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Original Research Article

Evaluation of Cognitive Reinforcement Potential of Turmeric in Colchicine Induced Cognitive Impairment in Mice

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Abstract

***Background*:** Cognitive impairment is a hallmark of neurodegenerative disorders, often associated with oxidative stress, neuroinflammation, and cholinergic dysfunction. Turmeric (Curcuma longa), known for its neuroprotective and antioxidant properties, has been investigated for its potential to mitigate cognitive deficits. This study evaluates the cognitive reinforcement potential of turmeric in colchicine-induced cognitive impairment in mice. ***Methods*:** Turmeric was extracted using cold extraction with 50% ethanol for maceration with daily agitation for 72 hrs as prescribed by the extraction protocol. Animals (mice) were acclimatized for two weeks at the Behavioural Laboratory and one-week daily cognitive trial using Morris Water Maze model was done. Furthermore, the animals were grouped according to the study design as 1: control-10 ml/kg p.o, 2: colchicine 0.5 mg/kg p.o, 3: colchicine 0.5 mg/kg and 500 mg/kg p.o turmeric, 4: colchicine 0.5 mg/kg and 1000 mg/kg p.o turmeric, 5: 1000 mg/kg p.o turmeric, 6: 1 mg/kg p.o donepezil and 0.5 mg/kg p.o colchicine; treated for fourteen(14) days and then the test was conducted for each group using same model. Cognitive function was assessed using standard behavioural paradigm, including the Morris water maze tests. ***Results*:** Mice treated with turmeric demonstrated a significant, dose-dependent improvement in cognitive function, with the 1000 mg/kg p.o turmeric group exhibiting the highest recovery. Turmeric administration led to enhanced memory retention, reduced escape latency, and improved discrimination indices, suggesting attenuation of colchicine-induced neurotoxicity. ***Conclusion*:** These findings support the cognitive reinforcement potential of turmeric, likely mediated through its antioxidant and anti-inflammatory mechanisms.

Keyword: Turmeric, Cognitive Function, Colchicine, Donepezil, Neurobehavioural.

BACKGROUND

Cognitive impairment is a defining feature of neurodegenerative disorders, including Alzheimer's disease (AD), which is characterized by progressive memory loss, neuroinflammation, oxidative stress, and cholinergic dysfunction (Chen *et al*., 2022). Various experimental models have been employed to mimic cognitive deficits, with colchicine-induced neurotoxicity serving as a well-established model for studying memory impairment. Colchicine, a microtubule destabilizing agent, disrupts axonal transport, impairs synaptic transmission, and induces neuronal degeneration, closely resembling the neuropathological changes observed in AD (Mehta *et al*., 2017). It also affects hippocampal integrity, leading to spatial and working memory deficits, making it a suitable model for assessing potential neuroprotective interventions.

Turmeric (*Curcuma longa*), a medicinal plant widely recognized for its neuroprotective properties, contains curcumin as its primary bioactive compound. Curcumin exhibits effective antioxidant, anti-inflammatory, and neurotrophic effects, which have been linked to its ability to modulate key signaling pathways involved in neurodegeneration (Hewlings & Kalman, 2017). Preclinical studies suggest that curcumin enhances cognitive function by reducing oxidative stress, inhibiting pro-inflammatory cytokines, and promoting synaptic plasticity (Kumar & Singh, 2020). Moreover, curcumin has been shown to

upregulate brain-derived neurotrophic factor (BDNF), which is essential for neuronal continued existence and cognitive function (Zhang *et al*., 2021).

The therapeutic potential of turmeric in cognitive impairment has been explored in several models of neurotoxicity. In colchicine-induced cognitive dysfunction, previous studies indicate that neuroinflammation and oxidative stress significantly contribute to hippocampal damage and cognitive decline (Sharma *et al*., 2018). Given curcumin's ability to attenuate these pathological features, its cognitive reinforcement potential warrants further investigation. Additionally, the dose-dependent effects of turmeric in modulating neurotransmitter systems, particularly the cholinergic and glutamatergic pathways, suggest its relevance as a natural therapeutic candidate for cognitive disorders (Mishra &Palanivelu, 2008).

This study aims to evaluate the cognitive reinforcement potential of turmeric in colchicine-induced cognitive impairment in mice. By assessing the effects of turmeric at different doses (500 mg/kg and 1000 mg/kg) in the presence of colchicine (1 mg/kg), this research seeks to determine its efficacy in ameliorating cognitive deficits and explore its potential as a neuroprotective agent. Findings from this study could provide insights into turmeric's role in cognitive enhancement and its applicability in managing neurodegenerative conditions.

METHODS

Extraction of Turmeric

Fresh turmeric rhizomes were sourced from the local market, washed thoroughly with distilled water to remove dirt and surface contaminants. The rhizomes were sliced into thin pieces and air-dried at room temperature (25–30°C) for 7–10 days to remove moisture content. Once dried, the turmeric pieces were ground into a fine powder using a mechanical grinder. The powder was sieved to ensure uniform particle size.

Extraction Process

A. Maceration Method:

1. Weigh 100 g of dried turmeric powder using an analytical balance.
2. Prepare 50% ethanol solution by mixing ethanol and distilled water in a 1:1 ratio.
3. Add 500 mL of 50% ethanol to the turmeric powder in a conical flask or glass container.
4. Seal the container and allow the mixture to stand at room temperature (25°C) for 48–72 hours, with occasional shaking to enhance extraction.
5. After maceration, the extract was filtered through Whatman No. 1 filter paper to remove solid residues.

B. Soxhlet Extraction (Alternative Method for Higher Yield):

1. Place 50 g of turmeric powder into a Soxhlet extractor.
2. Add 50% ethanol into the round-bottom flask and heat using a water bath at 60–70°C.
3. Allow continuous extraction for 6–8 hours until the solvent turns colorless.
4. The extract was cooled and filtered to remove residual particles.

Solvent Removal and Concentration

- The filtrate was concentrated using a rotary evaporator at 40–50°C under reduced pressure to remove excess ethanol.
- The filtrate at least level in the flask was turned into beaker and evaporated in a water bath at 50°C until a semi-solid crude extract was obtained.
- The concentrated extract was further freeze-dried to obtain a dry powder for experimental use.

Storage of Extract

- The dried extract was stored in an airtight amber glass container at 4°C to prevent degradation.

Animals and Experimental Design

Adult male mice (25–30 g) were obtained from the animal house breeding facility of the institution and housed under standard laboratory conditions (temperature: 22 ± 2°C, humidity: 50–60%, and a 12-hour light/dark cycle) with free access to food and water. The study was conducted in compliance with the National Institutes of Health (NIH) guidelines for the care and use of laboratory animals (National Research Council, 2011).

Mice were randomly separated into six groups (n = 6 per group):

- **Control group:** Received normal saline (10 ml/kg *p.o*).
- **Colchicine group:** Received colchicine (0.5 mg/kg,*p.o*) to induce cognitive impairment.
- **Turmeric 500 mg/kg** *p.o***+ Colchicine group:** Received colchicine (0.5 mg/kg, *p.o*) followed by turmeric extract (500 mg/kg, orally) for 14 days.
- **Turmeric 1000 mg/kg** *p.o***+ Colchicine group:** Received colchicine (0.5 mg/kg, *p.o*) followed by turmeric extract (1000 mg/kg, orally) for 14 days.
- Turmeric extract (1000 mg/kg, orally) for 14 days
- **Standard treatment group:** Received colchicine (0.5 mg/kg, *p.o*) and donepezil (1 mg/kg, orally) as a reference cognitive-enhancing drug for 14 days.

Induction of Cognitive Impairment

Cognitive impairment was induced using colchicine (0.5 mg/kg, p.o) following previously

established protocols (Mehta *et al*., 2017) with slight modifications.

Behavioural Studies

Morris Water Maze (MWM) Test

The MWM test, a widely used paradigm for assessing spatial learning and memory, was conducted on days 10–14 post-colchicine administration following the protocol described by Morris (1984) with minor adjustment. The experimental setup involved a circular water tank (120 cm diameter, 50 cm depth) filled with opaque water maintained at 25 ± 2°C. A submerged escape dais (10 cm diameter) was placed in the target quadrant 0.5 cm below the water surface and remained in a fixed position right through the training sessions. The test room contained external visual cues to facilitate spatial learning.

Training Phase (Days 10–13)

Mice underwent three trials per day for seven uninterrupted days with a maximum swim time of 60 seconds per trial. Mouse that failed to locate the dais within 60 seconds, was gently guided and allowed to remain on the platform for 10 seconds before removal. Escape latency (time taken to find the platform from any position: North, South, East and West) was recorded and used as a measure of spatial learning ability (Vorhees & Williams, 2006).

Probe Trial (Day 14)

On Day 14, a probe trial was conducted where the platform was removed, and each mouse was allowed to swim freely for 60 seconds. Time spent in the target quadrant, number of dais crossings, and swimming speed were recorded. Increased time spent in the target quadrant was considered indicative of cognitive improvement (D'Hooge& De Deyn, 2001).

Ethical Approval

Ethical approval was given by the institutions ethical committee before the commencement of this study. The study protocol was reviewed and approved under the reference number (NDU/PHARM/REC/25/002).

Statistical Analysis

Data were analysed using GraphPad Prism 9.3 (GraphPad Software, USA) and expressed as mean ± standard error of the mean (SEM). Group comparisons were performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant.

RESULTS

The table below presents the mean values of different experimental groups in comparison to the control group. Colchicine treatment resulted in a significantly higher mean value of time taken to identify the escape isle, indicating a notable deviation from the control. Turmeric and colchicine combined treatment showed significant reduction in the time taken to escape compared with control. Turmeric alone had a mean value of 4.17, which is slightly lower than the control, indicating a null effect of colchicine. Donepezil and colchicine combination resulted in a mean value of 4.84, which is close to the control value, suggesting a possible mitigating effect of donepezil against colchicine-induced changes (table 1).

Table 1: Evaluation of Turmeric, Colchicine on Cognition

Group	Treatment	Dose	M±SEM (s)	P value
1	Control	10 ml /kg	5.04±1.21$^{\#}$	-
2	Colchicine	0.5 mg/kg	28.13±2.64****	<0.0001
3	TMR+CCN	500 mg/kg +0.5 mg/kg	16.42±1.37****	<0.0001
4	TMR+CCN	1000 mg/kg +0.5 mg/kg	12.79±1.60***	<0.0001
5	TMR	1000 mg/kg	4.17±1.17	0.7578
6	DBZ + CCN	1mg/kg + 0.5 mg/kg +	4.84±1.17	0.7978

Data analysed by GraphPad Prism 9.3. One-way ANOVA with post hoc (Dunnett's) multiple comparisons test used to assess differences between treatment groups for cognition that showed statistical significance, **** and *** as defined in the *P* value column above when compared with the control group. TMR-Turmeric, CCN- Colchicine, DBZ-Donepezil

Spatial Navigation Study

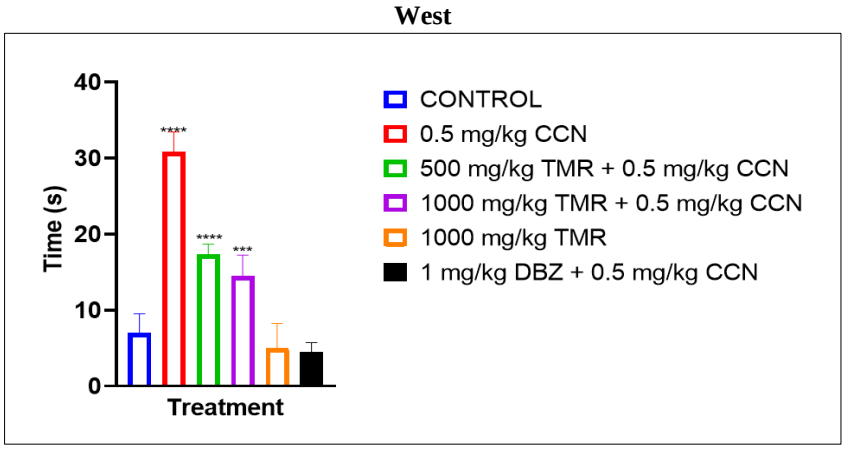


Figure 1: Data analysed by GraphPad Prism 9.3. One-way ANOVA with post hoc (Dunnett's) multiple comparisons test used to assess differences between treatment groups for cognition that showed statistical significance, ** and ***, p< 0.0001, 0.0002, when compared with the control group. CCN-Colchicine, TMR-Turmeric, DBZ- Donepezil**

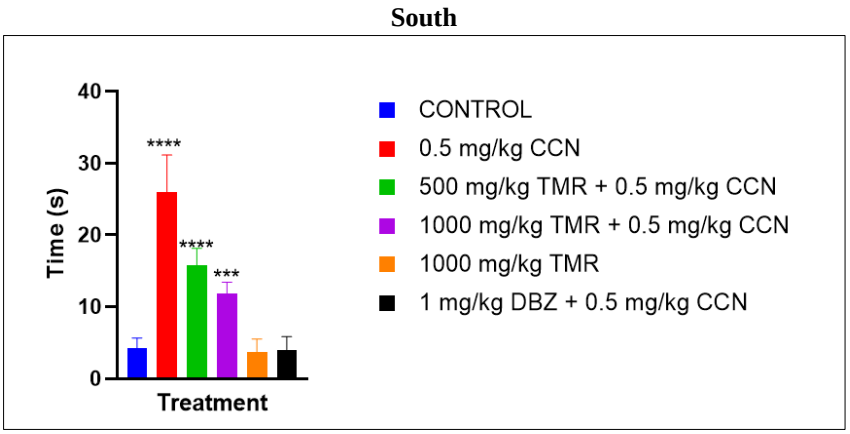


Figure 2: Data analysed by GraphPad Prism 9.3. One-way ANOVA with post hoc (Dunnett's) multiple comparisons test used to assess differences between treatment groups for cognition that showed statistical significance, ** and ***, p< 0.0001, 0.0002 when compared with the control group. CCN-Colchicine, TMR-Turmeric, DBZ- Donepezil**

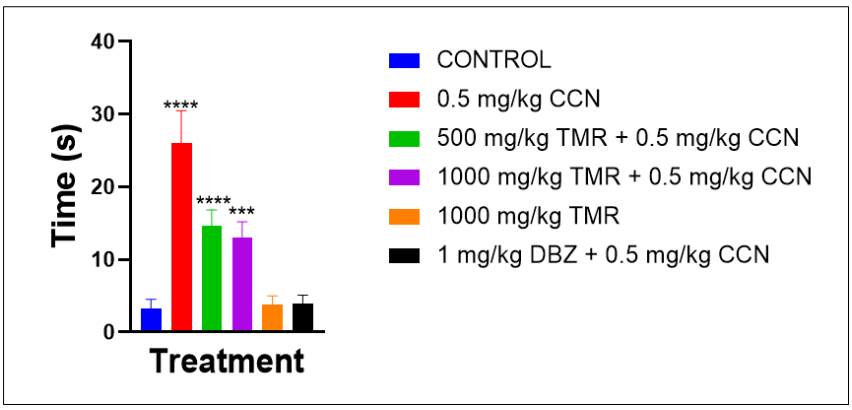


Figure 3: Data analysed by GraphPad Prism 9.3. One-way ANOVA with post hoc (Dunnett's) multiple comparisons test used to assess differences between treatment groups for cognition that showed statistical significance, ** and ***, p< 0.0001, 0.0002 when compared with the control group. CCN-Colchicine, TMR-Turmeric, DBZ- Donepezil**

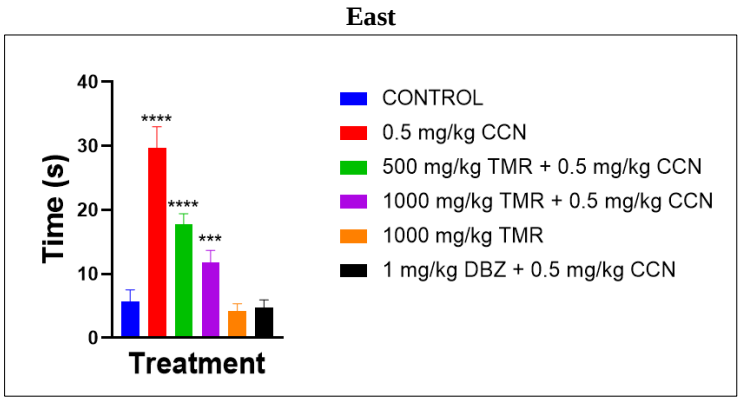
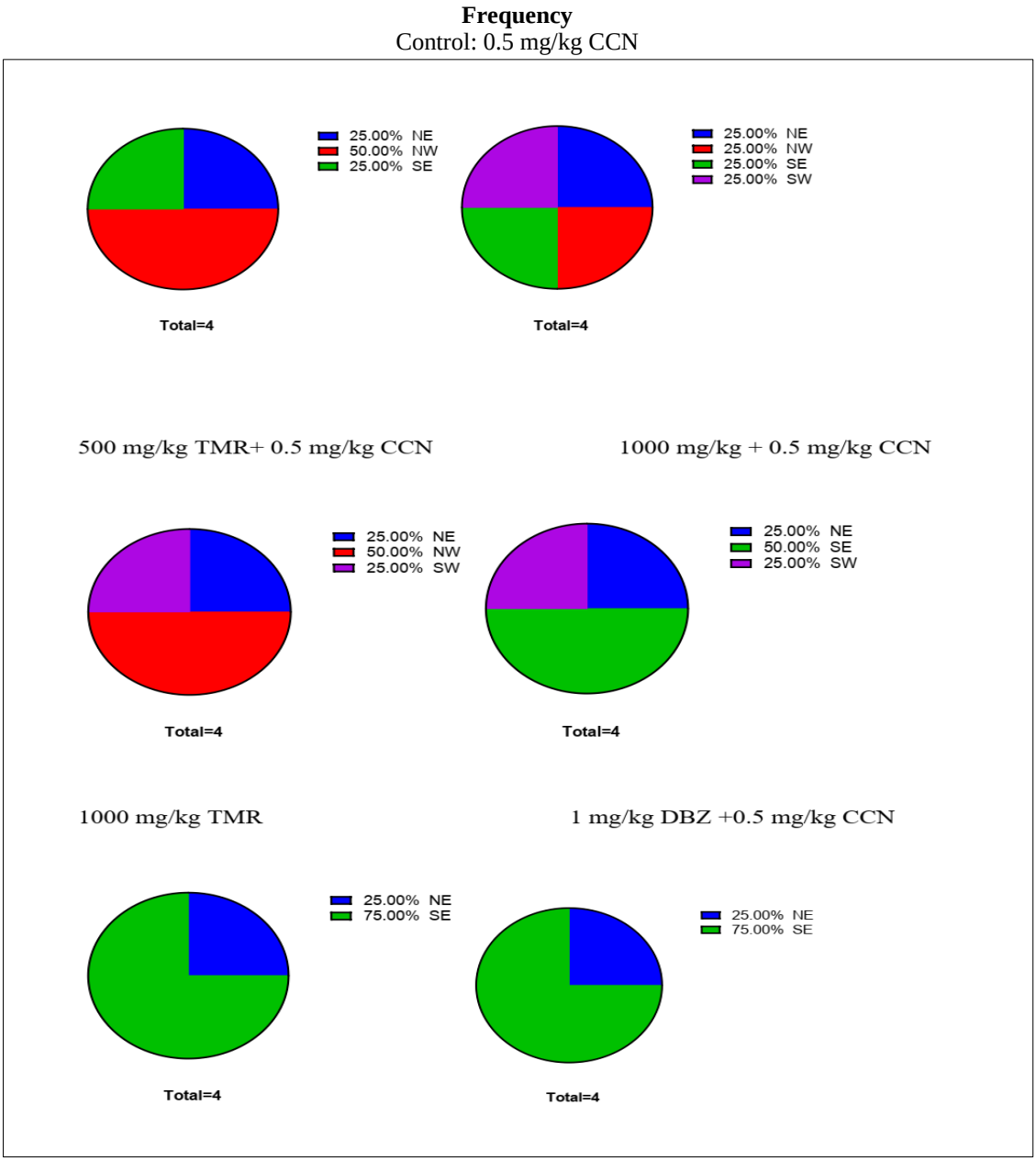


Figure 4: Data analysed by GraphPad Prism 9.3. One-way ANOVA with post hoc (Dunnett's) multiple comparisons test used to assess differences between treatment groups for cognition that showed statistical significance, ** and ***, p< 0.0001, 0.0002 when compared with the control group. CCN-Colchicine, TMR-Turmeric, DBZ- Donepezil**



DISCUSSION

Cognitive impairment, a hallmark of neurodegenerative disorders such as Alzheimer's disease (AD), is often characterized by deficits in learning, memory, and spatial navigation. Colchicine, a microtubule-disrupting agent, is known to induce cognitive dysfunction by impairing neuronal transport, promoting oxidative stress, and triggering neuroinflammation, primarily affecting the hippocampus (Mehta *et al*., 2017). The present study evaluates the cognitive reinforcement potential of turmeric (*Curcuma longa*) extract in colchicine-induced cognitive deficits in mice, revealing a significant improvement in cognitive function, especially in a dose-dependent manner (500 mg/kg and 1000 mg/kg). Furthermore, the results from spatial navigation assessments in the Morris water maze test indicated improved learning and memory in turmeric-treated groups, as evidenced by more efficient navigation from different quadrants (north, south, east, and west) to the escape platform.

Turmeric, rich in the polyphenol curcumin, has been extensively studied for its antioxidant, anti-inflammatory, neuroprotective, and cholinergic-enhancing properties (Mishra & Palanivelu, 2008). The present findings suggest that turmeric extract mitigates colchicine-induced neurotoxicity through multiple pharmacological mechanisms:

Colchicine-induced neurodegeneration is strongly linked to oxidative stress, which leads to mitochondrial dysfunction, lipid peroxidation, and neuronal apoptosis (Kamat *et al*., 2019). Curcumin has been shown to neutralize reactive oxygen species (ROS), enhance the doings of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px), and reduce oxidative damage in hippocampal neurons (Zhu *et al*., 2004). The significant cognitive improvement observed, particularly in the 1000 mg/kg turmeric group (table 1), may be attributed to enhanced neuroprotection against oxidative damage.

Neuroinflammation is a major contributor to cognitive impairment, and colchicine administration has been connected with elevated levels of pro-inflammatory cytokines such as TNF-α, IL-1β, & IL-6 in the brain (Heneka *et al*., 2015). Curcumin is a well-established inhibitor of nuclear factor-kappa B (NF-κB) signalling, which regulates inflammatory responses in microglia. By reducing neuroinflammatory markers, curcumin may prevent secondary neuronal damage and promote synaptic stability (Singh *et al*., 2010).

The cholinergic system, particularly the hippocampal and cortical acetylcholine (ACh) pathways, plays a crucial role in learning and memory (Bartus *et al*., 1982). Colchicine administration impairs acetylcholine (ACh) release and disrupts cholinergic signaling, leading to memory deficits (Mehta *et al*., 2017). Curcumin has been demonstrated to inhibit acetylcholinesterase (AChE), thereby increasing synaptic ACh availability and improving cognitive function (Mathew & Subramanian, 2014). The observed dose-dependent enhancement in spatial navigation performance in the turmeric-treated groups suggests a restoration of cholinergic neurotransmission and synaptic plasticity.

Hippocampal neurogenesis and synaptic remodeling are essential for cognitive function. Colchicine-induced toxicity leads to neuronal apoptosis, synaptic loss, and impaired brain-derived neurotrophic factor (BDNF) signalling, which is crucial for neuroplasticity (Xu *et al*., 2011). Curcumin has been reported to promote hippocampal neurogenesis, enhance synaptic connections, and upregulate BDNF expression, facilitating cognitive recovery (Mishra &Palanivelu, 2008). The improved spatial learning and faster navigation from multiple starting quadrants in the Morris water maze test support the hypothesis that turmeric enhances hippocampal synaptic strength and neuronal survival.

Cognitive function, particularly spatial learning and memory, is largely mediated by the hippocampus, prefrontal cortex, and associated neuronal circuits. Colchicine-induced neurotoxicity primarily affects the hippocampus, leading to disruptions in memory encoding, synaptic plasticity, and spatial navigation (Chaudhary *et al*., 2016). The anatomical effects observed in the present study align with the role of turmeric in hippocampal preservation and functional recovery.

The Morris water maze test assesses hippocampal-dependent learning by evaluating an animal's ability to locate a hidden escape platform from different quadrants (north, south, east, and west). The turmeric-treated groups exhibited significantly shorter escape latencies, suggesting improved spatial memory retention and efficient hippocampal function. The 1000 mg/kg group showed the most significant improvement, with mice quickly navigating from all quadrants to the escape platform, demonstrating enhanced reference memory (Table 1). The 500 mg/kg group exhibited moderate improvement, indicating partial protection against hippocampal damage.

These results suggest that turmeric facilitates hippocampal recovery, enhancing synaptic connectivity and neuronal signalling pathways. The prefrontal cortex (PFC) is a major player in executive function, working memory, and cognitive flexibility. Colchicine impairs PFC-dependent tasks by disrupting dopaminergic and cholinergic pathways (Kamat *et al*., 2019). Curcumin's ability to modulate dopaminergic transmission and

reduce neuroinflammation likely contributes to PFC-dependent cognitive improvements, further supported by the improved problem-solving abilities in the navigation task.

The amygdala, which interacts with the hippocampus in emotional processing and memory consolidation, is also vulnerable to colchicine-induced damage. Cognitive dysfunction often coexists with anxiety-like behaviours due to amygdalar dysfunction (Mathew & Subramanian, 2014). Curcumin's anxiolytic effects may help regulate amygdala-driven emotional responses, contributing toimproved cognitive stability and stress resilience.

The dose-dependent effects observed in the study suggest that turmeric's neuroprotective potential increases with higher doses (table 1, figure 1-4): the 500 mg/kg of turmeric led to moderate improvements, suggesting partial protection against oxidative damage and neuroinflammation. While the 1000 mg/kg of turmeric showed the most pronounced cognitive enhancement, likely due to greater BDNF expression, synaptic remodelling, and cholinergic enhancement. The turmeric-treated groups outperformed the colchicine-only group, demonstrating that turmeric effectively counteracts colchicine-induced neurotoxicity.

CONCLUSION

The results of this study indicate that turmeric extract significantly ameliorates colchicine-induced cognitive deficits through antioxidant, anti-inflammatory, cholinergic, and neurogenic mechanisms**.** The dose-dependent improvement in spatial navigation and cognitive performance suggests that turmeric not only protects hippocampal and cortical neurons but also facilitate ssynaptic plasticity and functional recovery**.** These findings highlight turmeric's potential as aneuroprotective agent in cognitive disorders and warrant further investigation into its therapeutic applications in neurodegenerative diseases such as Alzheimer's disease.

REFERENCES

- Ballard, C., Gauthier, S., Corbett, A., Brayne, C., Aarsland, D., & Jones, E. (2011). Alzheimer's disease. *The Lancet, 377*(9770), 1019–1031.
- Bartus, R. T., Dean, R. L., Beer, B., &Lippa, A. S. (1982). The cholinergic hypothesis of geriatric memory dysfunction. *Science, 217*(4558), 408–414.
- Chaudhary, P., Joshi, S. C., &Gajraj, A. (2016). Evaluation of colchicine-induced neurotoxicity in rats: A study on behavioral and biochemical parameters. *International Journal of Neuroscience, 126*(2), 123–132.
- Chen, X., Hu, Y., Cao, Z., Liu, Q., & Cheng, Y. (2022). The role of neuroinflammation in neurodegenerative diseases: Molecular mechanisms and therapeutic approaches. *Frontiers in Aging Neuroscience, 14*, 100573.
- D'Hooge, R., & De Deyn, P. P. (2001). Applications of the Morris water maze in the study of learning and memory. *Brain Research Reviews, 36*(1), 60–90.
- Heneka, M. T., Carson, M. J., El Khoury, J., Landreth, G. E., Brosseron, F., Feinstein, D. L., ... &Kummer, M. P. (2015). Neuroinflammation in Alzheimer's disease. *The Lancet Neurology, 14*(4), 388–405.
- Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A review of its effects on human health. *Foods, 6*(10), 92.
- Kumar, A., & Singh, A. (2020). A review on mitochondrial restorative mechanism of antioxidants in Alzheimer's disease and other neurological conditions. *Frontiers in Pharmacology, 11*, 634.
- Mehta, A., Prabhakar, M., Kumar, P., Deshmukh, R., & Sharma, P. L. (2017). Excitotoxicity: Bridge to various triggers in Alzheimer's disease. *European Journal of Pharmacology, 817*, 1–11.
- Mehta, A., Prabhakar, M., Kumar, P., Deshmukh, R., & Sharma, P. L. (2017). Excitotoxicity: Bridge to various triggers in Alzheimer's disease. *European Journal of Pharmacology, 817*, 1–11.
- Mehta, A., Prabhakar, M., Kumar, P., Deshmukh, R., & Sharma, P. L. (2017). Excitotoxicity: Bridge to various triggers in Alzheimer's disease. *European Journal of Pharmacology, 817*, 1-11.
- Mishra, S., &Palanivelu, K. (2008). The effect of curcumin (turmeric) on Alzheimer's disease: An overview. *Annals of Indian Academy of Neurology, 11*(1), 13.
- Mishra, S., &Palanivelu, K. (2008). The effect of curcumin (turmeric) on Alzheimer's disease: An overview. *Annals of Indian Academy of Neurology, 11*(1), 13.
- Morris, R. (1984). Developments of a water-maze procedure for studying spatial learning in the rat. *Journal of Neuroscience Methods, 11*(1), 47–60.
- National Research Council. (2011). *Guide for the care and use of laboratory animals* (8th ed.). National Academies Press.
- Paxinos, G., & Franklin, K. B. J. (2001). *The mouse brain in stereotaxic coordinates* (2nd ed.). Academic Press.
- Sharma, R., Kaur, G., & Singh, S. (2018). Curcumin and its derivatives: Therapeutic and medicinal applications in neurodegeneration. *Neuroscience and Biobehavioral Reviews, 85*, 175-186.
- Vorhees, C. V., & Williams, M. T. (2006). Morris water maze: Procedures for assessing spatial and related forms of learning and memory. *Nature Protocols, 1*(2), 848–858.

- Zhang, X., Yin, P., Fan, H., Sun, H., & Jiang, Y. (2021). Curcumin and neuroprotection: Mechanisms and pharmacological implications. *International Journal of Molecular Sciences*, *22*(11), 6085.