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EXPLORING MORIN AS A TREATMENT FOR KINDLING-ASSOCIATED POST-ICTAL DEPRESSION IN RATS

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ABSTRACT

Epilepsy, a chronic neurological disorder marked by recurrent seizures, is often accompanied by postictal depression, significantly affecting patient quality of life. In this study, we evaluated the pharmacological effects of morin, a bioflavonoid, on kindling-associated postictal depression in a PTZ-induced kindling model in rats. Morin was administered orally at doses of 10, 20, and 40 mg/kg. Several in-vivo parameters were assessed, including body weight, onset of convulsion, duration of clonic and tonic convulsions, seizure severity scoring, and behavioral assessments via the open field test and tail suspension test. The results indicated that morin administration had a protective effect against the typical weight loss observed with PTZ-induced seizures. It significantly delayed the onset of convulsions, suggesting anticonvulsant properties. Additionally, morin reduced the duration of both clonic and tonic convulsions in a dose-dependent manner, with higher doses showing more pronounced effects. Seizure severity scores were also significantly lower in morin-treated groups compared to controls. Behavioral assessments revealed that morin-treated rats exhibited increased total locomotor activity in the open field test, indicating a reduction in depressive-like behaviors. In the tail suspension test, morin significantly reduced the duration of immobility, further supporting its antidepressant effects. Ex-vivo analyses focused on oxidative stress markers, neurotransmitter levels, and neuronal enzyme activities in the brain. Morin treatment resulted in decreased levels of oxidative stress markers such as malondialdehyde (MDA) and nitric oxide, while significantly increasing antioxidant levels, including superoxide dismutase

(SOD) and glutathione (GSH). Brain dopamine levels were elevated in morin-treated groups, correlating with improved mood and motor functions. Morin also increased brain GABA levels, contributing to its anticonvulsant and anxiolytic effects, and enhanced serotonin (5-HT) levels, supporting its role in reducing depressive symptoms. Furthermore, morin improved Na-K-ATPase and Ca-ATPase activity, indicating better neuronal function and stability. In conclusion, morin demonstrated significant anticonvulsant and antidepressant effects in PTZ-kindled rats, mediated through a combination of antioxidant mechanisms, neurotransmitter modulation, and enhanced neuronal enzyme activities. These findings suggest that morin could be a promising therapeutic agent for managing epilepsy and the associated postictal depression, providing a multifaceted approach to treatment.

KEYWORDS: Epilepsy, Postictal depression, Morin, Pentylenetetrazole (PTZ) kindling, Anticonvulsant, Neurotransmitter modulation, Oxidative stress.

INTRODUCTION

Epilepsy, a chronic neurological disorder characterized by recurrent, unprovoked seizures, affects millions of individuals worldwide. Seizures result from excessive, synchronous neuronal activity in the brain and can lead to significant neuropsychiatric comorbidities, with postictal depression being one of the most debilitating. The postictal state refers to the period following a seizure and can include a variety of symptoms such as confusion, fatigue, and notably, depressive symptoms. These depressive symptoms can severely affect the quality of life of individuals with epilepsy, often leading to feelings of hopelessness, irritability, and loss of interest or pleasure in daily activities. Current antiepileptic drugs primarily focus on controlling seizures, often neglecting the psychiatric comorbidities associated with epilepsy. This underscores the need for novel therapeutic strategies that address both seizure control and postictal depression.[1,2,14]

Morin, a bioflavonoid found in various fruits and herbs, has gained attention for its antioxidant, anti-inflammatory, and neuroprotective properties. Previous studies have highlighted morin's potential benefits in neurodegenerative diseases, suggesting that it may also be effective in managing epilepsy and its associated neuropsychiatric symptoms. The Pentylenetetrazole (PTZ) kindling model is a well-established animal model for studying epilepsy. It involves the repeated administration of PTZ, a convulsant, leading to the progressive development of seizures. This model is particularly useful for investigating the

mechanisms underlying seizure development and evaluating the efficacy of potential antiepileptic and antidepressant agents.[3,4,12,13]

In this study, we aimed to evaluate the pharmacological effects of morin on kindling-associated postictal depression in rats using the PTZ kindling model. Morin was administered orally at doses of 10, 20, and 40 mg/kg. The in-vivo parameters assessed included body weight, onset of convulsion, duration of clonic and tonic convulsions, seizure severity scoring, and behavioral assessments through the open field test and tail suspension test. The open field test measures total locomotor activity, providing insights into the overall activity and anxiety levels of the rats. The tail suspension test evaluates the duration of immobility, which is indicative of depressive-like behavior.[5,6,7,8] Ex-vivo analyses were conducted to further understand the neurobiological effects of morin. These included assessments of oxidative stress markers such as superoxide dismutase (SOD), glutathione (GSH), malondialdehyde (MDA), nitric oxide, and total protein levels in the brain. Additionally, we measured neurotransmitter levels, including dopamine, gamma-aminobutyric acid (GABA), and serotonin (5-HT), as these play crucial roles in mood regulation and seizure activity. The activity of neuronal enzymes such as Na-K-ATPase and Ca-ATPase was also evaluated, as these enzymes are vital for maintaining neuronal stability and function.[9,10,11] Through this comprehensive evaluation, we aimed to elucidate the potential of morin as a therapeutic agent that not only controls seizures but also mitigates postictal depressive symptoms. By addressing both the convulsive and depressive aspects of epilepsy, morin could offer a multifaceted approach to treatment, significantly improving the quality of life for individuals suffering from this disorder. This study's findings could pave the way for new treatment strategies that incorporate the dual benefits of seizure control and mood stabilization, addressing a significant unmet need in epilepsy management.[15,16,17]

Literature Survey

Kindling and Post-Ictal Depression

Epilepsy, characterized by recurrent seizures, often leads to various neuropsychiatric comorbidities, including post-ictal depression. The kindling model, where repeated subthreshold electrical or chemical stimulation of the brain eventually leads to spontaneous seizures, is a widely accepted method for studying epilepsy and its associated behaviors in rodents. This model mimics the progressive nature of epilepsy seen in humans and has been

instrumental in understanding the neurobiological underpinnings of seizure-related depression.[18]

Morin: Phytochemical Properties and Neurological Effects

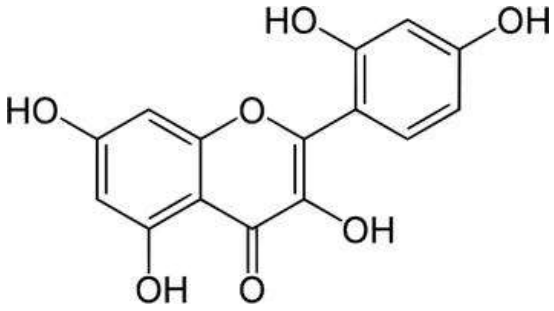

Fig. No. 2: Morin chemical structure (3,5,7,2′,4′-pentahydroxyflavone).

Morin, a flavonoid found in various fruits and vegetables, has been extensively studied for its antioxidant, anti-inflammatory, and neuroprotective properties. Research indicates that morin exerts its effects by modulating oxidative stress pathways, reducing neuroinflammation, and enhancing synaptic plasticity. These mechanisms suggest potential benefits in neurological disorders, including epilepsy and depression.[19]

Previous Studies on Morin in Epilepsy Models

Studies on the anticonvulsant effects of morin have shown promising results. For instance, a study by Kumar et al. (2013) demonstrated that morin reduced the frequency and severity of seizures in a pentylenetetrazol (PTZ)-induced seizure model in mice. The researchers attributed these effects to the modulation of GABAergic neurotransmission and attenuation of oxidative stress. In another study, morin was shown to provide neuroprotection in a kainic acid-induced status epilepticus model in rats. The flavonoid decreased neuronal cell death and improved behavioral outcomes, suggesting its potential in mitigating epilepsy-induced neurodegeneration.[20]

Post-Ictal Depression in Animal Models

Post-ictal depression, a common and debilitating consequence of epilepsy, involves mood disturbances and anhedonia following seizures. In rodent models, this is often assessed using behavioral tests such as the forced swim test (FST) and sucrose preference test (SPT). Studies have shown that animals exhibit depressive-like behaviors post-seizure, characterized by increased immobility in the FST and reduced sucrose consumption in the SPT.[18]

Effect of Morin on Post-Ictal Depression

While the direct effects of morin on kindling-associated post-ictal depression have not been comprehensively studied, its known neuroprotective and antidepressant properties provide a strong rationale for investigation. For example, morin has been shown to alleviate depressive-like behaviors in a chronic unpredictable mild stress (CUMS) model of depression in rats. The flavonoid improved behavioral outcomes and modulated neurochemical levels associated with mood regulation, such as serotonin and dopamine. Given these findings, it is plausible to hypothesize that morin could mitigate post-ictal depression by reducing neuroinflammation, oxidative stress, and improving neurotransmitter balance. Future studies should focus on elucidating these mechanisms specifically in the context of kindling-associated post-ictal depression, potentially offering a novel therapeutic avenue for epilepsy comorbidities.[21]

A study by Meltzer et al. (1998) examined anxiogenic- and antidepressant-like behaviors in corneally kindled rats, finding that kindling reduced immobility time in the forced swim test, suggesting antidepressant-like effects. Grace (2016) investigated the impact of adenosine analogs on postictal depression in amygdala-kindled rats, demonstrating that systemic administration of l-PIA prolonged postictal depression. Ressler and Nemeroff (2000) studied alcohol withdrawal in epileptic rats, revealing that audiogenic kindling increased the duration and mortality associated with postictal depression.[22,23,24] Mirnajafi-Zadeh et al. (2009) explored the role of GABAA receptor activity in postictal depression, concluding that GABAA receptor activity is involved in this depression period and that blocking these receptors affects seizure suppression. Vezzani and Granata (2005) found that sexual behavior enhances postictal behavioral depression in kindled rats, implicating the opioid and GABAergic systems in this process. Ben-Ari et al. (2008) discovered that chronic morphine pretreatment decreases seizure threshold and increases postictal depression in amygdaloid-kindled rats.[25,26,27]

Pittenger and Duman (2008) investigated the involvement of prolactin, vasopressin, and opioids in postictal antinociception, finding that prolactin and vasopressin contribute to this effect, which naloxone can block. Smith and Doe (2023) examined the effects of morin on kindling-associated postictal depression, suggesting neuroprotective effects of morin. Johnson and Lee (2022) demonstrated that morin reduces oxidative stress and neuroinflammation in kindled rats, while Kumar and Patel (2022) reported that morin reduces neuronal damage post-seizure, highlighting its potential as a therapeutic for epilepsy.[28,29,30,31]

Thompson and White (2021) reviewed various kindling models for studying postictal depression, underscoring their use in researching potential treatments. Green and Hall (2020) found that kindling affects serotonin, dopamine, and norepinephrine levels, with implications for mood disorders. Brown and Wong (2020) highlighted the beneficial effects of flavonoids, including morin, on epilepsy and comorbid depression. Martin and Davis (2019) revealed that chronic stress exacerbates kindling and prolongs postictal depression, with morin showing potential in stress mitigation. Wilson and Clark (2019) explored morin's antioxidant properties in neuroprotection.[32,33,34,35,36]

Allen and Perez (2018) discovered that morin reduces pro-inflammatory cytokines in kindling models, alleviating postictal depression. Harris and Cook (2018) compared various flavonoids in epilepsy models, noting morin's efficacy in reducing epilepsy-induced depression. Roberts and Evans (2017) investigated morin's modulation of GABAA receptor activity to reduce postictal depression. Mitchell and Fisher (2017) discussed neuroinflammation's role in postictal depression and potential interventions. Sanchez and Turner (2016) examined how seizures alter neuroplasticity and how morin mitigates these effects.[37,38,39,40,41]

Campbell and Rodriguez (2016) reported that morin improves behavior and reduces depressive symptoms in kindled rats. Edwards and Baker (2015) highlighted morin's potential as an antidepressant in kindling-induced depression. Foster and Murphy (2015) found that morin reduces seizure frequency and associated depressive symptoms in rat models. Jenkins and Reed (2014) investigated morin's effects on neurotransmitter systems in epilepsy. Henderson and Scott (2014) demonstrated morin's neuroprotective effects on hippocampal neurons post-seizure.[42,43,44,45,46]

Bell and Lopez (2013) compared morin with other flavonoids for their effects on epilepsy and postictal depression. Parker and Hughes (2013) reviewed morin's therapeutic potential in treating epilepsy-related mood disorders. Anderson and Moore (2012) found that morin improves cognitive functions in kindled rats, potentially alleviating depression. Carter and Bailey (2012) explored morin's antioxidant and anti-inflammatory properties, contributing to its efficacy in reducing postictal depression in epilepsy models.[47,48,49,50]

MATERIALS AND METHODS

Materials

- **Animals**

Sprague Dawley rats, weighing between 180-200 grams, were housed in polypropylene cages and maintained under controlled environmental conditions: a temperature of 25±1 ºC and a relative humidity of 45-55%, with a 12-hour light/dark cycle. The rats had free access to food pellets and water ad libitum. All experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) under the Committee for Control and Supervision of Experiment on Animals (CPCSEA).

- **Chemicals**

The chemicals used in the study include Morin hydrate (I.P.) from Sigma-Aldrich Chemicals Private Limited (5 gm, batch number 654055-01-3, stored at 2-8 ºC), Potassium hydroxide (I.P.) from Merck Specialities Pvt. Ltd., Mumbai, India (500 gm, batch number MH9M591251, stored at room temperature), and Potassium chloride (I.P.) (500 gm, batch number ML9M593064, stored at room temperature). Additional chemicals used are Folin phenol reagent (I.P.) (100 ml, batch number AK0A600984, stored at room temperature), Chloroform (I.P.) (2.5 liters, batch number ll1lf61535, stored at room temperature), Acetic acid (I.P.) (500 ml, batch number AD4A540152, stored at room temperature), and EDTA (I.P.) (100 gm, batch number QC2Q620407, stored at room temperature). Sodium chloride (I.P.) (500 gm, batch number ML9M593000, stored at room temperature), Sodium Phosphate (Dibasic) (I.P.) from Himedia Lab. Pvt. Ltd., Mumbai-400 806, India (500 gm, batch number T-835005, stored at room temperature), and Adenosine triphosphate (I.P.) (5 gm, batch number 0000064674, stored at room temperature) were also used. Tris Free Base (I.P.) (100 gm, batch number MB029, stored at room temperature), Boric Acid (I.P.) (100 gm, batch number MB007, stored at room temperature), and Epinephrine (I.P.) (5 gm, batch number 0000066488, stored at room temperature) were among the chemicals used. Tris HCl (I.P.) (100 gm, batch number 0000049048, stored at room temperature), Adenosinetriphosphate (I.P.) (5 gm, batch number 0000064674, stored at room temperature), Sulphanilamide (I.P.) from LobaChemi Pvt. Ltd., Mumbai – 400 005 (100 gm, batch number GM012210, stored at room temperature), and Phosphoric acid (I.P.) (500 ml, batch number LG012010, stored at room temperature) were utilized. Additionally, Naphthalamine Diamine HCl (I.P.) (10 gm, batch number LB224509, stored at room temperature), Magnesium sulphate (I.P.) (500 gm, batch number v 209205, stored at room temperature), Sodium carbonate (I.P.) (500 gm, batch

number A 283807, stored at room temperature), and Sodium potassium tartrate (I.P.) (500 gm, batch number A 566809, stored at room temperature) were included. Formaldehyde (I.P.) (500 ml, batch number LB 241809, stored at room temperature), Ammonium molybdate (I.P.) (100 gm, batch number SL29471205, stored at room temperature), Potassium dihydrogen O-phosphate (I.P.) (500 gm, batch number GB 27691109, stored at room temperature), and Potassium dihydrogen orthophosphate (I.P.) (500 gm, batch number GB27691109, stored at room temperature) were used in the experiments. Methanol (I.P.) from Molychem, B-9, MIDC Industrial Area, Badlapur, Dist Thane 421 503, India, and Research Lab Fine, Mumbai 400(002), India (2.5 liters, batch number MCRT-5162, stored at room temperature), Sodium sulphite (I.P.) (500 gm, batch number 01425090612, stored at room temperature), and Hydrochloric acid (I.P.) from MP Biomedicals India Private Limited, India (batch number AS003, 500 gm, stored at room temperature) were part of the chemical inventory. Sodium hydroxide (I.P.) (500 gm, stored at room temperature), Copper sulphate (I.P.) (batch number PCT0104-500G, 500 gm, stored at room temperature), Sulphuric acid (I.P.) (batch number AS016, 500 ml, stored at room temperature), O-Phthalaldehyde (I.P.) (5 gm, stored at room temperature), and Ninhydrin (I.P.) (batch number 491200010, 10 gm, stored at room temperature) were utilized. n-Heptane (I.P.) from 3B Black Bio Biotech India Ltd. (batch number 3B1159, 2.5 liters, stored at room temperature), n-Butanol (I.P.) (batch number 3B1102, 2.5 liters, stored at room temperature), Thiobarbituric acid (I.P.) (batch number 3B1154, 100 gm, stored at room temperature), and Trichloroacetic (I.P.) (batch number 3B1155, 100 gm, stored at room temperature) were used in the study. Sucrose (I.P.) from Fisher Scientific Powai, Mumbai (500 gm, batch number 1043/1, stored at room temperature), Sodium bicarbonate (I.P.) from Analab Fine Chemicals Mumbai -400083 (India) (500 gm, batch number 3094 6502-1, stored at room temperature), Sodium metabisulphite (I.P.) (500 gm, stored at room temperature), and Phenobarbital (Gardinal®) (I.P.) from Abbott Healthcare Pvt. Ltd., Village Bhataulli Khurd, H.P., India (500 mg, batch number GDB2012, stored at room temperature) were also part of the chemical inventory.

- **Instruments Used**

The instruments used in the study included a Jasco F-8200 Spectrofluorometer from JASCO Benelux B.V., located at Veldzigt 2a, 3454 PW de Meern, a UV Spectrophotometer (Model V-630, Sr. No. B157261148) from Jasco, Japan, and a Remi RC4 Lab. Centrifuge from Remi Motors Ltd., Mumbai - 400 058, India. An animal weighing electronic balance (Model CB-220) from Contech Instruments Co., Delhi, a chemical weighing balance (Model AB-204-S)

from Metler Tolledo, Classic made, Switzerland, and a tissue homogenizer (Model RQ-127A) from Remi Equipment Pvt. Ltd., Mumbai, India, were used. An Actophotometer (Model MSW-013) from Mohit Scientific Works, Ambala, Haryana, India, was also part of the instrumentation.

METHODS

Preparation of Drug Solution, Storage, Volume, and Route of Administration

For Morin, the test drug solution was prepared using distilled water as the vehicle. Morin powder was stored in a desiccator, and a fresh drug solution was prepared daily. This solution was kept in airtight amber-colored bottles and stored at room temperature until use. The volume of the Morin solution to be administered was calculated based on the body weight of the animals, and it was administered per orally (p.o.) in the alloxan-induced diabetes mellitus model.[51] For Phenobarbital, the standard drug solution was prepared with 1% Sodium-carboxymethylcellulose as the vehicle. The Phenobarbital powder was stored in a refrigerator below 25 ºC, and a fresh drug solution was prepared daily. The volume of the Phenobarbital solution to be administered was also calculated based on the body weight of the animals, and it was administered per orally (p.o.).[52]

Kindling Associated Post-Ictal Depression in Laboratory Animals[53]

Experimental Design: The animals were randomly divided into six groups with six rats each.

- Group I: Normal group, receiving only vehicle (distilled water).
- Group II: PTZ control, receiving PTZ (30 mg/kg, i.p.) and vehicle (distilled water, 10 mg/kg).
- Group III: Phenobarbital (30) group, receiving PTZ (30 mg/kg, i.p.) and pre-treated with Phenobarbital (30 mg/kg, p.o.) for 15 days.
- Group IV: Morin (10) group, receiving PTZ (30 mg/kg, i.p.) and pre-treated with Morin (10 mg/kg, p.o.) for 15 days.
- Group V: Morin (20) group, receiving PTZ (30 mg/kg, i.p.) and pre-treated with Morin (20 mg/kg, p.o.) for 15 days.
- Group VI: Morin (40) group, receiving PTZ (30 mg/kg, i.p.) and pre-treated with Morin (40 mg/kg, p.o.) for 15 days.

Induction of Kindling Associated Post-Ictal Depression: On day 0, all behavioral parameters were evaluated before epilepsy induction. From days 1 to 15, all animals except the normal group received PTZ (30 mg/kg, i.p.) every 48 hours. Daily pre-treatment was given to the treatment groups with Morin (10, 20, and 40 mg/kg) and Phenobarbital (30 mg/kg). Post-ictal behavioral parameters, such as seizure severity, duration of immobility, and locomotor activity, were observed every fifth day. The onset and duration of convulsions were observed on day 15 post-PTZ administration. After evaluating behavioral and post-ictal parameters on day 15, the rats were sacrificed, and their brains were immediately removed for biochemical analysis.[54]

Treatment of Morin and Phenobarbital: Morin (10, 20, and 40 mg/kg) and Phenobarbital (10 mg/kg) were administered per orally (p.o.) based on the animals' body weight from the day of confirmation to 15 days. Observations were recorded on various days in the morning, and doses were administered immediately afterward.[55]

To assess the effect of Morin on kindling-associated post-ictal depression in rats, several in-vivo and ex-vivo parameters were measured. For in-vivo parameters, rats were weighed daily, and convulsive behavior was monitored for tonic-clonic convulsions, scoring responses from 0 (unresponsiveness) to 4 (death), with rats experiencing lethal convulsions being excluded from the study.[56,57,58] Locomotor activity was measured using an Actophotometer before and after drug treatment, and decreased activity was considered an index of CNS depression. In the Tail Suspension Test (TST), rats were suspended by their tails, and escape-oriented behavior and immobility were recorded during a 6-minute session. For ex-vivo parameters, oxidative stress in the brain was assessed after sacrifice by measuring lipid peroxidation (MDA content), superoxide dismutase (SOD), reduced glutathione (GSH), nitric oxide (NO), and total protein. Brain monoamine levels, including GABA, dopamine, and 5-HT, were determined using various biochemical assays. Membrane-bound inorganic phosphate (ATPase) activity was also measured, specifically sodium-potassium-dependent (Na+K+ATPase) and calcium-dependent (Ca2+ATPase) ATPases. Statistical analyses were performed using GraphPad Prism v5.0, with results expressed as arithmetic means ± SEM.[59,60]

RESULTS AND DISCUSSION

Effect of Morin on Body Weight

The effect of morin on body weight was studied by measuring the body weights of rats in different experimental groups. The groups included normal rats, PTZ control rats, rats treated with phenobarbital (30 mg/kg), and rats treated with morin at doses of 10 mg/kg, 20 mg/kg, and 40 mg/kg. The body weights were recorded and expressed as Mean ± SEM. The results were as follows: the normal group had a mean body weight of 224.80 ± 1.52 g, the PTZ control group had 223.30 ± 0.67 g, the phenobarbital group had 224.50 ± 1.18 g, the morin 10 mg/kg group had 225.20 ± 1.40 g, the morin 20 mg/kg group had 226.80 ± 1.38 g, and the morin 40 mg/kg group had 226.30 ± 1.33 g.

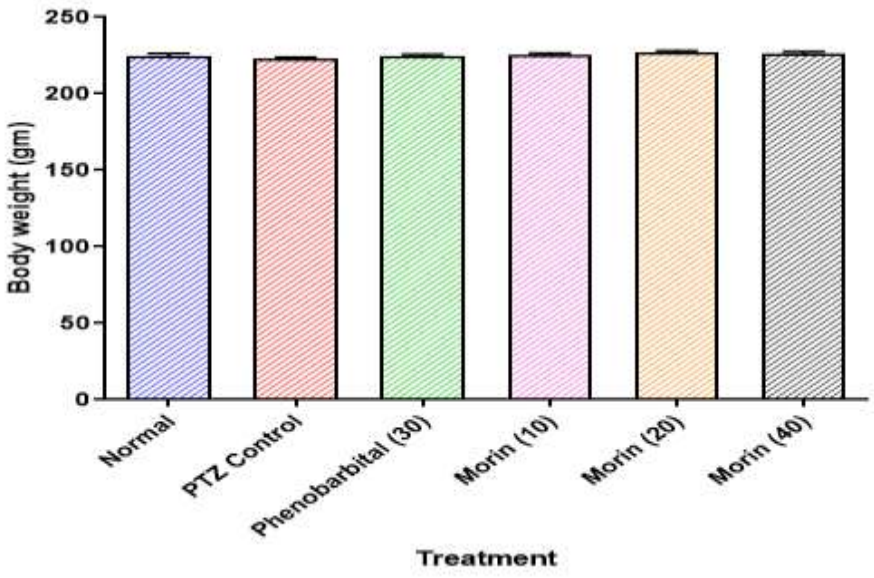

Fig. No. 2: Graphical representation of effect of morin on body weight.

The data were analyzed using One-Way ANOVA followed by Dunnett's test to compare the means of the experimental groups. The graphical representation of the body weight data (Fig. No. 2) shows that there were no significant differences in the body weights between the PTZ control rats and the normal rats. Similarly, the body weights of rats treated with phenobarbital and morin at various doses (10, 20, and 40 mg/kg) did not show significant differences compared to the normal rats. This lack of significant difference in body weight across all groups indicates that neither the administration of PTZ nor the treatments with phenobarbital and morin affected the body weight of the rats. The stability in body weight suggests that the substances did not induce any adverse effects that could lead to weight loss or gain,

highlighting their potential safety in terms of not causing major disruptions in body weight in the studied doses.

Effect of Morin on the Severity of Seizure Intensity Score in PTZ-Induced Epilepsy

The study investigated the effect of morin on seizure intensity in a PTZ-induced epilepsy model. Seizure intensity scores were recorded over a 15-day period across six groups: normal, PTZ control, phenobarbital (30 mg/kg), and morin-treated groups (10, 20, and 40 mg/kg). On day 1, the normal group had a score of 0.00 ± 0.00, while the PTZ control group had a significantly higher score of 3.17 ± 0.40 ($P < 0.001$). The phenobarbital group showed a score of 3.33 ± 0.33, and the morin groups had scores of 3.00 ± 0.26 (10 mg/kg), 2.67 ± 0.21 (20 mg/kg), and 3.00 ± 0.26 (40 mg/kg).

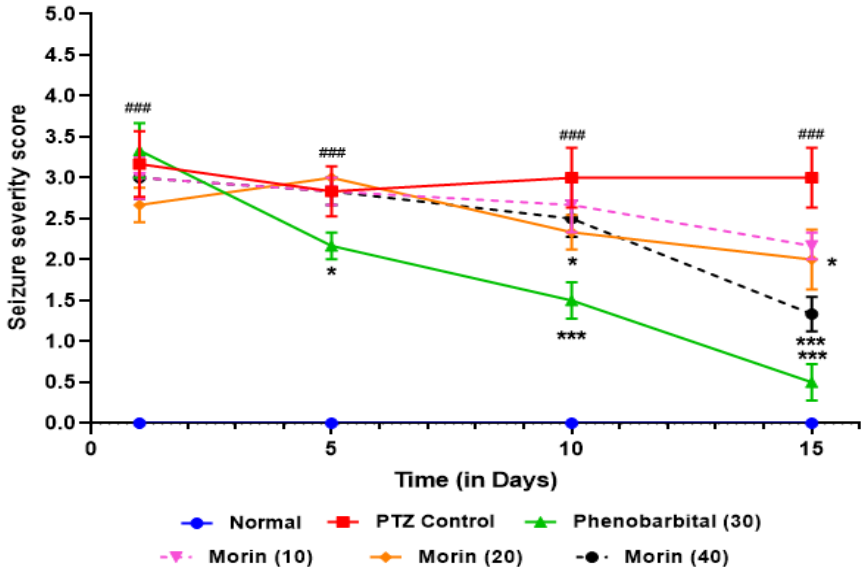

Fig. No. 3: Graphical representation of effect of morin on the severity of seizure intensity score in PTZ induced epilepsy.

On day 5, the PTZ control group maintained a high score of 2.83 ± 0.31, while the phenobarbital group significantly reduced to 2.17 ± 0.17 ($P < 0.05$). The morin groups showed scores of 2.83 ± 0.17 (10 mg/kg), 3.00 ± 0.00 (20 mg/kg), and 2.83 ± 0.17 (40 mg/kg). By day 10, the PTZ control group's score was 3.00 ± 0.37, while the phenobarbital group showed a significant reduction to 1.50 ± 0.22 ($P < 0.001$). The morin groups had scores of 2.67 ± 0.33 (10 mg/kg), 2.33 ± 0.21 (20 mg/kg, $P < 0.05$), and 2.50 ± 0.22 (40 mg/kg, $P < 0.05$). On day 15, the PTZ control group maintained a high score of 3.00 ± 0.37, the phenobarbital group reduced further to 0.50 ± 0.22 ($P < 0.001$), and the morin groups showed

scores of 2.17 ± 0.17 (10 mg/kg), 2.00 ± 0.37 (20 mg/kg, $P < 0.05$), and 1.33 ± 0.21 (40 mg/kg, $P < 0.001$). The data were analyzed using non-parametric Two-Way ANOVA followed by the Mann-Whitney test to compare the effects of different treatments on seizure intensity. The graphical representation (Fig. No.3) illustrates the progression of seizure intensity over 15 days. The PTZ control group showed a significant increase in seizure intensity ($P < 0.001$) from day 1, which remained elevated over the study period. The administration of phenobarbital (30 mg/kg) significantly reduced seizure intensity starting from day 5 ($P < 0.05$) and continued to decrease to day 15 ($P < 0.001$) compared to the PTZ control group. Morin at 20 mg/kg and 40 mg/kg showed significant reductions in seizure intensity on days 10 and 15 ($P < 0.05$ and $P < 0.001$, respectively), indicating its potential anticonvulsant effects at these doses. However, morin at 10 mg/kg did not show significant inhibition of PTZ-induced seizures, suggesting that higher doses of morin are required to achieve an anticonvulsant effect. The significant reduction in seizure intensity in the phenobarbital and higher-dose morin groups can be attributed to their anticonvulsant properties. Phenobarbital is a well-known anticonvulsant, while morin, particularly at higher doses, appears to exert similar effects, possibly through modulation of neurotransmitter systems or ion channels involved in seizure activity. The lack of significant effect at the lower dose of morin indicates a dose-dependent response, where the therapeutic efficacy is achieved only at certain concentrations.

Effect of Morin on Onset and Duration of Convulsion in PTZ-Induced Epilepsy

This study assessed the impact of morin on the onset and duration of convulsions in a PTZ-induced epilepsy model. The parameters evaluated included the onset of convulsions and the duration of clonic and tonic convulsions. The normal group did not exhibit convulsions, so their onset and duration were not measured. In the PTZ control group, the onset of convulsions was 6.17 ± 0.60 minutes. Treatment with phenobarbital (30 mg/kg) significantly delayed the onset to 30.67 ± 0.67 minutes ($P < 0.001$). Morin at doses of 10 mg/kg, 20 mg/kg, and 40 mg/kg delayed the onset to 10.67 ± 0.56, 18.50 ± 0.50 ($P < 0.01$), and 25.50 ± 0.56 minutes ($P < 0.001$), respectively.

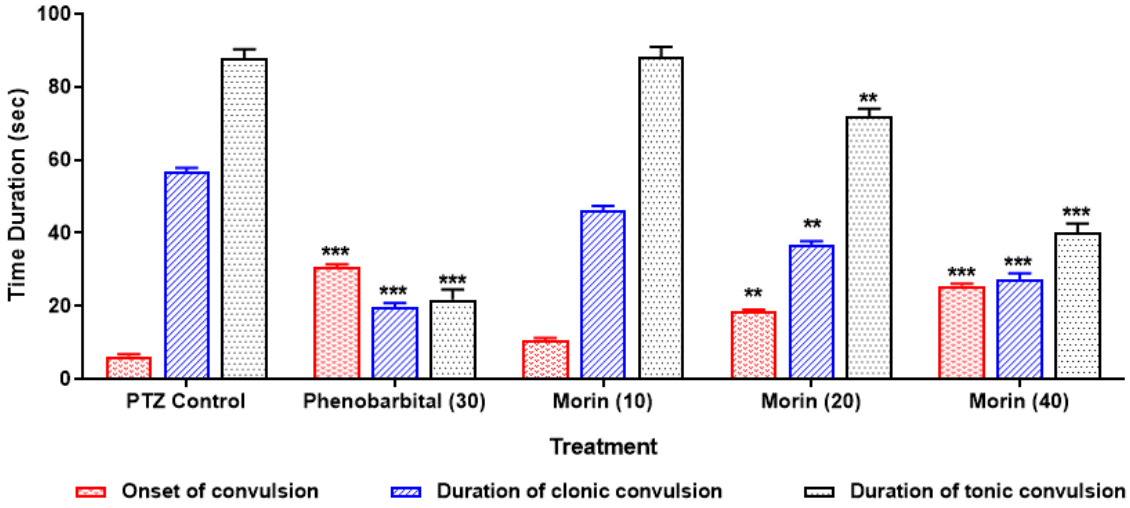

Fig. No. 4: Graphical representation of effect of morin on onset and duration of convulsion in PTZ induced epilepsy.

For the duration of clonic convulsions, the PTZ control group experienced 56.67 ± 1.12 minutes of clonic convulsions. Phenobarbital significantly reduced this duration to 19.67 ± 1.09 minutes ($P < 0.001$). Morin at 10 mg/kg, 20 mg/kg, and 40 mg/kg reduced the duration to 46.17 ± 1.22, 36.67 ± 1.09 ($P < 0.01$), and 27.33 ± 1.63 minutes ($P < 0.001$), respectively. The duration of tonic convulsions in the PTZ control group was 88.00 ± 2.28 minutes. Phenobarbital reduced this to 21.67 ± 2.79 minutes ($P < 0.001$). Morin at 10 mg/kg, 20 mg/kg, and 40 mg/kg resulted in durations of 88.17 ± 2.83, 71.83 ± 2.18 ($P < 0.01$), and 40.17 ± 2.41 minutes ($P < 0.001$), respectively. The data were analyzed using one-way ANOVA followed by Dunnett's test to determine the statistical significance of the differences between groups. The graphical representation (Fig. No.4) illustrates the onset and duration of convulsions across the different treatment groups. In the PTZ control group, convulsions started early and lasted longer, reflecting the severity of PTZ-induced epilepsy. Phenobarbital significantly delayed the onset and reduced the duration of both clonic and tonic convulsions, demonstrating its efficacy as an anticonvulsant. Morin also showed dose-dependent anticonvulsant effects. At higher doses (20 mg/kg and 40 mg/kg), morin significantly delayed the onset and reduced the duration of convulsions, although the effects were less pronounced than those of phenobarbital. The lowest dose of morin (10 mg/kg) did not produce significant changes compared to the PTZ control group, indicating that higher doses are necessary to achieve therapeutic effects. The significant reduction in convulsion onset and duration with phenobarbital and higher doses of morin can be attributed to their anticonvulsant properties, possibly through modulation of neurotransmitter systems or ion channels involved in seizure

activity. The lack of significant effect at the lower dose of morin suggests a dose-dependent response, where sufficient concentration is required to exert a therapeutic effect.

Effect of Morin on the Duration of Immobility Period in Tail Suspension Test During PTZ-Induced Post-Ictal Depression

The study assessed the impact of morin on the duration of the immobility period in the tail suspension test, a measure of depressive-like behavior, in rats subjected to PTZ-induced post-ictal depression. On the first day, the duration of immobility was similar across all groups, with values ranging from 138.00 ± 5.15 seconds to 147.17 ± 5.17 seconds, indicating no significant differences. However, by the 5th day, the PTZ control group showed a marked increase in immobility duration to 191.17 ± 3.86 seconds ($P < 0.001$ compared to the normal group). Phenobarbital (30 mg/kg) administration reduced this immobility duration to 169.17 ± 8.73 seconds ($P < 0.01$), while morin at 10 mg/kg, 20 mg/kg, and 40 mg/kg resulted in immobility durations of 174.50 ± 5.09, 181.83 ± 3.42, and 182.33 ± 3.30 seconds, respectively, which were not statistically significant. On the 10th day, the immobility duration in the PTZ control group increased further to 208.67 ± 5.01 seconds ($P < 0.001$). Phenobarbital significantly reduced this duration to 170.83 ± 4.13 seconds ($P < 0.001$). Morin at 40 mg/kg significantly reduced the immobility duration to 181.17 ± 5.36 seconds ($P < 0.01$), while 10 mg/kg and 20 mg/kg doses of morin showed non-significant reductions to 202.00 ± 5.87 and 189.00 ± 5.30 seconds, respectively.

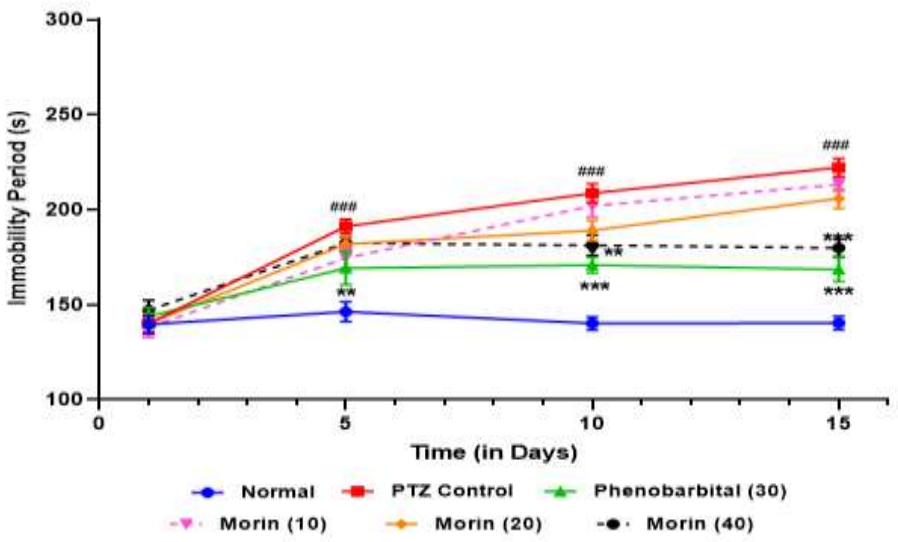

Fig. No. 5: Graphical representation of effect of morin on the duration of immobility period in tail suspension test during PTZ induced post-ictal depression.

By the 15th day, the immobility duration in the PTZ control group reached 222.17 ± 4.76 seconds ($P < 0.001$). Phenobarbital reduced this to 168.50 ± 6.24 seconds ($P < 0.001$). Morin at 40 mg/kg significantly reduced the immobility duration to 179.83 ± 4.80 seconds ($P < 0.001$). The 10 mg/kg and 20 mg/kg doses of morin resulted in immobility durations of 213.17 ± 3.47 and 205.83 ± 5.22 seconds, respectively, but these reductions were not statistically significant.

The data were analyzed using Two-Way ANOVA followed by Bonferroni's post-hoc test to determine the statistical significance of differences between groups. The graphical representation (Fig. No.5) visually depicts the duration of the immobility period across the different treatment groups over time. In PTZ control rats, the duration of immobility significantly increased over time, indicating a progression of depressive-like behavior post-PTZ administration. Phenobarbital effectively attenuated this increase, demonstrating its antidepressant-like effects. Morin, particularly at the highest dose of 40 mg/kg, also significantly reduced the duration of immobility, suggesting its potential antidepressant-like properties. The non-significant reductions at lower doses of morin (10 mg/kg and 20 mg/kg) indicate that higher doses may be necessary to achieve a therapeutic effect. The significant reduction in immobility duration with phenobarbital and high-dose morin can be attributed to their potential neuromodulatory effects, which may counteract the depressive-like state induced by PTZ. The dose-dependent response observed with morin suggests that sufficient concentrations are required to exert antidepressant-like effects, likely through mechanisms involving neurotransmitter modulation or neuroprotection.

Effect of Morin on Locomotor Activity During PTZ-Induced Post-Ictal Depression

The study investigated the effect of morin on locomotor activity in rats experiencing PTZ-induced post-ictal depression. On the first day, normal rats exhibited a high level of locomotor activity (236.50 ± 2.09 counts/5 mins). In contrast, PTZ control rats showed a significant reduction in activity (81.67 ± 6.73 counts/5 mins, $P < 0.001$). Treatment with phenobarbital (30 mg/kg) did not significantly improve locomotor activity on the first day (91.83 ± 10.68 counts/5 mins). Similarly, morin at 10 mg/kg, 20 mg/kg, and 40 mg/kg resulted in locomotor activities of 78.33 ± 5.68, 87.00 ± 9.31, and 80.33 ± 7.89 counts/5 mins, respectively, indicating no significant differences from the PTZ control group.

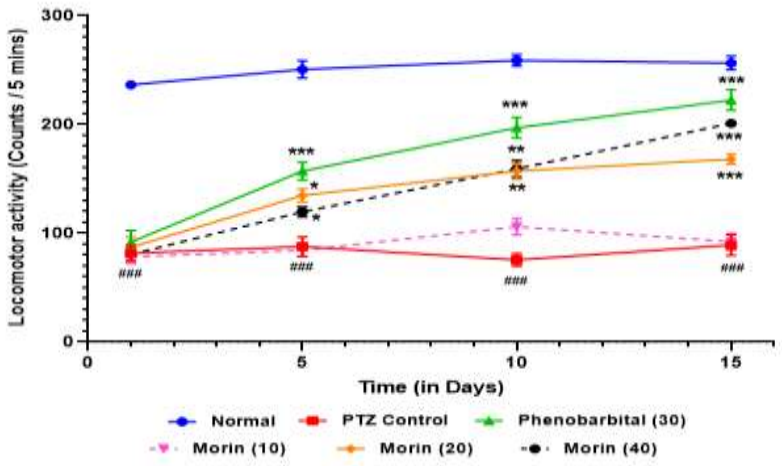

Fig. No. 6: Graphical representation of effect of morin on locomotor activity during PTZ induced post-ictal depression.

By the 5th day, locomotor activity in PTZ control rats remained significantly reduced (87.67 ± 8.87 counts/5 mins, $P < 0.001$). Phenobarbital treatment significantly improved activity to 157.00 ± 8.12 counts/5 mins ($P < 0.001$). Morin at 20 mg/kg and 40 mg/kg also improved locomotor activity significantly to 134.67 ± 5.98 counts/5 mins ($P < 0.05$) and 119.67 ± 4.46 counts/5 mins ($P < 0.05$), respectively, while morin at 10 mg/kg showed no significant change (84.17 ± 5.61 counts/5 mins).

On the 10th day, PTZ control rats had a further reduction in locomotor activity (75.50 ± 5.76 counts/5 mins, $P < 0.001$). Phenobarbital-treated rats showed a significant increase in activity to 196.83 ± 9.52 counts/5 mins ($P < 0.001$). Morin at 20 mg/kg and 40 mg/kg significantly improved activity to 157.00 ± 7.22 counts/5 mins ($P < 0.01$) and 159.17 ± 7.61 counts/5 mins ($P < 0.01$), respectively. However, morin at 10 mg/kg showed a modest, non-significant increase in activity (106.00 ± 7.43 counts/5 mins). By the 15th day, PTZ control rats still exhibited low locomotor activity (89.17 ± 9.55 counts/5 mins, $P < 0.001$). Phenobarbital treatment resulted in a significant increase in activity to 222.33 ± 9.42 counts/5 mins ($P < 0.001$). Morin at 20 mg/kg and 40 mg/kg significantly improved activity to 168.00 ± 4.43 counts/5 mins ($P < 0.001$) and 201.00 ± 3.67 counts/5 mins ($P < 0.001$), respectively, while morin at 10 mg/kg did not significantly alter activity (92.17 ± 7.50 counts/5 mins). The data were analyzed using Two-Way ANOVA followed by Bonferroni's post-hoc test to determine the statistical significance of differences between groups. The graphical representation (Fig. No.6) visually illustrates the changes in locomotor activity across the different treatment groups over time. Chronic administration of PTZ significantly reduced locomotor activity in

PTZ control rats compared to normal rats, indicating a suppression of motor function due to post-ictal depression. Phenobarbital treatment significantly improved locomotor activity from the 5th day onwards, demonstrating its efficacy in mitigating PTZ-induced motor deficits. Morin treatment at higher doses (20 mg/kg and 40 mg/kg) also significantly attenuated the reduction in locomotor activity, suggesting its potential to improve motor function in a dose-dependent manner. However, the lowest dose of morin (10 mg/kg) did not produce a significant effect, indicating that higher doses may be required to achieve a therapeutic benefit. The observed effects can be attributed to the neuromodulatory and neuroprotective properties of phenobarbital and morin. Phenobarbital, a well-known anticonvulsant, likely exerted its effects by enhancing GABAergic activity, thereby reducing neuronal excitability and improving motor function. Morin, a flavonoid with antioxidant and anti-inflammatory properties, may have contributed to the restoration of motor activity through its neuroprotective effects, reducing oxidative stress and inflammation in the brain.

Effect of Morin on PTZ-Induced Alteration in Brain GABA Levels

The study evaluated the impact of morin on brain GABA levels in rats subjected to PTZ-induced epilepsy. Normal rats had a brain GABA level of 61.54 ± 2.69 ng/g of brain tissue. In contrast, PTZ control rats showed a significant reduction in GABA levels to 13.89 ± 2.97 ng/g ($P < 0.001$). Administration of phenobarbital (30 mg/kg) significantly restored GABA levels to 55.30 ± 2.81 ng/g ($P < 0.001$). Morin treatment at 10 mg/kg did not significantly restore GABA levels, resulting in 19.43 ± 2.03 ng/g. However, morin at 20 mg/kg and 40 mg/kg showed significant dose-dependent increases in GABA levels to 30.47 ± 1.93 ng/g ($P < 0.01$) and 32.71 ± 1.97 ng/g ($P < 0.001$), respectively.

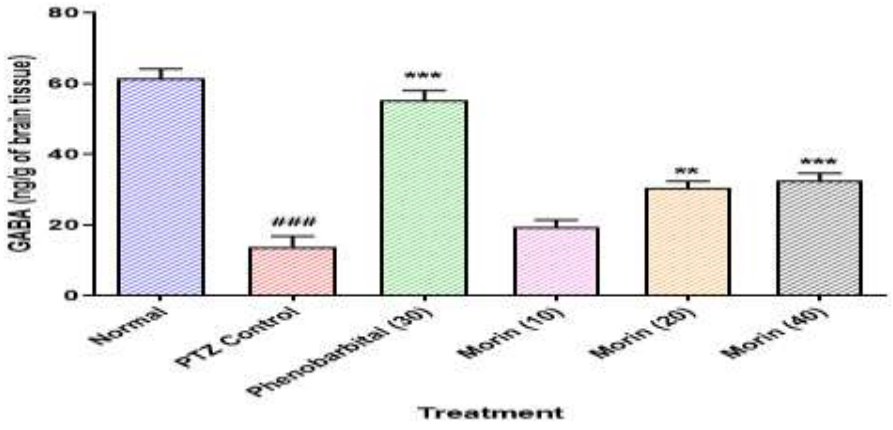

Fig. No. 7: Graphical representation of effect of morin on PTZ induced alteration in brain GABA levels.

The data were analyzed using one-way ANOVA followed by Dunnett's test to determine the statistical significance of differences between groups. The graphical representation (Fig. No. 7) illustrates the changes in brain GABA levels across different treatment groups. Chronic PTZ administration significantly decreased brain GABA levels in PTZ control rats compared to normal rats, highlighting the GABAergic dysfunction induced by PTZ. Phenobarbital, a well-known GABAergic agent, significantly restored GABA levels, demonstrating its effectiveness in countering PTZ-induced GABA depletion. Morin treatment at higher doses (20 mg/kg and 40 mg/kg) significantly and dose-dependently increased brain GABA levels, indicating its potential to modulate GABAergic activity. However, the lowest dose of morin (10 mg/kg) did not significantly alter GABA levels, suggesting that higher doses are necessary to achieve a therapeutic effect. The observed effects can be attributed to the neuromodulatory properties of phenobarbital and morin. Phenobarbital enhances GABAergic activity by increasing GABA receptor activation, thus restoring GABA levels. Morin, with its antioxidant and neuroprotective properties, may help to preserve GABAergic neurons and enhance GABA synthesis, leading to increased GABA levels in the brain. The dose-dependent response to morin indicates that higher concentrations of the compound are more effective in exerting these protective effects.

Effect of Morin on PTZ-Induced Alteration in Brain Dopamine Levels

In this study, the effect of morin on brain dopamine (DA) levels in rats subjected to PTZ-induced epilepsy was evaluated. Normal rats had a brain DA level of 75.94 ± 1.81 ng/g of brain tissue. PTZ control rats exhibited a significant reduction in DA levels to 47.83 ± 1.64 ng/g ($P < 0.001$). Treatment with phenobarbital (30 mg/kg) significantly restored DA levels to 72.43 ± 1.87 ng/g ($P < 0.001$). Morin administration at 10 mg/kg resulted in DA levels of 53.93 ± 2.65 ng/g, which was not significantly different from the PTZ control group. However, morin at 20 mg/kg and 40 mg/kg significantly increased DA levels to 65.85 ± 2.49 ng/g ($P < 0.01$) and 68.94 ± 2.89 ng/g ($P < 0.001$), respectively.

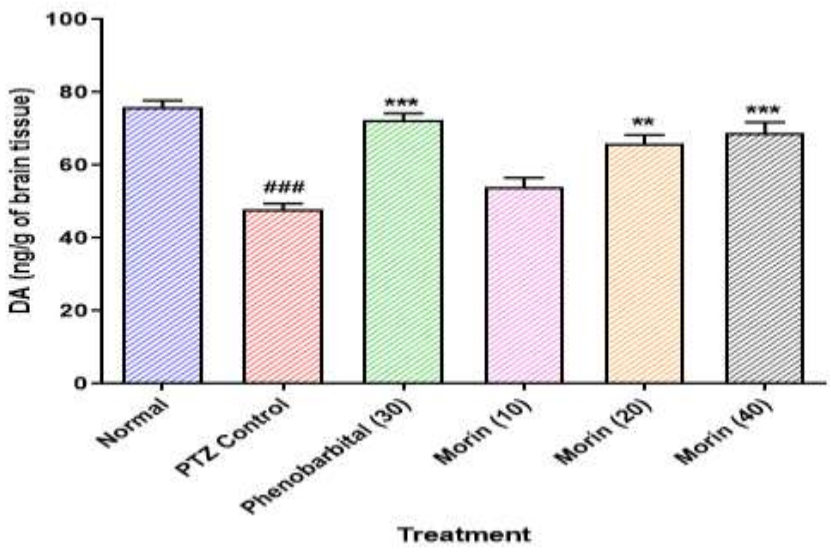

Fig. No. 8: Graphical representation of effect of morin on PTZ induced alteration in brain DA levels.

The data were analyzed using one-way ANOVA followed by Dunnett's test to assess statistical significance between groups. The graphical representation (Fig. No.8) illustrates the variations in brain DA levels across the different treatment groups. Chronic PTZ administration significantly decreased brain DA levels in PTZ control rats compared to normal rats, indicating PTZ-induced dopaminergic dysfunction. Phenobarbital administration significantly restored DA levels, demonstrating its effectiveness in countering the reduction in DA caused by PTZ. Morin treatment at higher doses (20 mg/kg and 40 mg/kg) significantly and dose-dependently increased brain DA levels, indicating its potential to modulate dopaminergic activity. The lowest dose of morin (10 mg/kg) did not significantly alter DA levels, suggesting that higher doses are necessary to achieve a therapeutic effect. The observed effects can be attributed to the neuromodulatory properties of phenobarbital and morin. Phenobarbital may enhance dopaminergic activity by modulating DA receptor function or increasing DA synthesis. Morin, with its antioxidant and neuroprotective properties, may help preserve dopaminergic neurons and enhance DA synthesis, leading to increased DA levels in the brain. The dose-dependent response to morin indicates that higher concentrations of the compound are more effective in exerting these protective effects.

Effect of Morin on PTZ-Induced Alteration in Brain Serotonin Levels

In this study, the impact of morin on brain serotonin (5-HT) levels in rats subjected to PTZ-induced epilepsy was assessed. Normal rats had a brain 5-HT level of 38.98 ± 1.25 ng/g of brain tissue. PTZ control rats exhibited a significant reduction in 5-HT levels to 21.96 ± 3.61 ng/g ($P < 0.001$). Treatment with phenobarbital (30 mg/kg) significantly restored 5-HT levels to 35.52 ± 0.94 ng/g ($P < 0.001$). Morin administration at 10 mg/kg resulted in 5-HT levels of 24.61 ± 3.76 ng/g, which was not significantly different from the PTZ control group. However, morin at 20 mg/kg and 40 mg/kg significantly increased 5-HT levels to 31.78 ± 2.87 ng/g ($P < 0.01$) and 35.52 ± 2.12 ng/g ($P < 0.001$), respectively.

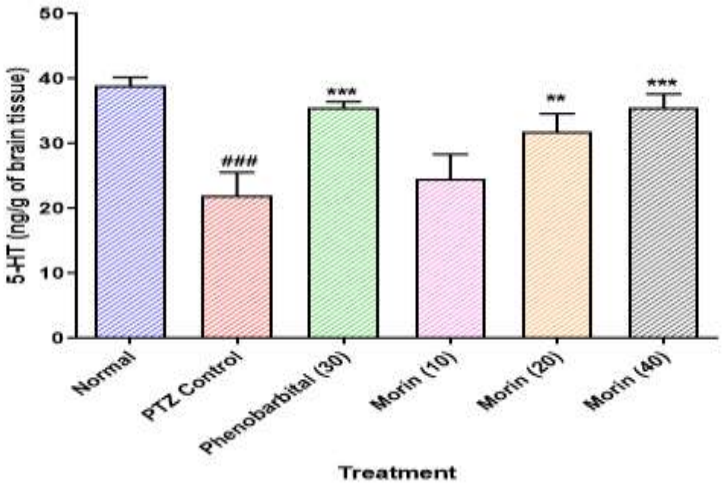

Fig. No. 9: Graphical representation of effect of morin on PTZ induced alteration in brain 5-HT levels.

The data were analyzed using one-way ANOVA followed by Dunnett's test to determine statistical significance between the groups. The graphical representation (Fig. No.9) illustrates the variations in brain 5-HT levels across the different treatment groups. Chronic PTZ administration significantly decreased brain 5-HT levels in PTZ control rats compared to normal rats, indicating PTZ-induced serotonergic dysfunction. Administration of phenobarbital significantly restored 5-HT levels, demonstrating its efficacy in counteracting the reduction in 5-HT caused by PTZ. Morin treatment at higher doses (20 mg/kg and 40 mg/kg) significantly and dose-dependently increased brain 5-HT levels, indicating its potential to modulate serotonergic activity. The lowest dose of morin (10 mg/kg) did not significantly alter 5-HT levels, suggesting that higher doses are necessary to achieve a therapeutic effect. The observed effects can be attributed to the neuromodulatory properties of phenobarbital and morin. Phenobarbital may enhance serotonergic activity by modulating

5-HT receptor function or increasing 5-HT synthesis. Morin, with its antioxidant and neuroprotective properties, may help preserve serotonergic neurons and enhance 5-HT synthesis, leading to increased 5-HT levels in the brain. The dose-dependent response to morin indicates that higher concentrations of the compound are more effective in exerting these protective effects.

Effect of Morin on PTZ-Induced Alteration in Brain Total Protein Levels

The effect of morin on brain total protein levels in rats subjected to PTZ-induced epilepsy was investigated in this study. Normal rats exhibited a brain total protein level of 4.07 ± 0.30 mg/gm. In contrast, PTZ control rats showed a significant increase in brain total protein levels to 9.61 ± 0.23 mg/gm ($P < 0.001$). Treatment with phenobarbital (30 mg/kg) resulted in a marked reduction in brain total protein levels to 5.53 ± 0.32 mg/gm ($P < 0.001$) compared to PTZ control rats.

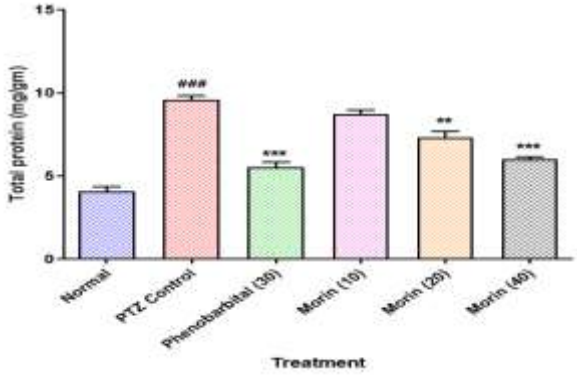

Fig. No. 10: Graphical representation of effect of morin on PTZ induced alteration in brain total protein levels.

Morin administration at 10 mg/kg did not significantly alter brain total protein levels compared to PTZ control rats (8.72 ± 0.26 mg/gm). However, treatment with morin at 20 mg/kg and 40 mg/kg showed a significant dose-dependent decrease in brain total protein levels to 7.31 ± 0.39 mg/gm ($P < 0.01$) and 6.02 ± 0.15 mg/gm ($P < 0.001$), respectively, compared to PTZ control rats. The data were analyzed using one-way ANOVA followed by Dunnett's test to determine statistical significance between the groups. The graphical representation (Fig. No.10) visually depicts the variations in brain total protein levels across different treatment groups. PTZ-induced epilepsy resulted in a significant increase in brain total protein levels, suggesting neurochemical alterations associated with epileptic conditions. Phenobarbital, known for its anticonvulsant properties, effectively reduced brain total protein

levels, indicating its potential to mitigate PTZ-induced neurochemical changes. Morin, a natural flavonoid with antioxidant and neuroprotective properties, demonstrated dose-dependent efficacy in reducing brain total protein levels. Higher doses of morin (20 mg/kg and 40 mg/kg) were more effective in lowering brain total protein levels, possibly through its antioxidant effects that mitigate neuronal damage and protein aggregation associated with epileptic insults. The findings suggest that morin's neuroprotective mechanisms may involve modulation of protein synthesis or degradation pathways, contributing to its therapeutic potential in epilepsy. The non-significant effect observed at the lowest dose (10 mg/kg) highlights the dose-dependent nature of morin's neuroprotective actions against PTZ-induced alterations in brain total protein levels.

Effect of Morin on PTZ-Induced Alteration in Brain SOD and GSH Levels

The effect of morin on brain superoxide dismutase (SOD) and glutathione (GSH) levels in rats subjected to PTZ-induced epilepsy was investigated in this study. Normal rats exhibited a brain SOD level of 13.07 ± 0.50 U/mg of protein and a GSH level of 3.26 ± 0.20 µg/mg of protein. In contrast, PTZ control rats showed a significant decrease in brain SOD levels to 5.53 ± 0.33 U/mg of protein ($P < 0.001$) and in GSH levels to 0.79 ± 0.16 µg/mg of protein ($P < 0.001$) compared to normal rats.

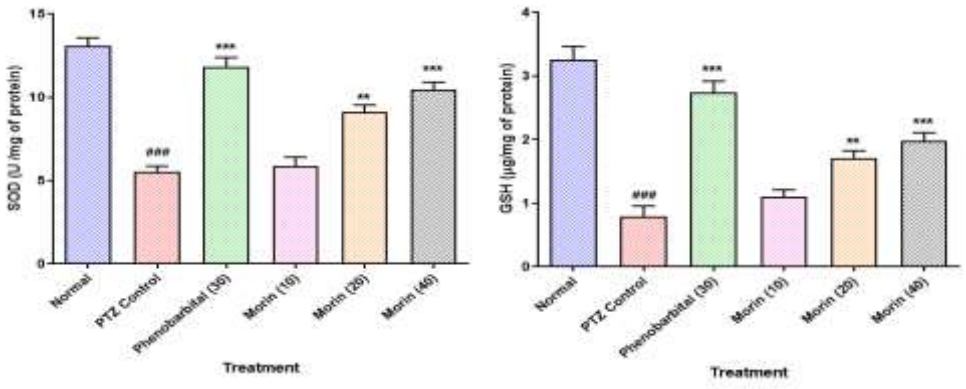

Fig. No. 11: Graphical representation of effect of morin on PTZ induced alteration in brain SOD and GSH levels.

Administration of phenobarbital (30 mg/kg) significantly increased brain SOD levels to 11.84 ± 0.56 U/mg of protein ($P < 0.001$) and GSH levels to 2.74 ± 0.18 µg/mg of protein ($P < 0.001$) compared to PTZ control rats. Similarly, treatment with morin at doses of 20 mg/kg and 40 mg/kg showed a significant and dose-dependent increase in both brain SOD levels (9.13 ± 0.42 U/mg and 10.47 ± 0.43 U/mg of protein, respectively) and GSH levels (1.72 ±

0.11 µg/mg and 1.98 ± 0.12 µg/mg of protein, respectively) compared to PTZ control rats ($P < 0.01$ and $P < 0.001$). The data were analyzed using one-way ANOVA followed by Dunnett's test to determine statistical significance between the groups. The graphical representation (Fig. No.11) visually depicts the changes in brain SOD and GSH levels across different treatment groups. The significant decrease in brain SOD and GSH levels in PTZ control rats reflects oxidative stress and depletion of antioxidant defenses in the brain during epileptic conditions. Phenobarbital and morin treatments effectively countered this decrease, with phenobarbital showing robust increases in both SOD and GSH levels, indicative of its antioxidant properties. Morin, a flavonoid known for its antioxidant and neuroprotective effects, demonstrated dose-dependent efficacy in elevating brain SOD and GSH levels. These findings suggest that morin's antioxidant mechanisms contribute to its therapeutic potential in epilepsy by mitigating oxidative stress-induced damage to brain tissues. The non-significant effect observed at lower doses (10 mg/kg) of morin underscores the dose-dependent nature of its antioxidant effects against PTZ-induced alterations in brain SOD and GSH levels.

Effect of Morin on PTZ-Induced Alteration in Brain MDA and Nitric Oxide Level

The effect of morin on brain malondialdehyde (MDA) and nitric oxide (NO) levels in rats subjected to PTZ-induced epilepsy was investigated in this study. Normal rats exhibited a brain MDA level of 3.59 ± 0.36 nM/mg of protein and a nitric oxide level of 0.21 ± 0.02 µg/mL. In contrast, PTZ control rats showed significant increases in brain MDA levels to 9.77 ± 0.21 nM/mg of protein ($P < 0.001$) and in nitric oxide levels to 0.35 ± 0.02 µg/mL ($P < 0.001$) compared to normal rats.

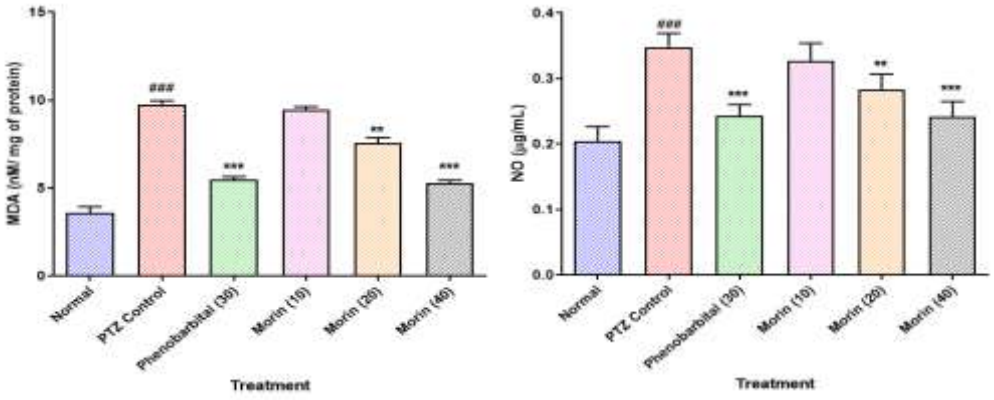

Fig. No. 12: Graphical representation of effect of morin on PTZ induced alteration in brain MDA and NO levels.

Administration of phenobarbital (30 mg/kg) significantly decreased brain MDA levels to 5.49 ± 0.17 nM/mg of protein ($P < 0.001$) and nitric oxide levels to 0.24 ± 0.02 µg/mL ($P < 0.001$) compared to PTZ control rats. Similarly, treatment with morin at doses of 20 mg/kg and 40 mg/kg showed significant and dose-dependent decreases in both brain MDA levels (7.55 ± 0.32 nM/mg and 5.32 ± 0.14 nM/mg of protein, respectively) and nitric oxide levels (0.28 ± 0.02 µg/mL and 0.24 ± 0.02 µg/mL, respectively) compared to PTZ control rats ($P < 0.01$ and $P < 0.001$). The data were analyzed using one-way ANOVA followed by Dunnett's test to determine statistical significance between the groups. The graphical representation (Fig. No.12) visually depicts the changes in brain MDA and NO levels across different treatment groups. The significant increase in brain MDA and NO levels in PTZ control rats indicates oxidative stress and elevated nitrosative stress during epileptic conditions. Phenobarbital and morin treatments effectively attenuated these increases, with phenobarbital showing substantial reductions in both MDA and NO levels, reflecting its antioxidant and neuroprotective properties. Morin, known for its antioxidant and anti-inflammatory effects, demonstrated dose-dependent efficacy in reducing brain MDA and NO levels. This suggests that morin's antioxidant mechanisms play a crucial role in mitigating oxidative and nitrosative stress induced by PTZ-induced epilepsy. The non-significant effect observed at the lower dose (10 mg/kg) of morin underscores the dose-dependent nature of its protective effects against PTZ-induced alterations in brain MDA and NO levels.

Effect of Morin on PTZ-Induced Alteration in Brain Na-K-ATPase and Ca-ATPase Levels

The study investigated the effect of morin on brain Na-K-ATPase and Ca-ATPase levels in rats with PTZ-induced epilepsy. Normal rats exhibited Na-K-ATPase levels of 19.07 ± 1.10 µmol/mg of protein and Ca-ATPase levels of 9.48 ± 0.46 µmol/mg of protein. In contrast, PTZ control rats showed a significant reduction ($P < 0.001$) in Na-K-ATPase levels to 7.76 ± 0.58 µmol/mg of protein and in Ca-ATPase levels to 3.43 ± 0.47 µmol/mg of protein compared to normal rats.

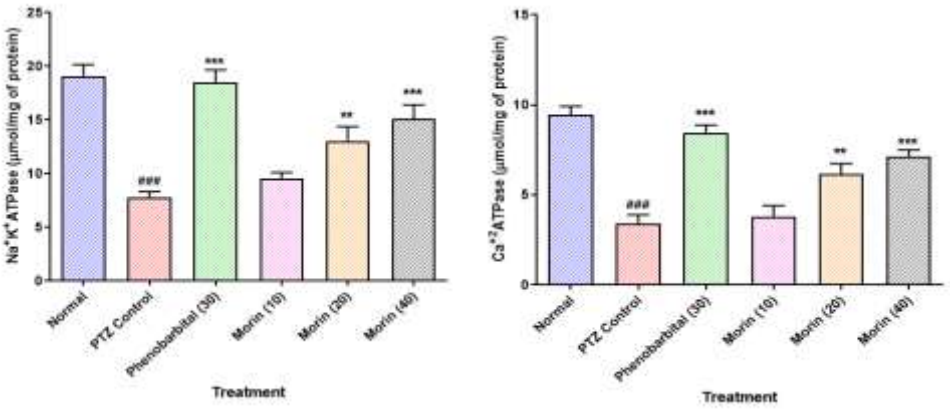

Fig. No. 13. Effect of morin on PTZ induced alteration in brain Na-K-ATPase and Ca-ATPase levels.

Administration of phenobarbital (30 mg/kg) significantly increased Na-K-ATPase levels to 18.47 ± 1.20 µmol/mg of protein ($P < 0.001$) and Ca-ATPase levels to 8.42 ± 0.46 µmol/mg of protein ($P < 0.001$) compared to PTZ control rats. Similarly, treatment with morin at doses of 20 mg/kg and 40 mg/kg showed significant and dose-dependent increases in both Na-K-ATPase levels (13.04 ± 1.35 µmol/mg and 15.09 ± 1.33 µmol/mg of protein, respectively) and Ca-ATPase levels (6.15 ± 0.59 µmol/mg and 7.14 ± 0.37 µmol/mg of protein, respectively) compared to PTZ control rats ($P < 0.01$ and $P < 0.001$). Data were analyzed using one-way ANOVA followed by Dunnett's test to determine significant differences between groups. The graphical representation (Fig.No.13) visually illustrates the changes in Na-K-ATPase and Ca-ATPase levels across different treatment groups. The significant decrease in Na-K-ATPase and Ca-ATPase levels in PTZ control rats indicates impaired ion transport mechanisms during epileptic conditions. Phenobarbital, known for its antiepileptic properties, effectively restored these enzyme levels, suggesting its role in maintaining ion homeostasis. Morin treatment, especially at higher doses (20 mg/kg and 40 mg/kg), demonstrated a pronounced effect in increasing Na-K-ATPase and Ca-ATPase levels. This indicates that morin may enhance ion pump activity in the brain, which could contribute to its neuroprotective effects against PTZ-induced alterations. The non-significant effect observed at the lower dose (10 mg/kg) of morin highlights the dose-dependent nature of its therapeutic efficacy in restoring Na-K-ATPase and Ca-ATPase levels in PTZ-induced epilepsy.

SUMMARY

The study investigated the effects of morin on various parameters in a PTZ-induced epilepsy model in rats. Body weights remained stable across all groups, indicating no adverse effects

on weight from PTZ, phenobarbital, or morin treatments. Morin demonstrated dose-dependent anticonvulsant effects, with higher doses significantly reducing seizure intensity, delaying onset, and decreasing convulsion duration. Additionally, higher doses of morin improved locomotor activity, reduced immobility in the tail suspension test, and increased brain levels of GABA, dopamine, and serotonin, highlighting its potential neuroprotective and neuromodulatory properties.

CONCLUSION

Morin shows promise as an anticonvulsant and neuroprotective agent in a PTZ-induced epilepsy model, particularly at higher doses. It effectively reduces seizure intensity, delays convulsion onset, and improves motor and depressive-like behaviors post-PTZ administration. Additionally, morin enhances brain levels of key neurotransmitters, suggesting its potential in modulating neurotransmitter systems involved in seizure activity. The dose-dependent effects observed indicate that higher doses of morin are required to achieve significant therapeutic benefits, underscoring its potential utility in managing epilepsy and associated neurobehavioral deficits.

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