herbal remedy on forced swimming endurance and tail suspension tests. Mojeaga at 20 mg/kg and fluoxetine

(20 mg/kg) significantly reduced the time of immobility when compared with control (P < 0.5).

Figure 1: Effect of Mojeaga herbal remedyon immobility time in forced swim test

Mojeagaextract tea at 20 mg/kg and fluoxetine (20 mg/kg) significantly reduced the immobility time when compared to control (P < 0.05). CON: Control, MHR: Mojeaga herbal remedy, FLU: Fluoxetine.The values were represented as the mean ± standard error of mean, n = 4.

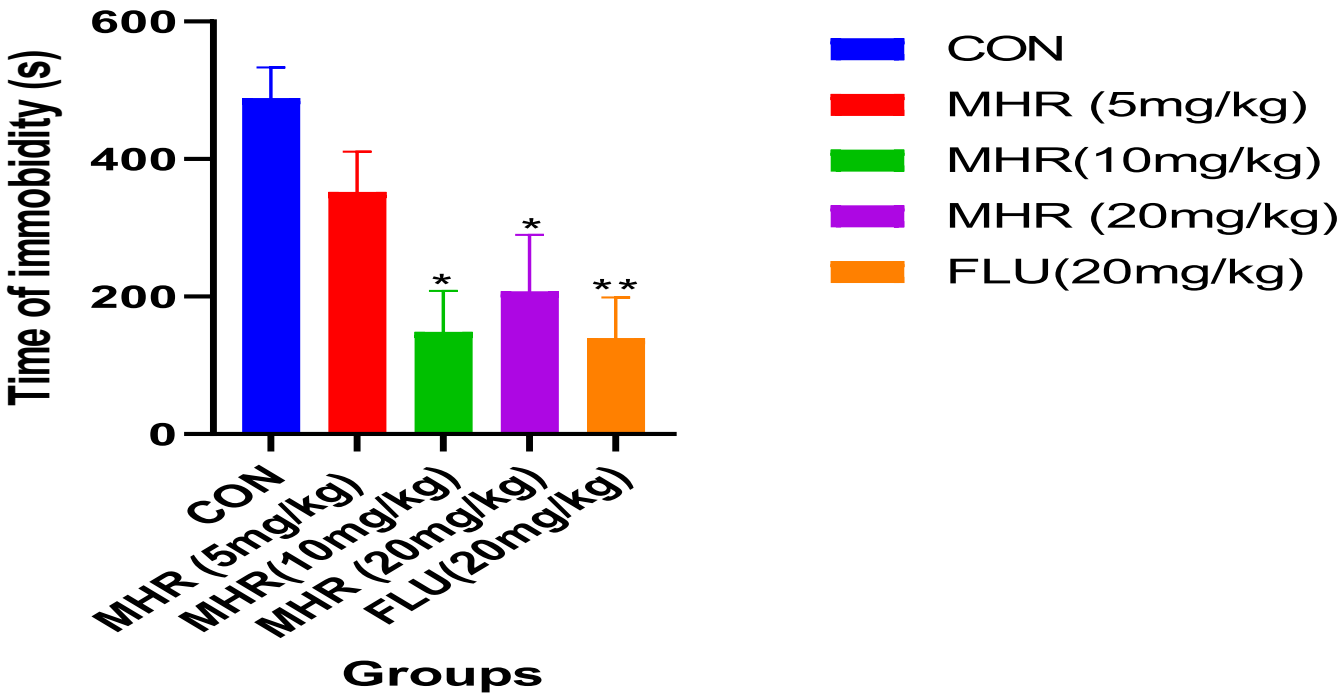

Figure 2**:** Effect of Mojeaga herbal remedy®on time of immobilityin tail suspension test

Mojeaga extract at 10 mg/kg and 20 mg/kg and fluoxetine (20 mg/kg) significantly reduced the immobility time when compared to the control (*P < 0.05; **P < 0.01). CON: Control, MHR: Mojeaga herbal remedy, FLU: Fluoxetine.The values were represented as the mean ± standard error of mean, n = 4.

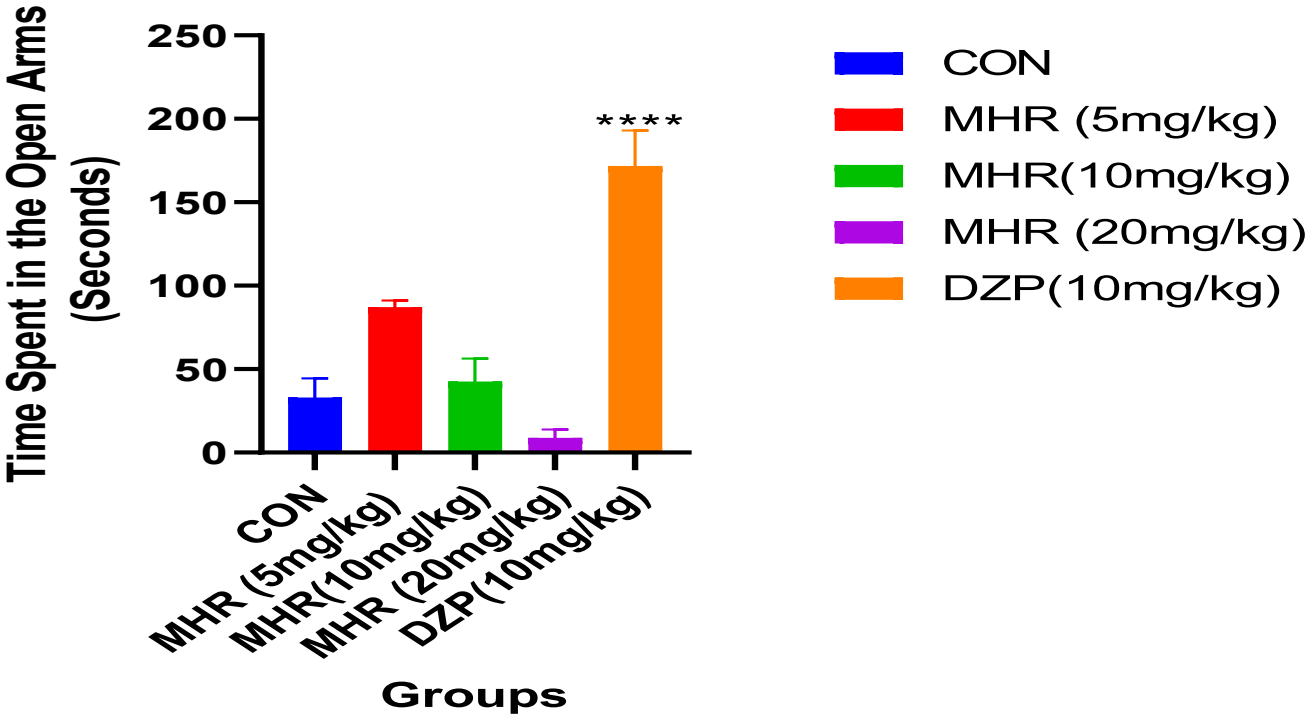

Figure 3a:Effect of Mojeaga herbal remedy® on time spent in the open arm in elevated plus maze test

Mojeaga herbal remedy has no effect ontime spent in the open arm, while diazepam 10 mg/kg) significantly increased the time spent in the open arm when compared to control, ($P< 0.0001$). CON: Control, MHR: Mojeaga herbal remedy, DZP: Diazepam.The values were represented as the mean ± standard error of mean, n = 4.

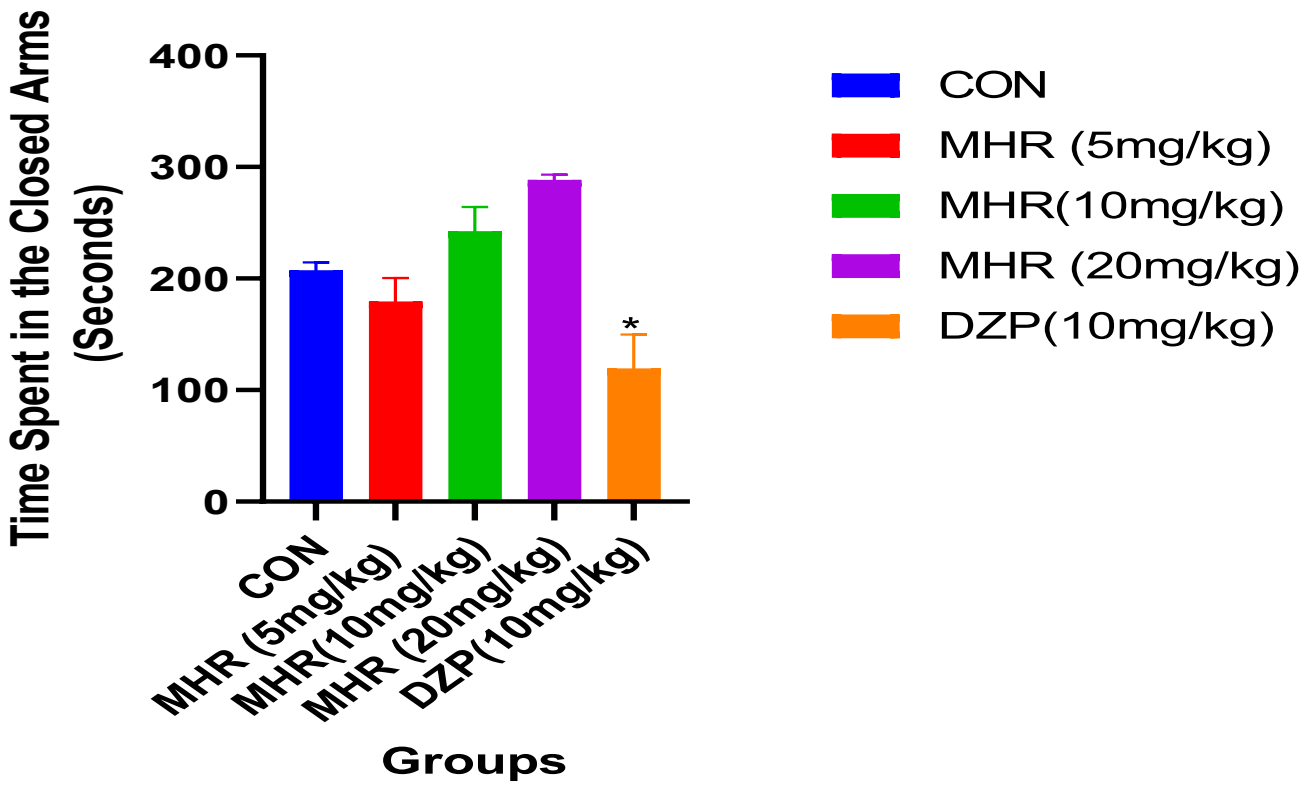

Figure 3b:Effect of Mojeaga herbal remedy® on time spent in the closed arm in elevated plus maze test

Mojeaga herbal remedy increased the time spent in the closed arm, and diazepam (10 mg/kg) significantly decreased the time spent in the closed arm when compared to control ($P < 0.05$). CON: Control, MHR: Mojeaga herbal remedy, DZP: Diazepam.The values were represented as mean ± standard error of mean., n = 4.

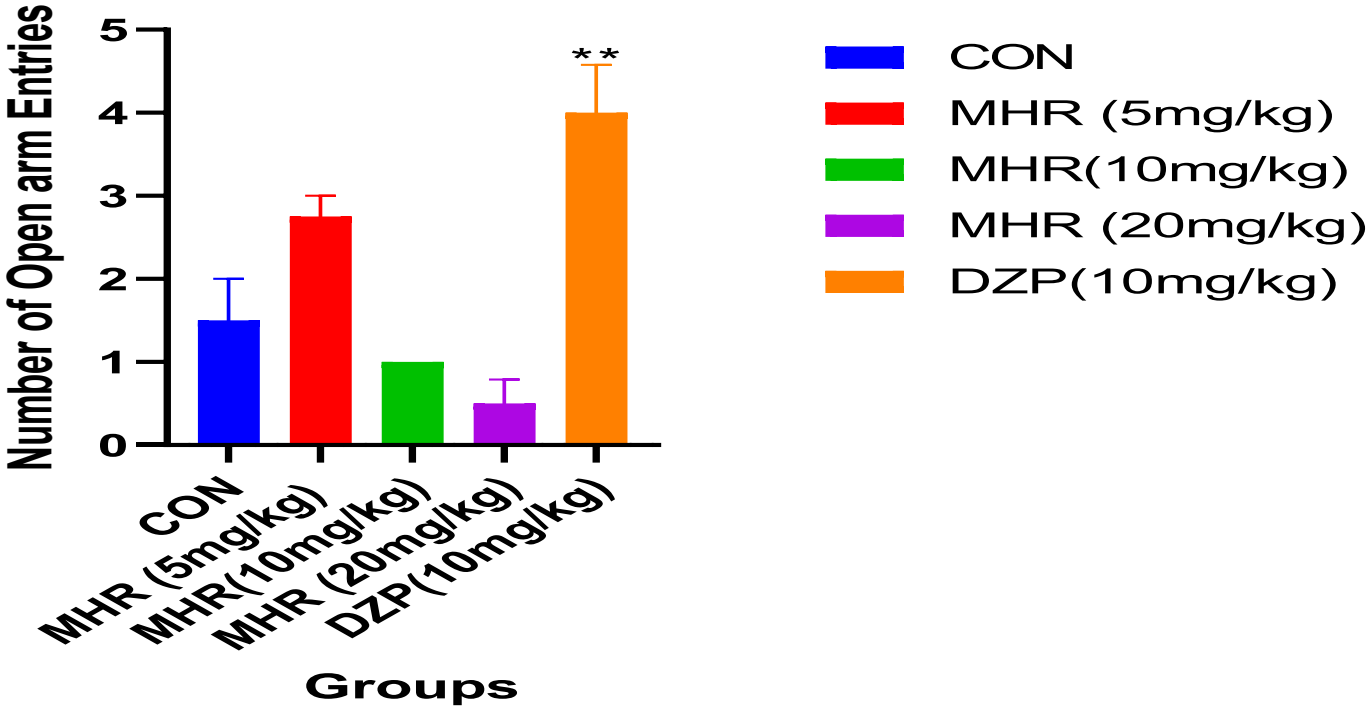

Figure 3c: Efect of the Mojeaga herbal remedy®onnumber of open arm entries in elevated plus mazetest

Mojeaga herbal remedy reduced the number of open arm entries, and diazepam 10 mg/kg) significantly increased the number of open arm entries when compared to control ($P < 0.01$).CON: Control, MHR: Mojeaga herbal remedy, DZP: Diazepam. The values were represented as the mean ± standard error of mean, n = 4.

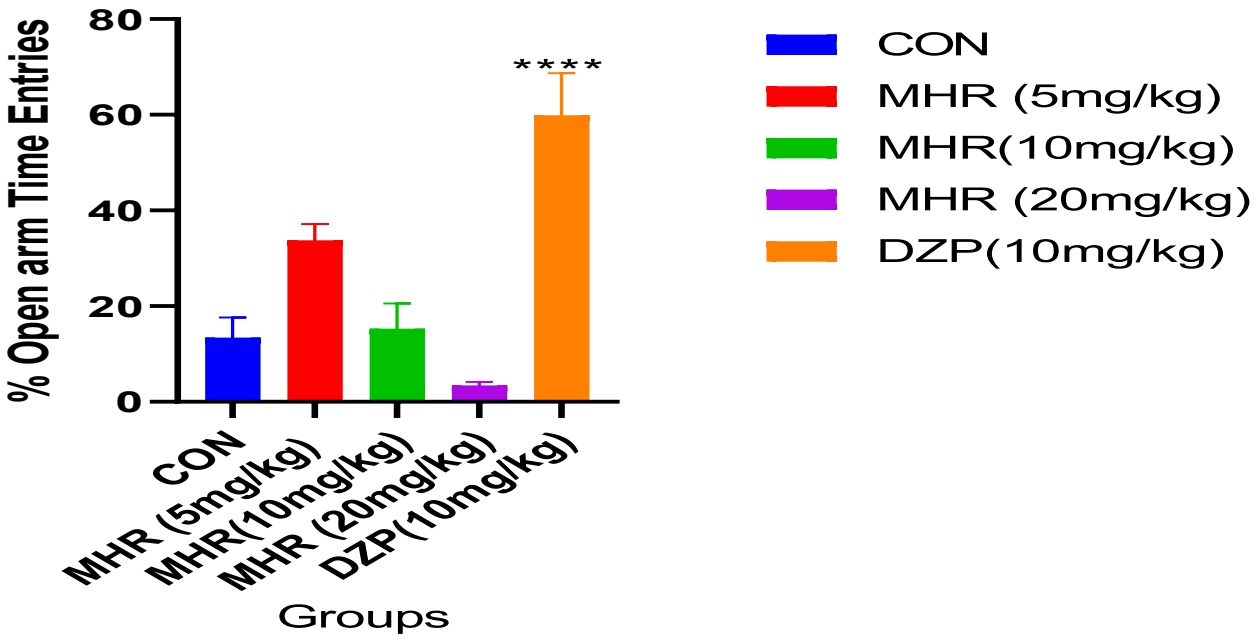

Figure 3d: Effect of the Mojeaga herbal remedy®on elevated plus maze test

Mojeaga herbal remedy extract reduced percentage open arm time entries and diazepam (10 mg/kg) significantly increased the percentage of open arm entries when compared to the control (**P < 0.01).CON: Control, MHR: Mojeaga herbal remedy, DZP: Diazepam. The values were represented as the mean ± standard error of mean, n = 4.

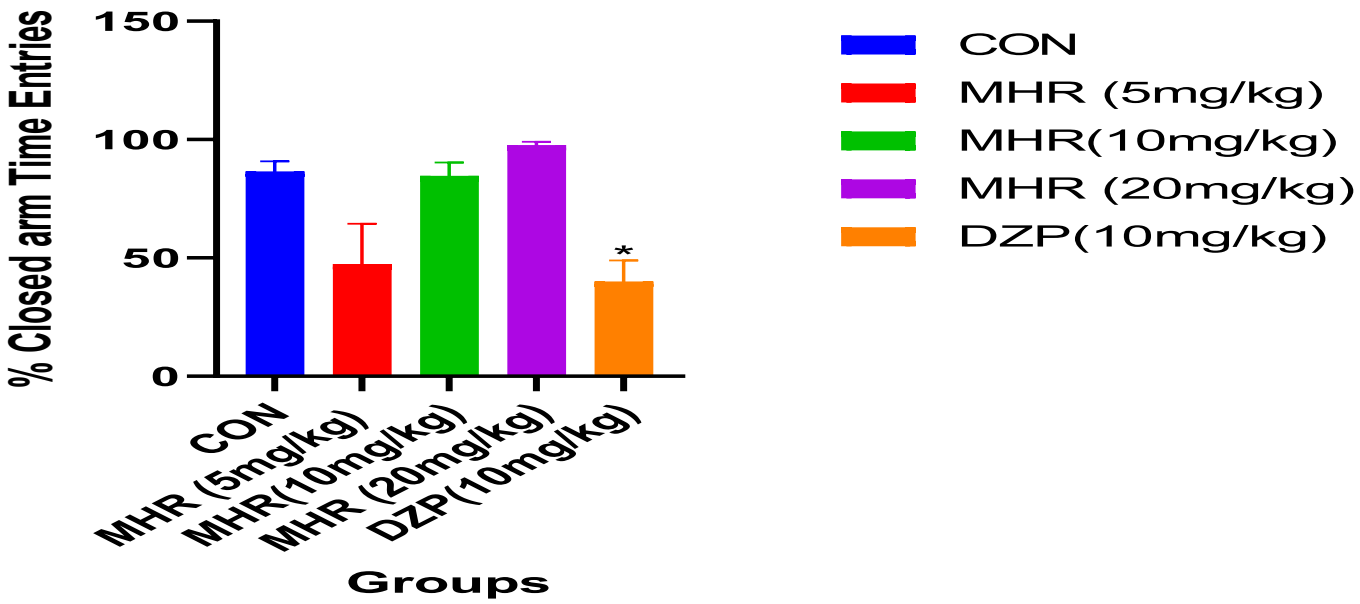

Figure 3e: Effect of Mojeaga herbal remedy®on percentageof closed arm time entries inelevated plus maze**.**

Mojeaga herbal remedy extract increased percentage closed arm time entries and diazepam (10 mg/kg) significantly decreased the number of percentage closed arm entries when compared to control ($P < 0.05$).CON: Control, MHR: Mojeaga herbal remedy, DZP: Diazepam. The values were represented as the mean ± standard error of mean,n = 4.

Table 1. Effect of the Mojeaga herbal remedy®on strychnine-induced convulsion in mice

Treatment	Dose	Number of Animals	Number of Convulsed Animals	Number of Deaths	% Protection
Control	Distilled water (10ml/kg)	4	4	4	0
M. Extract	5mg/kg	4	4	4	0
M. Extract	10mg/kg	4	4	4	0

M. Extract	20mg/kg	4	4	4	0
Diazepam	10mg/kg	4	3	3	25

Mojeaga herbal remedy® at all dose levels (5, 10, and 20 mg/kg) showed no percentage protection against strychnine-induced convulsion. The standard drug Diazepam (10 mg/kg) showed (25%)percentage protection.M: Mojeaga herbal remedy.The values were represented as the mean ± standard error of meanmean ± standard error of mean, n = 4.

Table 2: Effect of Mojeaga herbal remedy® on Pentylenetetrazol-induced convulsions

Treatment	Dose	Number of animals	Number of convulsed animals	Number of deaths	% Protection
Control	Distilled water (10ml/kg)	4	4	0	0
M. Extract	5mg/kg	4	4	0	0
M. Extract	10mg/kg	4	4	0	0
M. Extract	20mg/kg	4	4	0	0
Diazepam	10mg/kg	4	2	0	50

Mojeaga herbal remedy® at all dose levels (5, 10, and 20 mg/kg) showed no percentage protection against pentylenetetrazol-induced convulsion. The standard drug Diazepam (10 mg/kg) significantly increased the percentage protection (50%) compared to that of control distilled water (10 mg/kg). M: Mojeaga herbal remedy.The values were represented as the mean ± standard error of mean, n = 4.

Discussion

Mojeaga herbal remedy at higher doses and the standard drug, fluoxetine at 20 mg/kg, significantly reduced the duration of immobility in both the forced swim and the tail suspension test. The forced swimming endurance test is a widely recognized behavioral paradigm used to assess depressive-like states in rodents, particularly their susceptibility to behavioral despair

(Uwaya*et al*., 2024). This assay gauges each animal's stress response by measuring their behavioral adaptation to an inescapable situation, namely the perceived threat of drowning, thus serving as a reliable model for evaluating helplessness and affective disorders (Can *et al*., 2012). The tail suspension test elicits immobility in mice subjected to an inescapable stressor, serving as an established model of behavioral despair that is indicative of depression-like states and psychological stress (Gonzalez-Trujano *et al*., 2016). The ability of Mojeaga herbal remedy® extract to reduce the time of immobility in forced swim and tail suspension tests suggests its antidepressant activity. Ali and Engidawork (2022), Tsala *et al*. (2010), and Foyet*et al*. (2011) independently demonstrated that the administration of *Carissa spinarum* root bark and *Alafia multiflora* stem bark extracts significantly reduced immobility time, indicating potential antidepressant-like effects. Fluoxetine is a commonly prescribed drug for the treatment of depression (Sun *et al*., 2019; Perez-Caballero *et al*., 2014; Sommi *et al*., 1897) belonging to the class of antidepressant drugs called serotonin selective reuptake inhibitors (SSRIs). Its effects are mediated by the inhibition of serotonin reuptake into the presynaptic terminal, thereby increasing serotonergic activity (Sun *et al*., 2019; Perez-Caballero *et al*., 2014; Sommi *et al*., 1897). Mojeaga herbal remedy® may thus be inhibiting serotonin reuptake into the presynaptic terminal. Previous reports have shown that Mojeaga herbal remedy® contains bioactive compounds like flavonoids, alkaloids, tannins, saponins, terpenoids, and phenols that have the potential to change behaviors that are similar to depression (Moragrega and Rios, 2021; Khushboo and Sharma, 2017; Ittiyavirah and Paul, 2013; Singh *et al.,* 2012). Research confirms that phytochemicals in medicinal plants like

flavonoids, alkaloids, tannins, saponins, cardiac glycosides, oxalates, steroids, terpenoids, and phenols are associated with various health benefits(Sabndare*et al.,* 2013). The antidepressant property of the Mojeaga herbal remedy® could therefore be a result of the phytochemical component present in the plants (Swati*et al.,* 2012). The effect may be a result of *A. laxiflora and S. bicolour* in the remedy. It has been reported that *A. laxiflora* possesses antidepressant properties, possibly by affecting the PI3K-Akt and MAPK signaling pathways (Jain *et al.,* 2024). Another report also indicated that the leaf extract of *S. bicolour* had sedative activity, which is a central nervous system-related effect (Nwinyi and Kwanashie, 2009).

The elevated plus maze (EPM) is a widely utilized method for assessing anxiety-related behaviours in rodents (de Figueiredo Cerqueira *et al.,*2023). This model involves a plus-shaped elevated maze with two open arms and two enclosed arms, designed to measure the natural conflict between rodents aversion to open spaces and their exploratory tendencies (Arabo*et al.,* 2014).The exploration pattern of an animal in the EPM is commonly characterized by a set of measures related to the number of entries in and time spent on the two arm types (Arantes*et al.,* 2013). The amount of time spent in the open arms, the percentage of open arm entries, and the total number of open arm entries are unaffected by Mojeaga extract at all doses (Figures 3a, b, c, and d). However, the Mojeaga extract increased the time spent in the closed arm (Figures 3c and d). Diazepam (10 mg/kg) decreased the amount of time spent in the closed arm, increased the amount of time spent in the open arms, and percentage of open arm entries (Figures 3a, b, c and d).Diazepam, a fast-acting and long-lasting benzodiazepine, is commonly prescribed for the treatment of anxiety disorders, acute seizures, severe muscle spasms, and spasticity associated

with neurological disorders (Calcaterra and Barrow, 2014). It works by making the effects of gamma-aminobutyric acid (GABA) stronger. GABA is the brain's main neurotransmitter for inhibition (Nutt and Malizia, 2001). In particular, diazepam binds allosterically at the point where the alpha and gamma subunits of GABA-A receptor chloride ion channels meet. This binding increases the number of times that the chloride channels open, which makes the conductance of chloride ions higher (Weintraub, 2017). As a result, the neuronal membrane becomes more hyperpolarized, which lowers excitability. This has effects that calm, stop seizures, and relax muscles (Nutt and Malizia, 2001). Studies have shown that for a medicinal plant to possess anxiolytic properties there should be an increase in time spent in open arm entries, the number of open arm entries, and the percentage of time of entries of the rodent on the elevated plus maze (Zouhra *et al*., 2016; Rabbani *et al*., 2003). The results from this study indicate that Mojeaga herbal remedy® does not possess anxiolytic properties.

Mojeaga herbal remedy® did not protect against seizures caused by strychnine and Pentylenetetrazol in this study (Tables 1 and 2). Diazepam, on the other hand, a standard drug, showed 25% protection in strychnine-induced convulsion and 50% protection in Pentylenetetrazol-induced convulsion (Tables1 and 2). Strychnine and Pentylenetetrazol-induced seizure models are standard chemical methods to screen anticonvulsant agents in the laboratory. Strychnine-sensitive glycine receptors are ligand-gated chloride channels found in the brain and spinal cord (Stojanović *et al*., 2022). Strychnine blocks the glycine receptor, which is a chloride channel (Brams *et al*., 2011). Glycine receptors (GlyR) mediate inhibitory neurotransmission by binding to glycine, an amino acid neurotransmitter (Rajendra *et al.,* 1997). By

blocking the glycine receptor, strychnine stops glycine from attaching and calming down nerve signals, which causes too much muscle tightening (Brams *et al*., 2011). The drug PTZ works by blocking GABAergic neurotransmission by acting against GABA-A receptors, leading to seizures (Cremer *et al*., 2009). The results of this study showed that diazepam protected the animals against both strychnine- and PTZ-induced seizures while Mojeaga herbal remedy®, at 5 mg/kg, 10 mg/kg, and 20 mg/kg did not. *A. laxiflora,* which is a component of Mojeaga extract has been reported to exhibit anti-anxiety and anticonvulsant activities at doses of 400 mg/kg, 800 mg/kg, and 1600 mg/kg (Nwonu*et al*., 2018b; Bum *et al*., 2009). The lack of anti-anxiety and anticonvulsant effects of the Mojeaga herbal remedy, as observed in this study, may be a result of the low doses used.

Conclusion

The findings of this study indicate that Mojeaga Herbal Remedy® exhibits significant antidepressant-like activity, while lacking observable anxiolytic and antiepileptic effects at the doses used.

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Conflict of interest

There is no conflict of interest, the authors claim.

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