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Possible neuropharmacological effects of *Adenia trilobata* (Roxb.) in the Swiss albino mice model

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Abstract

Background: Known colloquially as akandaphal in Bangladesh, *Adenia trilobata* has some traditional uses. Its leaves and stems are extracted with pure methanol (MEATL, MEATS) and fractioned by n-hexane (NFATL, NFATS). The in vivo anxiolytic activity was evaluated by elevated plus maze (EPM) testing and hole-board test (HBT), whilst the locomotor activity was examined using the open-field test (OFT) and hole-cross test (HCT) and the antidepressant activity was assessed with the forced swimming test (FST) and the tail suspension test (TST).

Results: Regarding the anxiolytic activity, the 400-mg/kg doses of MEATL, NFATL, MEATS and NFATS exhibited maximum percentages of entry into the open arm of 33.85%, 32.23%, 30.06% and 41.84%, respectively, compare with the diazepam (69.33%). During HBT, MEATL (400 mg/kg) and NFATL (400 mg/kg) demonstrated 51.67 ± 0.88 and 57.67 ± 3.18 instances of head-dipping relative to diazepam (64.33 ± 3.16), whilst the locomotor activity showed a dose-dependent reduction in square movements and number of hole crossings. During FST and TST, the NFATL (400 mg/kg) exhibited rates of 43.32% and 57.71% time spent immobile, whilst fluoxetine experienced rates of 54.79% and 55.74%.

Conclusion: *Adenia trilobata* could be a potential component for the treatment of neuropharmacological defects. Further study is required.

Keywords: *Adenia trilobata*, Neuropharmacological effects, Anxiolytic, Locomotor, Antidepressant

Background

Traditional medicine is an essential part of ethnopharmacology and continues to promote the investigation of pharmacological activities for therapeutic uses [1]. Emerging ethnopharmacological information continually adds to the disclosures of new antinociceptive substances from plants [2]. Phytotherapy dependent on this information is additionally being used as a guide for the advancement of central nervous system depressant, sedative and anxiolytic drugs [3].

Depression is one of the five most common diseases in existence around the world. By the end of 2020, it may become the second leading cause of disability globally. Depression is ordinarily introduced as mood swings, trouble with speculation and physical problems such as migraine, disturbed rest and loss of energy [4, 5]. Roughly 80% to 90% of the current literature suggests that depressive behaviours might be the result of anxiety symptoms [6]. The coexistence of anxiety and depression predicts poor results with a higher level of treatment obstruction than that

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with either disorder happening alone. Further, if they overlap with each other, it can complicate the diagnosis and delay treatment [7]. Moreover, anxiety and depression are common symptoms in Alzheimer's disease and the elongation of their duration and severity can lead to dementia [8]. There are several drugs useful for the treatment of depression and anxiety. Tricyclic antidepressants, monoamine oxidase inhibitors, serotonin–norepinephrine reuptake inhibitors and serotonergic antidepressants are mostly used for the treatment of depression, whereas benzodiazepines are useful due to their anti-anxiety, sedative and muscle-relaxant activities [9–12]. Though they have several beneficiary effects, these medications also lead to unfavourable impacts. As such, some researchers are focusing on medicinal plants to elucidate compounds that are similarly effective but with less side effects. As indicated by the World Health Organisation (WHO), around 75% of the total global populace depends upon traditional medicine for health care or remedies [13].

Adenia trilobata (family: Passifloraceae), colloquially known as akandaphal, is distributed in the Chittagong District, Assam, Myanmar, Pakistan and eastern and western Himalayas. According to a previous report, the leaves of this plant are useful in the treatment of headache, knee pain, snake bite and stomach trouble [14, 15]. In our previous research, extracts of *A. trilobata* with different fractionations showed antioxidant, cytotoxicity, thrombolytic, antinociceptive and antidiarrheal activities [16].

As a follow-up, the present study assessed the anxiolytic, locomotor and antidepressant activities of methanol (MEATL, MEATS) and n-hexane (NFATL, NFATS) extracts of *A. trilobata* leaves and stems.

Methods

Chemicals

Diazepam and fluoxetine were procured from Square Pharmaceuticals Ltd., Dhaka, Bangladesh, whereas all other chemicals and reagent were of analytical grade.

Animals

Swiss albino mice of either sex (aged 6–7 weeks old and weighing 25–35 g) were obtained from the appropriate source. The animals were familiarised with the laboratory conditions for 14 days at room temperature (25 °C ± 2 °C) with a 12-h light/dark cycle with food pellets and ample water supply. For the animal experiments, all efforts were made to minimise the suffering of the animals. At the end of the observation period, all mice were euthanised using diethyl ether anaesthesia. This study was approved by the institutional animal ethical committee according to governmental guidelines under an approved reference number [17]. All sections of this report adhere to the Animal Research: Reporting of In Vivo Experiments guidelines for reporting animal research.

Collection and preparation of plant materials

The detailed extraction process of *A. trilobata* was as described in research by Barua et al. [16], whereas the fractioning of n-hexane extract was performed according to the protocol of Kupchan et al. [18]. The sample was stored at 4 °C until further use.

Experimental design

This study was conducted using four separate groups containing five Swiss albino mice each. The groups were stratified as the negative control (1% Tween-80 solution) group, reference drug group and two test groups (200 and 400 mg/kg): Meanwhile, the four test samples were the methanol extract of *A. trilobata* leaves (MEATL), n-hexane fraction of *A. trilobata* leaves (NFATL), methanol extract of *A. trilobata* stem (MEATS) and n-hexane fraction of *A. trilobata* stem (NFATS), respectively. Fluoxetine was used to discern the antidepressant activity in a dose of 10 mg/kg body weight (b.w.) delivered via an intraperitoneal route (IP), whereas diazepam was used for the anxiolytic and locomotor activity assessments and was delivered as a dose of 1 mg/kg (b.w., IP). As a negative control, 1% Tween-80 in water was received as a dose of 10 mL/kg (b.w.) by oral gavage.

Anxiolytic activity

Elevated plus maze (EPM) test

The EPM test was used to explore the anxiolytic activity of the extract of *A. trilobata* in Swiss albino mice. The EPM apparatus consisted of two open arms (5 × 10 cm^2) and two closed arms (5 × 10 × l5 cm^3) with a mid-point (5 × 5 cm^2) [19, 20]. Swiss albino mice of either sex were used in this study and the treatment was as described in the experimental design section. After 60 min, each group of mice was individually placed in the midpoint of the apparatus and the numbers of entries into the open and closed arms, respectively, were counted. The study recorded for 5 min. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia.

$$\%\text{Entry into the open arm} = \frac{\text{Number of entries in the open arm}}{\text{Number of entries in the open arm} + \text{number of entries in the closed arm}} \times 100$$

Hole-board test (HBT)

The HBT assessed the anxiolytic activity of the extract of *A. trilobata*. The device was made up of a wooden box with a size of 40 × 40 × 25 cm^3 with 16 evenly distributed holes, each measuring 3 cm in diameter. The apparatus was elevated from the floor to a height of 25 cm. The treatment of each group was as described in the experimental design section. After 30 min of dosing, each mouse was placed in the apparatus and we counted the number of head dips over 5 min and determined the latency of the first head dip [21, 22]. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia.

Locomotor and exploratory activity

Open field test (OFT)

The locomotor and exploratory behaviours of the extract of *A. trilobata* in Swiss albino mice were previously determined by Saleem et al. [23]. The apparatus of the OFT construct used a wooden square with a wall height of 40 cm, which was coloured in black and white sections alternatively, totalling 25 equal squares in the box. After the treatment of the groups, as described in the experimental design section, mice were placed in the apparatus and their movements for 3 min were assessed at 0, 30, 60, 90 and 120 min of observation. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia.

Hole-cross test (HCT)

The locomotor and exploratory behaviour analysis using the hole-cross apparatus was previously carried out by Takagi et al. [24]. A wooden box with dimensions of 30 × 20 × 14 cm^3 with a 3-cm hole located in the centre of the box was positioned at the height of 7.5 cm. The treatment of the group was as described in the experimental design section. After the treatment, each mouse was individually placed in the apparatus and the number of holes crossed was counted for 3 min at 0, 30, 60, 90 and 120 min of observation. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia.

Antidepressant activity

Forced swim test (FST)

The antidepressant activity was assessed by FST according to the previously explained method of David et al. [25]. The treatment of the groups was as described in the experimental design section. Sixty minutes after the administration of extract and reference drug mice were individually placed in a plastic apparatus measuring 25 × 15 × 25 cm^3, which was filled with water (15 cm) with a consistent water temperature of 25 °C ± 2 °C. The placement of individual mice in the apparatus was recorded for 6 min, with the initial 2 min considered as the adjustment time and the remaining 4 min measured as the immobile time. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia. The following equation was used to calculate the percentage of inhibition of immobility:

$$\text{Inhibition } (\%) = \frac{\text{A} - \text{B}}{\text{A}} \times 100$$

where A is the mean immobility time of the control and B is the mean immobility time of the test sample, respectively.

Tail suspension test (TST)

The TST was used to evaluate the antidepressant activity of *A. trilobata* extracts according to a previously explained method [26]. The treatment of the groups was as described in the experimental design section. Sixty minutes after treatment, mice were individually hung by their tails using adhesive tape positioned nearly 1 cm from the tip of the tail. The recoding and percentage of immobility were calculated as the TST results. At the end of the experiment, the mice were euthanised using diethyl ether anaesthesia.

Statistical analysis

The study results were expressed as mean ± standard error of the mean, where $p < 0.05$, $p < 0.01$ and $p < 0.001$ were considered to be statistically significant. The statistical analysis followed by one-way analysis of variance (ANOVA) (Dunnett's test), comparing the test groups to the negative control (1% Tween-80) using GraphPad Prism version 8.4 (GraphPad Software Inc., San Diego, CA, USA).

Results

Effect of different extracts of *A. trilobata* on anxiolytic activity in the EPM test

EPM testing is mostly used to investigate anxiolytic behaviour in mice. Table 1 presents the results of EPM

Table 1 Anxiolytic activity of different extract of *A. trilobata* on elevated plus-maze test

Group (mg/kg)	Entry into open arm (%)
Control	30.33 ± 0.88
Diazepam (1)	69.33 ± 1.15[c]
MEATL 200	23.97 ± 0.88[ns]
MEATL 400	33.85 ± 1.26[ns]
NFATL 200	25.48 ± 2.95[ns]
NFATL 400	32.23 ± 2.42[a]
MEATS 200	22.75 ± 0.87[ns]
MEATS 400	30.06 ± 0.88[ns]
NFATS 200	23.14 ± 2.44[ns]
NFATS 400	41.84 ± 3.19[a]

ns non-significant; *MEATL* methanol extract of *A. trilobata* leaves, *NFATL* n-hexane fraction of *A. trilobata* leaves, *MEATS* methanol extract of *A. trilobata* stem, *NFATS* n-hexane fraction of *A. trilobata* stem
The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the negative control (1% Tween-80) using GraphPad Prism version 8.4
The results were expressed in mean ± SEM (standard error mean)
[a]$p < 0.05$ considered as statistically significant
[c]$p < 0.001$ considered as statistically significant

Table 2 Anxiolytic activity of different extract of *A. trilobata* on hole-board test in mice

Group (mg/kg)	No. of head dipping	Latency of first head dipping (s)
Control	26.33 ± 0.88	8.33 ± 0.88
Diazepam (1)	64.33 ± 3.16[c]	2.0 ± 0.57[a]
MEATL 200	39.33 ± 2.33[b]	6.33 ± 2.40[ns]
MEATL 400	51.67 ± 0.88[c]	5.67 ± 0.88[ns]
NFATL 200	43.0 ± 2.89[c]	5.67 ± 1.76[ns]
NFATL 400	57.67 ± 3.18[c]	5.33 ± 1.76[ns]
MEATS 200	31.0 ± 1.53[ns]	8.0 ± 2.65[ns]
MEATS 400	40.33 ± 2.33[c]	7.0 ± 1.53[ns]
NFATS 200	34.67 ± 0.88[ns]	7.53 ± 0.33[ns]
NFATS 400	46.33 ± 1.86[c]	4.67 ± 0.45[ns]

ns non-significant, *MEATL* methanol extract of *A. trilobata* leaves, *NFATL* n-hexane fraction of *A. trilobata* leaves, *MEATS* methanol extract of *A. trilobata* stem, *NFATS* n-hexane fraction of *A. trilobata* stem
The results were expressed in mean ± SEM (standard error mean)
[a]$p < 0.05$ considered as statistically significant
[b]$p < 0.01$ considered as statistically significant
[c]$p < 0.001$ considered as statistically significant

testing, where diazepam (1 mg/kg) led to a significant degree of ($p < 0.001$) increased entry into the open arms (69.33% ± 1.15%) as compared with the negative control (30.33% ± 0.88%). The ANOVA of the 400 mg/kg dose of NFATL and NFATS similarly showed a significant degree of ($p < 0.05$) increased entry into the open arms (32.23% ± 2.42% and 41.84% ± 3.19%, respectively). In general, different extracts of *A. trilobata* triggered a significant dose-dependent reduction in anxiety behaviour. Also, the other doses of *A. trilobata* extracts showed a nonsignificant ($p > 0.05$) reduction in terms of entry into the open arms when compared with the negative control group.

Effects of anxiolytic activity following the administration of *A. trilobata* extract during HBT

During the HBT, the number of head dips was significantly increased in a dose-dependent manner for MEAT L, NFATL, MEATS (400 mg/kg) and NFATS (400 mg/kg) relative to in the negative control group. A similar effect was observed following treatment with diazepam, whereas nonsignificant activity was observed for the 200-mg/kg doses of MEATS and NFATS. Furthermore, the latency for the first head dip showed significant behaviour in correlation with diazepam, whilst the outcomes of other treatments of *A. trilobata* had no significance. Table 2 presents the anxiolytic activity recorded during HBT.

Effects of different extracts of *A. trilobata* on locomotor activity during OFT

Locomotor activity was assessed by counting the number of square movements in the open-field apparatus at different interval times. In contrast, all doses of *A. trilobata* extract triggered a reduction in the movements with time. The positive control, diazepam, exposed a significant ($p < 0.001$) reduction of movements at 90 and 120 min of observation, whilst no findings of significance were observed at 0, 30 or 60 min of observation. However, the MEATS (200 mg/kg) correlated with significant square movements at 0, 30 and 120 min of observation. Fig. 1 presents the locomotor activity noted during OFT.

Effects of different extracts of *A. trilobata* on locomotor activity during HCT

The locomotor activity of the *A. trilobata* extracts was observed by the crossing of the hole in the hole-cross apparatus. The diazepam exhibited significant numbers of ($p < 0.001$) hole crossings at 0, 60, 90 and 120 min of observation, with significant treatment differences ($p < 0.01$) relative to the negative control group noted at 30 min. Meanwhile, all doses of the *A. trilobata* extracts showed a dose-dependent reduction in the number of hole crossings. Fig. 2 presents the locomotor activity observed during HCT.

Effects of different extracts of *A. trilobata* on depression-like behaviour during FST

The antidepressant activity of *A. trilobata* extracts was assessed using the FST. Statistical analysis by ANOVA revealed a significant ($p < 0.001$) length of time of immobility for all treatments of *A. trilobata* and fluoxetine except MEATL (200 mg/kg) ($p > 0.05$). The 400-mg/kg doses of MEATL, NFATL, MEATS and NFATS, respectively, triggered maximum percentages of inhibition

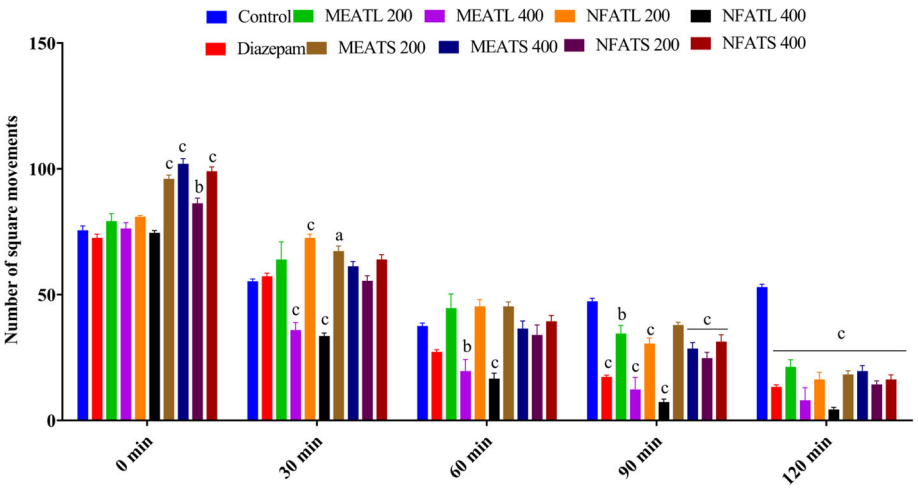

Fig. 1 Locomotor activity of different extracts of *A. trilobata* on open field test in mice. The results were expressed in mean ± SEM, where $^{a}p < 0.05$, $^{b}p < 0.01$ and $^{c}p < 0.001$ were considered as statistically significant. The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the negative control (1% Tween-80) using GraphPad Prism version 8.4. MEATL, methanol extract of *A. trilobata* leaves; NFATL, n-hexane fraction of *A. trilobata* leaves; MEATS, methanol extract of *A. trilobata* stem; NFATS, n-hexane fraction of *A. trilobata* stem

(30.48%, 43.32%, 30.22% and 39.73%, respectively), whilst fluoxetine as the standard drug exhibited an immobility percentage of 54.79%. Table 3 presents the antidepressant activity of *A. trilobata* extracts seen during FST.

Effects of different extracts of *A. trilobata* on depression-like behaviour in TST

During the TST, the treatment of *A. trilobata* extracts and fluoxetine led to a significant ($p < 0.001$) reduction in immobility in comparison with the negative control, with the treatments showing a dose-dependent reduction pattern. The 400-mg/kg doses of MEATL, NFATL, MEATS and NFATS exhibited maximum percentages of inhibition of 42.65%, 57.71%, 55.91% and 55.55%, respectively, which was almost similar to that of the standard drug fluoxetine (55.74%). Table 4 presents the antidepressant activity of *A. trilobata* extracts during TST.

Discussion

Complementary and alternative medicine (CAM) has become an important part of the treatment of chronic diseases. Natural products are one CAM aspect with the potential to facilitate the development of new compounds for novel therapeutic applications. Amongst

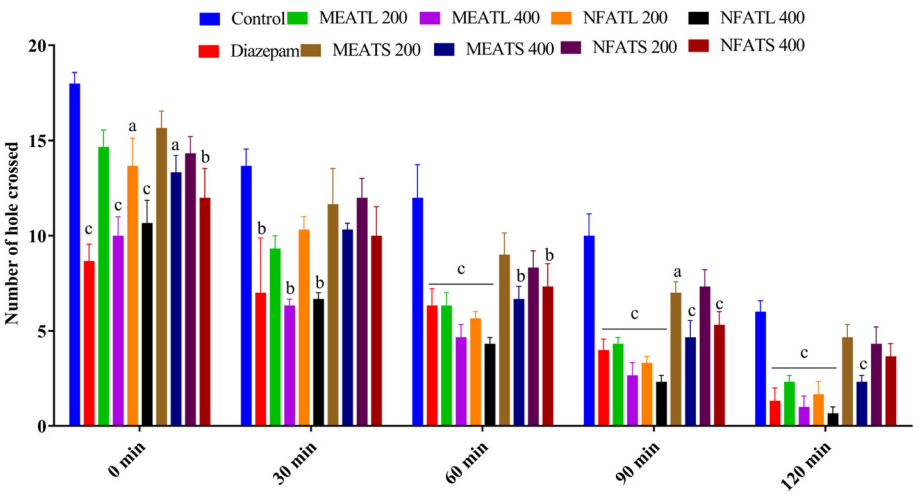

Fig. 2 Locomotor activity of different extracts of *A. trilobata* on hole-cross test in mice. The results were expressed in mean ± SEM, where $^{a}p < 0.05$, $^{b}p < 0.01$ and $^{c}p < 0.001$ were considered as statistically significant. The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the negative control (1% Tween-80) using GraphPad Prism version 8.4. MEATL, methanol extract of *A. trilobata* leaves; NFATL, n-hexane fraction of *A. trilobata* leaves; *MEATS*, methanol extract of *A. trilobata* stem; NFATS, n-hexane fraction of *A. trilobata* stem

Table 3 Antidepressant activity of different extracts of *A. trilobata* on forced swimming test in mice

Group (mg/kg)	Immobile time	Inhibition (%)
Control (10 mL/kg)	194.67 ± 2.91	-
Fluoxetine (20)	88.0 ± 1.15[c]	54.79
MEATL 200	183.0 ± 6.51[ns]	5.99
MEATL 400	135.33 ± 2.91[c]	30.48
NFATL 200	159.0 ± 4.73[c]	18.32
NFATL 400	110.33 ± 4.06[c]	43.32
MEATS 200	161.67 ± 4.91[c]	16.95
MEATS 400	130.0 ± 3.61[c]	30.22
NFATS 200	169.33 ± 1.76[c]	13.01
NFATS 400	117.33 ± 3.84[c]	39.73

ns non-significant, *MEATL* methanol extract of *A. trilobata* leaves, *NFATL* n-hexane fraction of *A. trilobata* leaves, *MEATS* methanol extract of *A. trilobata* stem, *NFATS* n-hexane fraction of *A. trilobata* stem
The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the negative control (1% Tween-80) using GraphPad Prism version 8.4
The results were expressed in mean ± SEM (standard error mean)
[c] $p < 0.001$ considered as statistically significant

other areas of study, the use of CAM or natural products in the treatment of neurodegenerative disease is a topic of interest for the researcher [27].

Anxiolytics properties exert their pharmacological activity by increasing γ-aminobutyric acid (GABA)-ergic neurotransmission in the brain [28]. The anxiolytic activity was assessed herein by EPM testing and the HBT. GABA receptors are directly l with anxiolytic effects, whilst the GABA-A receptor plays a key role in balancing neuronal inhibition and excitation [29]. In EPM testing, the presence of an agent with anxiolytic behaviour increases the frequency of entry into the open arms [30]. In our study, Swiss albino mice treated with different extracts of *A. trilobata* at different doses showed a significant percentage of entries into the open arms. Ultimately, the maximum percentage of entries ($p < 0.05$) was observed for the 400-mg/kg doses of NFATL and NFATS. Meanwhile, the extracts of *A. trilobata* exhibited a dose-dependent reduction in anxiety. Diazepam also triggered a significant percentage of entries into the open arms. The HBT is useful for assessing anxiety in rodent animals, whereas the increased number of head dips is considered as an anxiolytic behaviour [31, 32]. It is reported that head dipping by rodents is directly connected with the animals' emotional state [33]. In HBT, the number of head dips was significantly increased in a dose-dependent manner for MEATL, NFATL, MEATS and NFATS (400 mg/kg), with a similar observation made for diazepam as well.

Table 4 Antidepressant activity of different extracts of *A. trilobata* on tail suspension test in mice

Group (mg/kg)	Immobile time	Inhibition (%)
Control (10 mL/kg)	186.0 ± 1.69	-
Fluoxetine (20)	82.33 ± 1.19[c]	55.74
MEATL 200	158.33 ± 4.01[c]	14.87
MEATL 400	106.67 ± 3.47[c]	42.65
NFATL 200	144.0 ± 4.36[c]	22.58
NFATL 400	78.67 ± 1.33[c]	57.71
MEATS 200	113.0 ± 2.65[c]	39.24
MEATS 400	82.0 ± 2.08[c]	55.91
NFATS 200	118.33 ± 4.91[c]	36.38
NFATS 400	82.67 ± 3.71[c]	55.55

ns non-significant, *MEATL* methanol extract of *A. trilobata* leaves, *NFATL* n-hexane fraction of *A. trilobata* leaves, *MEATS* methanol extract of *A. trilobata* stem, *NFATS* n-hexane fraction of *A. trilobata* stem
The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the negative control (1% Tween-80) using GraphPad Prism version 8.4
The results were expressed in mean ± SEM (standard error mean)
[c] $p < 0.001$ considered as statistically significant

To discern the impact of *A. trilobata* extracts on the central nervous system during the PFT and HCT, the numbers of square movements and holes crossed are considered as the locomotor effects, respectively [34, 35]. In our study, the decrease in locomotion triggered by the *A. trilobata* extracts might correlate with the antidepressant activity due to sensory neurons having an excitatory response to motor neurons and spinal interneurons in relation to muscle compaction in locomotion. In addition, GABAergic interneurons regulate this pathway by suppressing the sensory afferents at the presynaptic level [36]. Since the degree of excitability of the central nervous system is estimated by locomotion, this decrease in motor action suggests the *A. trilobata* extracts might have sedative effects.

The anxiolytic and locomotor or sedative effects of benzodiazepines (e.g. diazepam) are known to increase the activity of GABA-A. Benzodiazepines bind at the α subunit, which opens the chloride ion channel, leading to hyperpolarisation. The biological effects of the *A. trilobata* extracts might be responsible for the GABA-A receptor, benzodiazepines, and nonbenzodiazepine agents. The anxiolytic and locomotor effects of benzodiazepines might result from the activation of glycine neurotransmitters in the brain [35, 37].

The FST and TST are widely used apparatuses for assessing the effects of antidepressants in rodents. Both tests are sensitive to quantifying the impact of all kind of antidepressant drugs (e.g. selective serotonin reuptake inhibitors, monoamine oxidase inhibitors and tricyclics) [38, 39]. In our study, the 400-mg/kg extract dose led to greater reductions in immobility similar to those of the standard drug fluoxetine. In an attempt to predict a positive outcome, *A. trilobata* extracts were assessed regarding their locomotor effects; however, the 400-mg/kg

dose of such did not demonstrate significant locomotion effects except for at a few points during the total observation time. Moreover, these reduction effects on FST and TST were thought to be due to antidepressant effects rather than locomotor-enhancing effects. According to the researcher, the GABA-A receptor is responsible for depression-like behaviours. Patients deficient in GABA as well as who show a decreased level in the GABA-A receptor might suffer from depression. As such, agents that mimic the GABAergic receptor might be effective in reducing the severity of depression [40]. The finding that *A. trilobata* extracts show antidepressant effects might be due to the activation of the GABAergic system.

Conclusion

According to the present study, *A. trilobata* extracts are a potential source of neuropharmacological effects and exhibit significant anxiolytic, locomotor and antidepressant activities. Notably, the anxiolytic and antidepressant effects might be mediated by the GABAergic system. However, further research is required to predict the possible mechanisms that are behind the neuropharmacological effects of *A. trilobata*.

Abbreviations

MEATL: Methanol extract of *A. trilobata* leaves; NFATL: n-Hexane fraction of *A. trilobata* leaves; MEATS: Methanol extract of *A. trilobata* stem; NFATS: n-Hexane fraction of *A. trilobata* stem; EPM: Elevated plus maze; HBT: Hole-board test; OFT: *Open field test*; *HCT*: *Hole-cross test*; FST: Forced swimming; TST: Tail suspension test; b.w.: Body weight; IP: Intraperitoneal route; SEM: Standard error mean

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Authors' contributions

MAIA, NB and AMT planned and designed the research. MAS, MAUC and TBE arranged the whole facilities for the research and supervised the whole research. MAIA, NB and AMT conducted the entire laboratory works with NA and RJP and MNM. MAIA, NB and AMT imparted in study design and interpreted the results putting efforts on statistical analysis with MNM and MAUC. AMT, MAIA, NB, AMT and TBE participated in the manuscript draft and has thoroughly checked and revised the manuscript for necessary changes in format, grammar and English standard. All authors read and agreed on the final version of the manuscript. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study approved by the Institutional Animal Ethical Committee, Department of Pharmacy, International Islamic University Chittagong, Bangladesh, according to governmental guidelines under the reference of Pharm/PND/150/20-2019. For ethical reasons, each animal was used only once and all animals were sacrificed at the end of the study. *Adenia trilobata* was freshly collected from the Hajarikhil Hill tract area, Chittagong, Bangladesh, in February 2019, which was authenticated by an expert plant taxonomist Md. Anwarul Islam, Department of Botany, Jahangirnagar University, Savar, Dhaka-1342, Bangladesh, under accession number Anwar-0311.

Consent for publication

Not applicable

Competing interests

Authors declared that they have no conflict of interest.

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