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Research Article

Effects of *Mimosa pudica* Linn. Extract on Reducing Seizures, Memory Impairment, and Emotional Disorders in a Mouse Model of Temporal Lobe Epilepsy Induced by Trimethyltin

Hoang Hai Nguyen[1], Quang Tuan Kiet Le[1], Nguyen Minh Tho Ho[1], Ngoc Phuc Nguyen[1], Thanh Binh Nguyen[2,3], Quynh Dieu Trinh[4], Lam Truong Tuong[1], Phi Hoang Yen Tran[1], Huynh Nhu Mai[1,*]

1 University of Medicine and Pharmacy at Ho Chi Minh city, Ho Chi Minh city, 700000, Vietnam
2 Thu Dau Mot University, Binh Duong, 820000, Vietnam
3 Pham Ngoc Thach University of Medicine, Ho Chi Minh city, 700000, Vietnam
4 Ton Duc Thang University, Ho Chi Minh city, 700000, Vietnam

ABSTRACT

Mimosa pudica Linn., commonly known as "Mắc cỡ" in Vietnam, is a medicinal plant with anti-inflammatory, antibacterial, anxiolytic, and antidepressant properties. Despite its potential, there is a limit to the amount of research on its effects on conditions such as seizures and associated emotional impairment, as well as memory impairment. This study aims to investigate the impact of improving memory and emotional impairment of the extract on the mice induced with trimethyltin (2.5 mg/kg, i.p.). *Mimosa pudica* Linn. was extracted with 96% ethanol at a ratio of 1:15 (w/v). Mice were divided into 5 groups: control group, disease group, positive control group receiving galantamine 10 mg/kg/day for memory and behavior test or carbamazepine 10 mg/kg/day for seizure score, and treatment groups receiving extract (200 mg/kg/day and 400 mg/kg/day). The effects of treatment were assessed using the Elevated Plus Maze (EPM) for emotional disorders; the Morris Water Maze (MWM) and the Novel Object Recognition (NOR) for memory improvement. Compared to the control group, the extract at both doses increased the number of entries and time mice spent in the open arm in the EPM. In the MWM model, the extract at both doses increased the time mice spent swimming in platform area and decreased the time mice needed to find the escape platform during training days. Mice receiving extract at both doses spent more time exploring the new object in NOR. In summary, the MP extract has the effects of reducing seizures, ameliorating emotional disorders and memory impairment in mice injected with trimethyltin.

Keywords:
Mimosa pudica Linn.; Trimethyltin; Seizures; Memory impairment

1. INTRODUCTION

According to WHO, epilepsy is a chronic noncommunicable disease of the brain that affects around 50 million people worldwide, making it one of the most common neurological disorders globally[1]. The prevalence of epilepsy is higher in developing countries, accounting for about 80% of cases. The risk of early death in people with epilepsy is three times higher than in the general population[2]. Nowadays, with advances in science, technology, and medicine, there is hope for better treatment strategies, including medication and non-drug therapies, to stabilize or even cure the condition. However, human trials for epilepsy still have

***Corresponding author:**
***** Huynh Nhu Mai Email: mhnhu@ump.edu.vn

many limitations, hence the need to conduct research on an animal model that simulates epilepsy.

The organotin compound trimethyltin chloride (C_3H_9ClSn) (TMT) is a potent neurotoxin that selectively targets and damages nerve cells in the limbic system, especially the dentate gyrus[3]. Animals exposed to TMT develop behavioral changes (hyperactivity and aggression), impaired cognition (memory loss and decreased learning ability), and spontaneous seizures. TMT induces selective cell death in the nervous system, with severity and extent varying depending on the species studied and the dosage[4].

The *Mimosa pudica* Linn. is a popular plant in Vietnam and some countries in the region. Studies have shown that the *Mimosa pudica* extract (MP extract) brings about many impressive effects in medical treatment such as anti-inflammatory, antibacterial, sedative, antidepressant, and especially strong anti-seizure properties and can reduce other symptoms associated with epilepsy[5]. However, there is still a limit to the number of in-depth scientific research on this plant's effects such as reducing the symptoms of temporal lobe epilepsy. Therefore, the effects of reducing seizures, reducing memory impairment, and emotional disorders of MP extract in mice exposed to TMT were investigated in this study.

These above issues are the reason for investigating the reduction of seizure, memory impairment and emotional disturbances of MP extract in Temporal Lobe Epilepsy simulating model caused by trimethyltin.

2. MATERIALS AND METHODS

2.1. Animals

Young male Swiss albino mice that were 5 - 6 weeks old and weighed 25 ± 2 g were purchased from the Pasteur Institute in Ho Chi Minh city. They were acclimatized to the environment for 14 days prior to the experiment. All the experiments were carried out in the laboratory of the Department of Pharmacology, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam and in strict accordance with the guidelines for care and use of laboratory animals. The experiments were approved by the Ethics Committee for Animal Research of University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam (Number 590/GCN - HDDDNCTDV).

2.2. Plant material

Mimosa pudica Linn. was purchased from Thanh Binh herbal tea CO., LTD in Ho Chi Minh City and identified by amplifying the rbcL gene and comparing with data from the GenBank of BLAST search results at NCBI[6]. The plants were ground and extracted using 96% ethanol (EtOH). 200 g of *Mimosa pudica* Linn. powder was soaked in 96% EtOH solvent at room temperature with a medicinal herb/solvent ratio of 1:15 (kg/l). The extract was then obtained and the solvent was removed under decreased pressure to yield the concentrated extract. The experiments were conducted in Department of Medicinal Chemistry, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City.

2.3. Acute toxicity

The procedure of acute toxicity followed the Guidelines for preclinical and clinical trials of Traditional Medicine and Herbal Medicines by the Vietnam Ministry of Health[7] and OECD[8,9] with slight modifications. All animals were fasted overnight, with free access to water and weighed before oral administration of the MP extract. The mice were divided into 2 groups (n = 10 each group). Group 1 (Control) received distilled water orally at a dose of 0.1 ml/10g; Group 2 (MP extract) received the MP extract at maximum concentration of the extract in water that can go through the feeding tube. The animals were then observed for any abnormalities in the first 24 hours and changes in general behaviors, physical condition, waste, and mortality rate in 72 hours. If any deaths were recorded, the dead subject would be kept for macroscopic analysis, and the lethal dose of 50% of the animals tested (LD50) would be determined by testing on new groups of mice with a different dose range. Based on the number of animals that died within each dose, calculate the LD50 using the Karber – Behrens formula. If no death was recorded in 72 hours, the mice were then observed and their body weights and abnormalities (if any) were recorded within 14 days.

2.4. Experimental design for evaluating seizure score and histopathology

The mice were divided into 5 groups (n = 10 each group).

Group 1 (Control): distilled water, p.o.

Group 2 (TMT): TMT (2.5 mg/kg, i.p.) and distilled water, p.o.

Group 3 (MP 200 mg/kg): TMT (2.5 mg/kg, i.p.) and MP extract (200 mg/kg/day, p.o.)

Group 4 (MP 400 mg/kg): TMT (2.5 mg/kg, i.p.) and MP extract (400 mg/kg/day, p.o.)

Group 5 (CBZ): TMT (2.5 mg/kg, i.p.) and carbamazepine (10 mg/kg/day, p.o.).

All the reagents [TMT (146498, Sigma-Aldrich, U.S.A), Carbamazepine (Novartis Farma S.p.A. Italy)] and MP extract were prepared immediately before use. The dosage of TMT[10], MP 200 and MP 400 were chosen

based on our pilot study and previous studies[11]. The treatment started 7 days prior to TMT injection. After injected with TMT, the mice were scored for seizures every day and were sacrificed on day 2. The brains of the mice were then perfused and 15 μm sections were prepared for H&E staining to evaluate histopathology on the DG region.

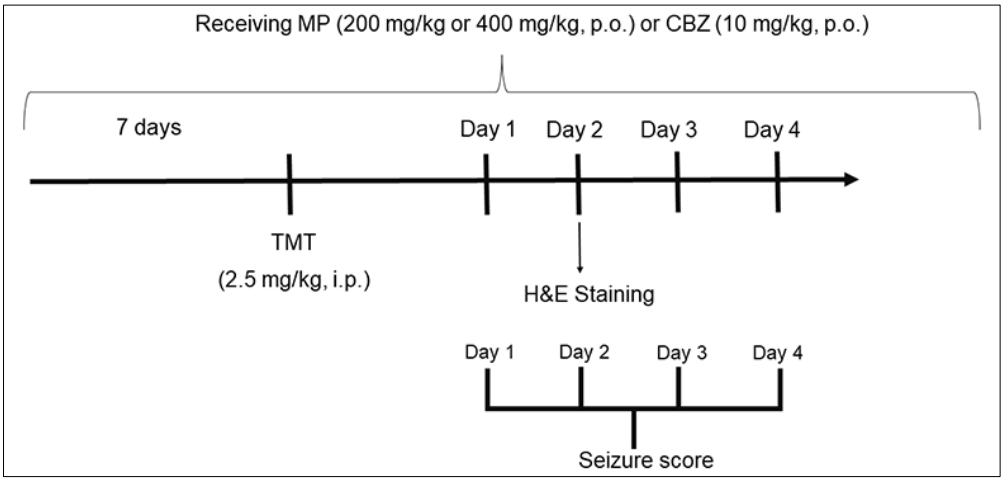

Figure 1. Experimental design for evaluating the protective effect of MP extract on seizure score and histopathology in DG region induced by TMT.

2.5. Seizure score

The seizure score test was performed daily from day 1 to day 4 after TMT injection. Mice were released into a fully lit place (in a 40 x 40 x 30 cm cage) and their behaviors were observed. Behavioral changes were assessed according to the seizure score as follows:
Aggression = 1 score; Weak tremor = 2 scores; Systemic tremor = 3 scores; Tremor and spasmodic gait = 4 scores; Death = 5 scores[12].

Seizure score = Daily average seizure score of all the mice in group ± SEM

2.6. Perfusion

The procedures of perfusion were carried out as previously described[13]. Briefly, mice were perfused transcardially with 50 mL of ice-cold PBS (10 mL/10 g body weight) followed by 4% paraformaldehyde (20 mL/10 g body weight). Brains were collected and stored in 4% paraformaldehyde for 2 days at 4°C. The brains were then transferred to a 30% (w/v) sucrose solution.

2.7. H&E staining

Brains were embedded in paraffin using a Tissue-TEK TEC 5 tissue embedding machine (Sakura Finetek Japan.Co, Tokyo, Japan) and 15 μm sections were prepared using a CUT4060 machine (Microtec Viet Nam, Ho Chi Minh, Vietnam). These sections were stained with hematoxylin and eosin according to a standard protocol[14]. The surviving nerve cells in DG were counted using Java-based image processing program ImageJ (NIH Image, https://imagej.net/ij/). The experiments were conducted in Tissues and Cells Unit, Biomedical Research Center, Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam.

2.8. Experimental design for the model of memory impairment and emotional disorder

The mice were divided into 5 groups (n = 10 each group).

Group 1 (Control): distilled water, p.o.

Group 2 (TMT): TMT (2.5 mg/kg, i.p.) and distilled water, p.o.

Group 3 (MP 200 mg/kg): TMT (2.5 mg/kg, i.p.) and MP extract (200 mg/kg/day, p.o.)

Group 4: (MP 400 mg/kg): TMT (2.5 mg/kg, i.p.) and MP extract (400 mg/kg/day, p.o.)

Group 5 (Gal): TMT (2.5 mg/kg, i.p.) and Galantamine (10 mg/kg/day, p.o.)

The treatment started from 7 days prior to TMT injection until 14 days after injection. After 14 days of TMT injection, mice were evaluated for memory impairment and anxiety based on 3 models: Elevated Plus Maze (EPM), Novel object recognition (NOR) and Morris Water Maze (MWM) model[10]. All the experiments were conducted in Laboratory Animal House, Department of Pharmacology, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City.

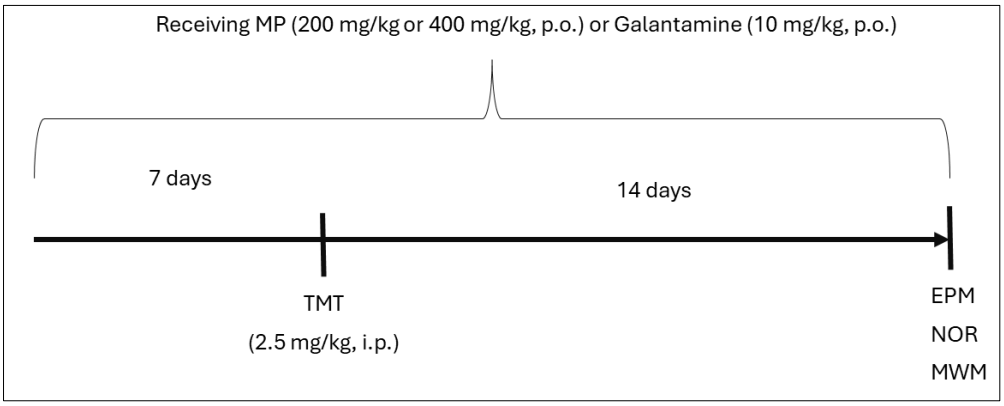

Figure 2. Experimental design for evaluating the protective effect of MP extract on the model of memory impairment and emotional disorder induced by TMT.

2.9. Elevated Plus Maze (EPM)

Elevated Plus Maze was performed as previously described[15,16]. The mice were injected with TMT and received medication for 14 consecutive days. On the 14th day, 60 minutes after taking the medication, each mouse was placed in the center of the experimental apparatus, with its face towards an open arm.

Number of entries = the number of entries into the open arm in 5 minutes

Time (s) = Time the mice spent in the open arm (s)

2.10. Novel Object Recognition (NOR)

Novel Object Recognition was performed as previously described[17].

The familiarization session: the mouse freely explored the box for 5 minutes.

The training session: the mouse was exposed to two identical objects for 5 minutes, during which the time it interacted with the objects was recorded (the mouse was considered to be exploring when it showed signs of sniffing and active observation).

The testing session: the mice were presented with one of the previous objects and a new object in the opposite corners of the box for 5 minutes, during which the time it interacted with the new and old object was recorded. The test apparatus was cleaned with alcohol before the next animal was tested.

$$\%\text{Time} = \frac{a}{a+b} \times 100$$

a: time mice interacted with the new object (s)

b: time mice interacted with the old object (s)

2.11. Morris Water Maze (MWM)

Morris Water Maze was performed as previously described[18]. The training phase began by placing the mouse on the escape platform for 20 seconds to allow orientation to the external cues. After orientation, the mice were gently lowered by the tail into a quarter of the pool that did not contain the escape platform. The maximum swimming time of the mouse was 60 seconds. If the mouse did not reach the platform after 60 seconds of swimming, the mouse was then gently guided to the platform and allowed to stand on the platform for 20 seconds before being removed from the pool. After being removed from the pool, the mouse was manually dried. The mouse was tested over 5 days, twice a day, about 30 minutes apart. All trials were conducted at nearly the same time each day to minimize changes in performance over time within the day. The test phase was performed 24 hours after the final training session. During the test phase**,** the escape platform was removed from the pool and the mouse was allowed to swim freely for 1 minute. The target quadrant was the quadrant containing the platform. The swimming process of the mouse was recorded. In the training phase the time mice reached the platform was recorded and calculated as follows:

Time (s) = time the mice spent to find the platform (s)

In the test phase, the time mice spent swimming in the target quadrant was recorded and %Time was calculated as follows:

$$\%\text{Time} = \frac{Time\ mice\ spent\ swimming\ in\ the\ target\ quadrant\ (s)}{60}$$

2.12.Statistical analysis

Data were presented as Mean ± SD (standard deviation) or SEM (standard error of mean). Statistical analysis was conducted using one-way analysis of variance (one-way ANOVA), repeated-measures ANOVA (Morris Water Maze test) followed by post hoc Tukey's test. Results were considered statistically significant at a value of $P < 0.05$. GraphPad Prism 8.0.2 (GraphPad Software Inc., San Diego, CA, USA) was used to perform all statistical analysis.

3. RESULTS

3.1. Acute toxicity

No abnormalities in mice were observed after 72 hours, and no death were recorded. Mice were regularly monitored for 14 days; no aberrant behaviors were observed, mice ate, drank, and urinated normally, and their weights remained consistent. The weights of mice receiving the MP extract were not different from the control group. After 14 days, mice were sacrificed; there were no abnormalities in form or color of the mice's internal organs, and there was no difference between the control group and the treated group.

3.2. Effect of MP extract on seizure score

The effect of MP extract on seizure is shown in Figure 3. The mice started seizing after 1 day, peaking on day 2; then the level of seizures gradually decreased. After 4 days of injecting TMT, mice began to stop having seizures and after 8 days of testing, mice completely stopped having seizures in all test groups.

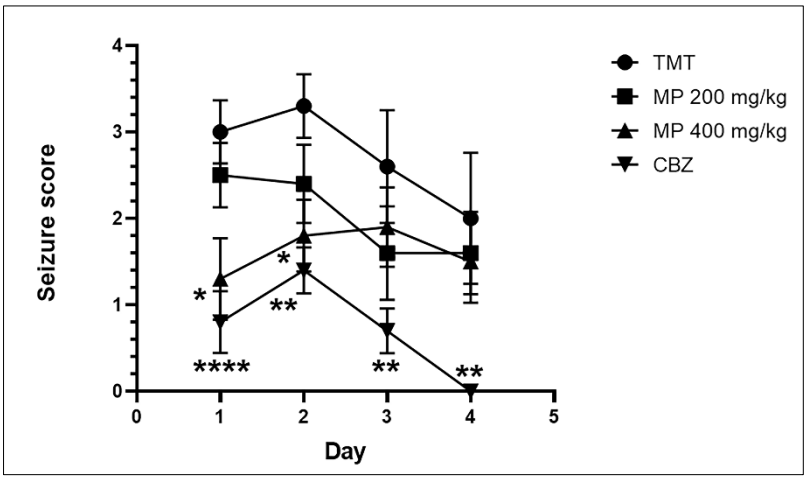

Figure 3. Seizure scores in 4 days. The data were presented as mean ± SEM (n=10 mice in each group) using one-way analysis of variance (one-way ANOVA) followed by post hoc Tukey's test. *P < 0.05; **P < 0.01; ****P < 0.0001 vs TMT group. TMT = trimethyltin, MP = *Mimosa pudica* Linn. extract, CBZ = carbamazepine.

The death rate of mice is shown in Table 1. Mice receiving the MP extract at both doses showed reduced death rate during the testing days, while no mortality in the CBZ group was recorded.

Table 1. Death rate of mice after TMT injection

	Day 1	Day 2	Day 3	Death rate
Control	0	0	0	0%
TMT	1	1	1	30%
MP 200 mg/kg	0	1	0	10%
MP 400 mg/kg	1	0	0	10%
CBZ	0	0	0	0%

3.3. Effect of MP extract on DG histology

DG histology after injecting TMT for 2 days is shown in Figure 4A. The cell loss was observed in the DG in the TMT group but was not observed in the MP 200 mg/kg and 400 mg/kg groups. Figure 4B reveals the comparisons of the surviving nerve cells in DG in the other 4 groups with Control group. The results were shown as percentage (%). As seen in Figure 4B, the percentage of surviving nerve cells in TMT group decreased significantly as compared to the control group. All treatment groups (MP 200, MP 400 and CBZ) showed protective effects against TMT-induced nerve cell loss, though the differences were not statistically significant.

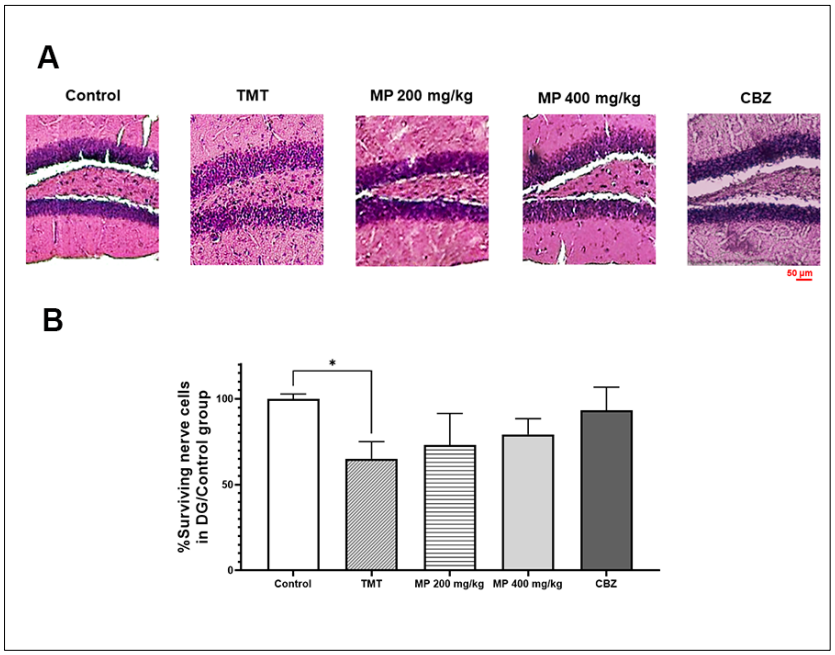

Figure 4. H&E staining in DG region on day 2 of TMT injection at 4x magnification (A), Percentage of surviving nerve cells in DG in other groups compared to Control group (B). The data were presented as mean ± SD (n=3 mice in each group) using one-way ANOVA followed by post hoc Tukey's test. TMT = trimethyltin, MP = *Mimosa pudica* Linn. extract, CBZ = carbamazepine. Scale bar = 50 µm.

3.4. Effect of MP extract on EPM

As shown in Figure 5A, TMT decreased the number of times mice entered the open arm when compared to the control group ($P < 0.05$). The numbers of entries in the MP extract at 400 mg/kg and the galantamine groups were higher than the TMT group ($P < 0.05$). The MP 200 mg/kg also elevated both the time mice spent in the open arm and the number of entries compared to TMT, though the difference was not statistically significant.

According to Figure 5B, mice only receiving TMT spent much less time in the open arm as compared to the control group ($P < 0.001$). Both MP extract at 400 mg/kg and galantamine significantly increased the time mice spent in the open arm, with the differences being $P < 0.05$ vs. TMT and $P < 0.01$ vs. TMT, respectively.

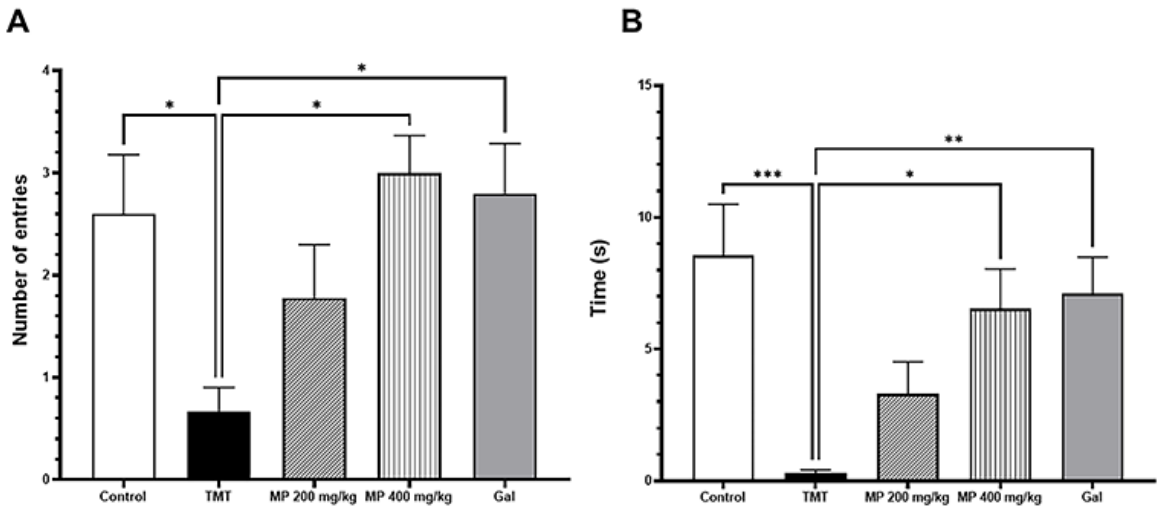

Figure 5. The effect of MP extract on number of entries into the open arm (A) and time mice spent in the open arm (B) in Elevated plus maze (EPM). The data were presented as mean ± SEM (n=10 mice in each group) using one-way ANOVA followed by post hoc Tukey's test. *P < 0.05; **P < 0.01; ***P < 0.001. TMT = trimethyltin, MP = *Mimosa pudica* Linn. extract, Gal = galantamine.

3.5. Effect of MP extract on NOR

As shown in Figure 6, the treatment with MP extract at both doses at 200 mg/kg (P < 0.0001) and 400 mg/kg (P < 0.001) significantly increased the time mice spent exploring the new object compared to the TMT group. The time mice spent exploring the new object accounted for 74% and 73% of the total exploration time in MP 200 mg/kg and MP 400 mg/kg, respectively. Meanwhile, mice receiving only TMT spent significantly less time exploring the new object in comparison with the control group (P < 0.05), accounting for 51% of the total exploration time.

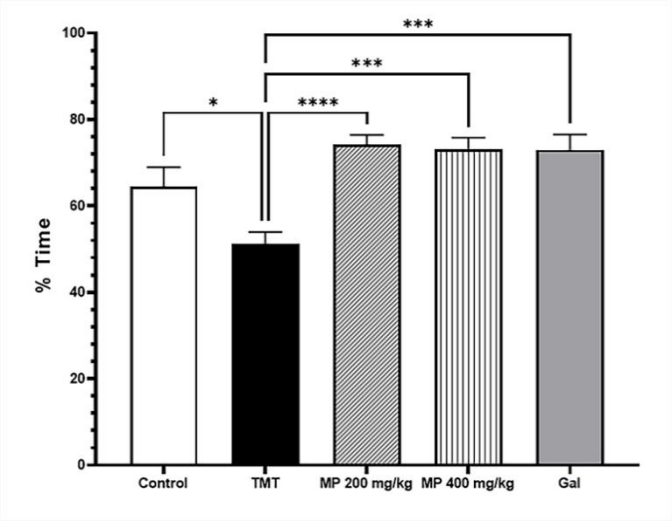

Figure 6. The effect of MP extract on the percentage of time mice explored new objects in Novel object recognition (NOR). The data were presented as mean ± SEM (n=10 mice in each group) using one-way ANOVA followed by post hoc Tukey's test. *P < 0.05; ***P < 0.001; ****P < 0.0001. TMT = trimethyltin, MP = *Mimosa pudica* Linn. extract, Gal = galantamine.

3.6. Effect of MP extract on MWM

According to Figure 7A, the time for mice to find the escape platform decreased significantly in all groups throughout the experiment. On the 5th day of the experiment, the time for mice to find the escape platform of MP 200 mg/kg and MP 400 mg/kg groups were respectively 20.5 and 22.95 seconds, while this figure of the group only injected with TMT was 36.05 seconds.

The effect of MP extract on the swimming time in the platform area is shown in Figure 7B. The treatment with MP extract at both doses at 200 mg/kg (P<0.05) and 400 mg/kg (P < 0.01) significantly increased the time mice spent swimming compared to the TMT group. These figures accounted for 18.67% and 20.0% of the total swimming time respectively, and approximately twice the swimming time of mice injected with TMT.

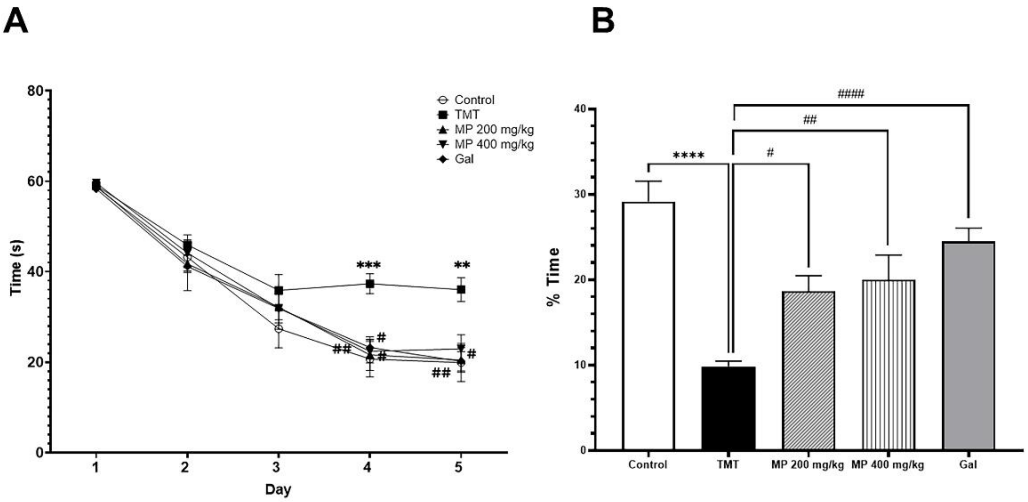

Figure 7. The effect of MP extract on the time required to find the escape platform (A) and percentage of time swimming in the platform area (B) in Morris water maze (MWM). The data were presented as mean ± SEM using one-way ANOVA with repeated-measures for the time required to find the escape flatform (A), one-way ANOVA for percentage of time swimming in the platform area (B) followed by post hoc Tukey's test. **P < 0.01, ***P < 0.001, ****P < 0.0001 vs Control group. #P < 0.05, ##P < 0.01, ####P < 0.0001 vs TMT group. TMT = trimethyltin, MP = *Mimosa pudica* Linn. extract, Gal = galantamine.

4. DISCUSSION

Mimosa pudica Linn. is a medicinal herb that has long been used worldwide, therefore its safety has been verified. Previous studies have indicated that the MP extract did not exert any detrimental effects when administered up to a level of 2000 mg/kg/day[19]. Long-term testing in mice showed no abnormalities after oral administration of the extract in 21 days[20] and 28 days[21]. After being administered a dose of 2.5 mg/kg of TMT, mice exhibited onset of seizures after one day, peaking after two days. A reduction in the severity of seizures was observed by the fourth day post-TMT administration, therefore the seizure score was usually recorded until 4 days of experiment. Moreover, the death rate also peaked after two days (Table 1), and the nerve cell loss was confirmed at this time-point (Figure 4). Those results were consistent with the results of other studies on TMT models[22]. This could be due to TMT-induced nerve cell loss in the DG, which would cause anomalies in neurotransmitters, leading to spontaneous seizures. During the experimental process, a mortality rate of 30% was noted in mice following TMT injection, in contrast to a 0% rate in those administered carbamazepine, and 10% in those receiving MP extract. This could be due to TMT inhibiting the activity of the Na^+/K^+ - ATPase, causing the death of heart cells[23]. The results showed that MP extract helped reduce the severity of seizures and mortality rate in mice after TMT injection

Mice injected with TMT showed symptoms of central nervous system disturbances such as seizures, memory impairment, and emotional disorders. These neurological damages are attributed to TMT-induced loss of nerve cells in the hippocampal dentate gyrus (DG) area, which is responsible for learning, memory, and emotional processing in mice[4,24]. Several hypotheses have been proposed to explain TMT-induced cell loss mechanism, including oxidative stress, glutamate toxicity, neuroinflammation, intracellular calcium overload, impaired neural transmission, and mitochondrial dysfunction[25]. Still, the precise mechanism behind TMT-induced nerve cell loss remains unclear. In this study, we observed early post-TMT injection nerve cell loss in the hippocampus DG on day 2 (Figure 4). Nonetheless, these DG nerve cells showed spontaneous regenerative recovery[26]. This explains why, post 4 days of TMT injection, symptoms like tremors and seizure in mice reduced, though other impacts like memory reduction, learning impairment, and emotional disorders persisted (Figures 5-7).

The elevated plus maze (EPM) is widely used for assessing anxiolytic and sedative drug effects. This model is based on two behavioral traits in mice: exploratory inclination and self-defense instinct. The exploratory preference of mice is expressed by their tendency to go out to the open arms and the defensive instinct is expressed by their tendency to stay in the closed arms. Mice injected with TMT spent most of their time choosing to be in the closed arms, the reason could be due to TMT reducing the function of the GABA receptor and causing neurological disorders[27]. The MP extract may have an agonistic effect on GABA/benzodiazepine receptor complex and tend to act as diazepam, since flavonoids and diazepam are structurally similar. Therefore, anxiolytic activity of the MP extract may be due to the presence of flavonoids and alkaloids[28]. Other studies showed that the extract had anxiolytic and sedative effects in various mouse models[5].

Other studies on novel object recognition (NOR) indicated that two brain regions, the perirhinal cortex and the hippocampus, influence outcomes[29]. The perirhinal cortex plays a role in object recognition and relaying signals to the hippocampus for memory storage. Within this study's scope, we evaluated TMT's impact on the hippocampus but not on the perirhinal cortex. Therefore, we were unable to determine the precise cause of TMT-induced short-term memory loss, whether it was due to object non-recognition or memory impairment. However, other studies have shown that DG nerve cells function as a portal for information to enter the hippocampus, and they also take on the responsibility of processing incoming data before storing it in the CA[30]. Therefore, the nerve cell loss in the DG significantly affected the learning and memory abilities of mice exposed to TMT.

In the Morris water maze (MWM), mice administered the MP extract showed a shorter platform location time and spent more time in the platform area compared to the TMT group. The reason could be that TMT damaged the nerve cells in areas of the hippocampus such as CA1, CA3, DG, which are associated with memory degradation and spatial cognition impairment in mice[4]. As mentioned above, DG cells play a crucial role in the learning and memory activities of mice as they enable the mice to retain and process information. Studies indicated that mice losing around 90% of the DG cells would have difficulty in navigating previously directed mazes, thus it would see this as its first time entering the maze the next time it entered[31]. Another study demonstrated that mice exposed to TMT experienced memory impairment, as evidenced by their increased time needed to locate the platform[10]. Memory decline is due to TMT-induced hippocampal nerve cell damage, which is crucial for memory and learning in mice. Cell loss in hippocampus is related to the mice's learning and memory abilities, which aligns with previous publications[32,33].

Mimosa pudica Linn. is commonly used as a herbal medicine in some Asian countries and the effect of reducing seizures in mice caused by strychnine, pentylenetetrazol, isoniazid have been shown in previous studies[19,34]. In addition, other research also

showed the antidepressant effect of the extract on rats[35]. Botanical studies showed that the MP extract contains components such as flavonoids, tannins, terpenoids, coumarins, alkaloids, steroids, phenols, and saponins[5]. Based on the present knowledge of the chemical constituents, it is not possible to confirm the exact mechanism of the *Mimosa pudica*'s effect on anticonvulsant and antidepressant activities, however there are articles indicating that the active ingredients in the plant act as a benzodiazepine-like in the nervous system and regulate GABA-mediated chloride channels in animal models of anxiety, sedation and convulsions[28]. Further studies are needed to isolate the biologically active substances responsible for these effects. To the best of our knowledge, this is the first study to demonstrate the effects of reducing seizure, anxiety, and enhancing memory of the MP extract on TMT model, but additional investigation is required to precisely identify the mechanism behind these effects.

Mimosa pudica, *Valeriana officinalis*, *Piper methysticum*, *Matricaria chamomilla*, and *Passiflora incarnata* all have anticonvulsant and anti-anxiety properties, but each plant has a different mechanism of action and various active components that contribute to their effects[36]. *Mimosa pudica* Linn. has been known as a long-standing traditional remedy due to its wide range of therapeutic properties[35]. Therefore, its safety and efficacy on humans have been verified. However, this is the first time it has been used to treat temporal lobe epilepsy induced by TMT. Although initial results showed the therapeutic potential of MP, its precise molecular mechanism of action is still unclear. To fully understand its mechanism, efficacy, safety, and any potential toxicities, more research is needed. That should be defined as the next and most crucial step for translating these findings to clinical settings. Once we have a comprehensive understanding of it, clinical trials on humans can be conducted to validate the therapeutic potential.

5. CONCLUSIONS

The *Mimosa pudica* Linn. extract at 400 mg/kg/day had the effect of reducing seizure and improving emotional disorder. MP extract at both doses 200 mg/kg/day and 400 mg/kg/day could improve short-term and long-term spatial memory in mice injected with trimethyltin.

6. ACKNOWLEDGEMENTS

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Author contribution

H.H.N: Methodology, data curation, writing draft, investigation; Q.T.K.L: Methodology, writing - original draft; N.M.T.H: Visualization, methodology, data curation; N.P.N: Methodology, validation, formal analysis; T.B.N: Methodology, H&E staining, visualization; Q.D.T: Methodology, validation; L.T.T: Methodology, investigation; P.H.Y.T: Writing – original draft, methodology, formal analysis; H.N.M: Writing – review & editing, validation, conceptualization, supervision, formal analysis

Conflict of interest

The authors declare no conflict of interest.

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Ethics approval

The animal experiments were approved by the Ethics Committee for Animal Research of University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam (Number 590/GCN- HDDDNCTDV).

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