© 2026 Akter F, et al. This is an open access article distributed under the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (https://creativecommons.org/licenses/by-nc-sa/4.0/). ISSN 2518-6299 (print), 2520-5048 (online)

Original Article

Analysis of the Effects of *Phyllanthus emblica* (Amloki) Fruit on Colchicine Induced Memory Deficit and Hippocampal Oxidative Stress in Male Long-Evans Rats

Fhamida Akter[1], Mahatab Bin Mostafa[2], Puspita Basak[3], Rokhsana Binte Amin[4]

Abstract

Background: *Oxidative stress plays a crucial role in the development of several serious diseases, such as inflammation, neurodegenerative disorders, liver cirrhosis, atherosclerosis, cardiovascular diseases, cataracts, diabetes, and cancer. Compounds that can effectively scavenge free radicals possess significant potential for improving these diseases. This research was conducted to evaluate the impact of the ethanolic extract of Phyllanthus emblica (EEPE) on memory and oxidative stress in the hippocampus induced by colchicine in male Long-Evans rats.* ***Materials and Methods:*** *This experimental study was conducted at KM Fariduddin Animal Research Laboratory, Department of Physiology, Bangladesh Medical University (BMU). Here total 24 male Long-Evans rats were divided into 4 groups (6 rats/group). Based on treatments these were normal control (NC), sham control (SC), colchicine control (ColC), pre colchicine PE (Pre PE Exp). For evaluation of memory performance specially reference memory (RM), Morris water maze (MWM) test [Mean escape latency (EL) in acquisition phase, number of target crossing (TC) and time spent in target (TT) in probe trial] was done. Then, after sacrifice, hippocampal tissue was collected for estimation of malondialdehyde (MDA) and glutathione peroxidase (GPx) to assess oxidative stress status. The statistical analysis was done by one way ANOVA followed by Bonferroni post hoc test where $p<0.05$ was considered as statistically significant.* ***Results:*** *In this study, RM performance colchicine caused significantly higher mean EL ($p<0.001$) in acquisition as well as significantly ($p<0.001$) lower TC and TT in ColC rats in comparison to those SC rats. In contrast, significantly lower mean EL ($p<0.001$) in acquisition phase along with significantly higher TC and TT ($p<0.001$) were found in Pre PE Exp rats, than those of ColC rats. ColC rats exhibited significantly higher MDA levels ($p<0.001$) and significantly lower GPx activity ($p<0.001$) compared to SC rats. However, pre-colchicine PE (Pre PE Exp) groups of rats showed significantly ($p<0.01$) lower MDA as well as significantly higher ($p<0.05$) GPx in comparison to those of ColC rats. Moreover, when we compared all these memory and oxidative stress variables between our experimental and NC rats, they were statistically non-significant.* ***Conclusion:*** *Phyllanthus emblica (Amloki) can improve colchicine induced forgetfulness and intrahippocampal oxidative stress in male Long-Evans rats.*

Keywords: *Phyllanthus emblica* (PE), Colchicine, malondialdehyde, glutathione peroxidase, hippocampus, Oxidative stress, Morris water maze (MWM) test.
Received: October 16, 2025; **Accepted:** December 02, 2025
https://doi.org/10.3329/emcj.v11i1.90000

Introduction

Oxidative stress is the imbalance between reactive oxygen species (ROS) and the antioxidant opposing forces[1]. It can induce damage to cellular membranes resulting in lipid peroxidation, protein oxidation and DNA and RNA damage. As a consequence, malondialdehyde (MDA), protein carbonyls, 8-hydroxyguanine etc., are produced[2]. This MDA can be measured as an indirect index of oxidative stress[3]. On the other hand, various antioxidants are the scavenging molecules that limit or prevent the damaging effects of ROS and repairs cell damage. The common antioxidants include superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH), vitamin E, β carotene, vitamin C, taurine, L-carnitine, coenzyme Q compound 10 etc[4]. The brain is particularly vulnerable to oxidative stress due to its high metabolic demand, abundance of easily oxidizable components, and comparatively limited antioxidant defense mechanisms[5].

Colchicine, an alkaloid drug, destroys microtubular assembly, decreases axoplasmic transport[6], increases free radical generation and causes

[1]Assistant Professor, Department of Physiology, Eastern Medical College, Cumilla, Bangladesh.
[2]Registrar, Department of ENT & HNS, Dhaka Community Medical College, Dhaka, Bangladesh.
[3]Assistant Professor, Department of Physiology, Monno Medical College, Manikganj, Bangladesh.
[4]Lecturer, Department of Pathology, Shaheed Ziaur Rahman Medical College, Bogura, Bangladesh.

Adress of Correspondence: Dr. Fhamida Akter, Assistant Professor, Department of Physiology, Eastern Medical College, Cumilla, Bangladesh. E-mail: shompadjmc@gmail.com

oxidative stress[7]. The hippocampus, located in the most medial part of the temporal lobe cortex, plays a crucial role in the formation as well as maintenance of memories. Oxidative stress is the most common cause of memory impairment. Phyllanthus emblica (PE), popularly known as 'Amloki', is an essential medicinal fruit that offers a broad spectrum of health benefits. Studies have indicated that its fruit is hepatoprotective[8], functions as an antitussive[9], and has anti-pyretic and analgesic properties[10]. It is also recognized for its antidiabetic effects[11], antimalignant properties[12] and anti-malarial effects[13]. Additionally, it exhibits anti-inflammatory[14], hypolipidemic[15], nephroprotective [16] and antimicrobial properties[17]. PE, which is very rich in vitamin C, is a very well-known antioxidant vitamin. Moreover, PE also contains tannin and polyphenol compounds in a very large amount both of which have marked antioxidant property[18].

In recent times, oxidative stress has been identified as a key underlying pathology in various diseases, and PE contains antioxidant components. So, the present study was designed to evaluate the effects of *Phyllanthus emblica* (PE) 700 mg/kg for 7 days on memory performance as well as hippocampal oxidative stress markers before colchicine induced memory impairment in male Long-Evans rats.

Materials and Methods

Study design: This experimental study was conducted in the K M Fariduddin animal laboratory of the Department of Physiology of Bangladesh Medical University (BMU), Dhaka, Bangladesh from March 2023 to February 2024. Ethical clearance for this study was obtained from the Institutional Review Board of BMU (Reg No: 4469). ***Drugs and chemicals:*** Normal saline (Opso Saline Ltd, Bangladesh), gentamicin (Incepta Pharmaceuticals Ltd, Bangladesh), thiopental sodium (Gonosasthaya Pharmaceuticals Ltd), di-ethyl ether (MERCK, Germany) and Ethanol (MERCK, Germany) were purchased from local market. Colchicine was obtained from Incepta Pharmaceuticals Ltd, Bangladesh.

Collection and identification of plant materials: The fresh leaves of PE were collected from Haziganj Upazila under the Chandpur district, Bangladesh, in August 2023 and and was identified by an expert taxonomist at the Bangladesh National Herbarium, Mirpur, Dhaka, Bangladesh. A voucher specimen (accession no. DACB 90617) was deposited in the herbarium for future reference.

Extract collection: A method for preparing a crude ethanolic extract from the fruits of the *PE* plant has been described previously by Uddin et al., 2016[19]. Initially, 5 kg of fruits were collected, washed to eliminate dirt, and shade dried for 30 minutes. The seeds were then removed, and seed-free fruits underwent an additional drying process for 7 days using irregular sun drying techniques. Following this, the dried fruits were ground manually into a powder, yielding approximately 500 grams, which was stored in an airtight container. The powder was soaked in 2.5 liters of 98% ethanol in an amber-colored glass bottle, which was sealed and left at room temperature (24-27ºC) for 7 days with frequent shaking to facilitate extraction. After this period, the mixture was filtered through cotton and Whatman (Grade no.1) filter paper. The resulting filtrate was concentrated and evaporated at 50°C using a rotatory evaporator under reduced pressure to obtain the crude extract. Finally, dried crude ethanolic extract was stored at 4°C for future use.

Procurement and maintenance of animals: A total of 30 male Long-Evans rats, aged approximately 8 weeks and weighing around 225 grams, were collected from BMU central animal house. The rats were housed in specially designed plastic cages, with 6 rats per cage, under a controlled 12-hour light/dark cycle[20]. The ambient temperature was kept at 27°C, which is within the thermoneutral zone for rodents, ranging from 27-28°C[21]. During the acclimatization phase, the rats had unrestricted access to standard laboratory food and cooled boiled water *ad libitum*[22]. All experimental procedures complied with the guidelines established by the Animal Experimentation Ethics Committee (AEEC) on May 15, 2023, from the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDRB). Furthermore, the experiments were conducted under the supervision of an expert veterinarian of Bangladesh Agricultural University, Mymensingh, Bangladesh. To reduce circadian effects, all experiments were performed during daytime hours, specifically between 08:00 and 16:00 hours[23].

Experimental setup and animal grouping: On the basis of treatments, all the rats were randomly divided into four (4) groups, with six (6) rats in each group: a) Normal control (NC): No stereotaxic surgery (SS); no treatment; healthy rats b) Sham control (SC): Hippocampal infusion of 1 µl Normal saline (NS) by SS c) Colchicine control (ColC): Hippocampal infusion of 15 µg of colchicine in 1 µl NS by SS and d) Pre colchicine PE (Pre PE Exp): Intraperitoneal (i.p) administration of ethanolic extract of *Phyllanthus emblica* (EEPE) 700 mg/kg for 7 days followed by hippocampal infusion of 15 µg of colchicine in 1 µl NS by SS.

After 7 days of room acclimatization of all rats, for memory evaluation of NC rats, Morris water maze (MWM) test was performed. On 8th day 1 µl Normal saline infusion (SC rats), as well as 15 µg of colchicine in 1 µl NS infusion (ColC rats) in

hippocampus was given by stereotaxic surgery. Then, after 12 days of post-surgical period MWM test was done for memory performance of these two groups of rats. In case of experimental (Pre PE Exp) rats after 7 days of room acclimatization, i.p 700 mg/kg EEPE was applied on 8Th to 14th day. On 15th day, 15 µg of colchicine in 1 µl NS was infused on hippocampus by stereotaxic surgery in experimental rats. After that 12 days of post-surgical period Pre PE Exp rats were checked by MWM for memory. Following the experimental period, the rats were sacrificed, and brain tissues (hippocampus) were extracted for the estimation of hippocampal malondialdehyde (MDA) and glutathione peroxidase (GPx).

Hippocampal colchicine application by stereotaxic surgery: Considering previous studies[24,25], colchicine was administered into the rat hippocampus through stereotaxic surgery (SS). Each rat was subjected to an overnight fasting period before the surgery, although it was allowed to drink water. On the day of the operation, the rat was deeply anesthetized with thiopental sodium (45 mg/kg, i.p.). It was subsequently placed in a stereotaxic frame for precise positioning. The scalp was carefully incised and reflected. A Hamilton micro syringe was used to infuse 15 µg of colchicine in 1 µl normal saline into each hippocampus. The control rats were administered a vehicle injection. Infusion was performed at the following coordinates relative to bregma: -3.6 mm anterior-posterior, ±2 mm lateral-medial, and -3.4 mm dorso-ventral. The administration of colchicine and/ or normal saline into the hippocampus was conducted very slowly over 1 minute, and the micro syringe was maintained in position for the next minute (60 seconds) before being gently withdrawn. The scalp was subsequently closed with sutures. Right after the surgery, the rat was placed in a post-operative cotton bed for 2 days, with all aseptic measures and care taken for feeding until it recovered from surgical stress. Gentamycin (5 mg/kg, i.p) was given post operatively to avert sepsis.

Memory assessment by Morris Water Maze (MWM) test:

Test tools and circumstances: Memory was evaluated using the Morris Water Maze (MWM) test. According to previous researchers[26,27], the apparatus consisted of a large circular pool (150 cm in diameter X 50 cm high) filled with water. The entire inner surface of the pool and the platform were coated with non-toxic black paint to eliminate visual cues. The pool was situated in a room with additional maze cues, which the rats could use for spatial orientation. Eight starting positions-north (N), south (S), east (E), west (W), northeast (NE), northwest (NW), southeast (SE), and southwest (SW) were designated and the pool was divided into four arbitrary quadrants. A black, circular platform (15 cm diameter × 28 cm height) was positioned in the center of the NE quadrant, with its top submerged 2 cm below the water surface to remain hidden from view.

Reference memory test: At first rats were swimming for 3 minutes without platform for consecutive 3 days for instrumental acclimatization as well as for habituation phase of Reference memory version. Then in acquisition phase, the rats were given four trials per day over 6 consecutive days kept in a fixed position (that was NE quadrant). In each trial, the rats were released from a different starting point in a different sequence each day and given 60 sec to find the platform and to climb onto it. A 50 sec (20 sec on platform and 30 sec for self-drying) intertrial time was permitted. The time taken by each rat to reach the platform, referred to as the mean escape latency (EL), measured from the moment the rat entered the water until it reached the platform, was recorded using a stopwatch to evaluate learning ability. Similar 4 trials were given for all rats for consecutive 6 days. During the first trial of each day, rats reached the platform by chance, representing the information stage. In the subsequent trials, they were required to locate the platform in its fixed position over six days, reflecting learning and memory performance. About 24 hours after last trial of day 6 (that was on day 7), the platform was removed from pool and final spatial probe trial was given to assess learning strength/ retrieval. In this probe trial, rats were allowed to swim *ad libitum* for 60 sec during which target crossings (TC) (TC; number of passing the quadrant of MWM by rats, within 60 seconds from where the platform was removed) and time spent in target (TT) (TT; the time spent in the quadrant, from where the platform was removed within 60 seconds) were measured.

Hippocampal separation and tissue preparation: The rats were sacrificed via decapitation while under di-ethyl ether anesthesia. The brain tissues were quickly extracted, and the hippocampal tissues were immediately dissected from the brain. The dissected hippocampi were cut into small pieces and washed with ice-cold phosphate-buffered saline (PBS) (0.1 M, pH: 7.40) to thoroughly remove any excess blood. Then the tissue pieces were weighed and homogenized in PBS according to the ratio of Weight (gm): Volume (mL) = 1:4 with a glass homogenizer on ice. The homogenate was then centrifuged at 3,500 rpm for 10 minutes, and the resulting supernatants were used for the analysis of all biochemical parameters. If there was any unintended delay, then the supernatant was kept at -20°C in laboratory.

Hippocampal oxidative stress markers assay: Hippocampal malondialdehyde (MDA) and

OPEN ACCESS

glutathione peroxidase (GPx) level were measured immediately by ELISA by using Elab Science Biotechnology kit (USA). The micro-ELISA plate provided in this kit has been pre-coated with an antibody specific to Rat GPx and MDA. Samples or standards are added to the wells and mixed with the antibodies. Following incubation, a biotinylated detection antibody and Avidin-Horseradish Peroxidase (HRP) conjugate are added. After washing away free components, a substrate solution is introduced, and the reaction is stopped with a stop solution. The resulting color change is measured spectrophotometrically at a wavelength of 450±2 nm, allowing for the determination of MDA and GPx concentrations by comparing optical densities to a standard curve.

Statistical analysis: The results were presented as mean ± SEM for the measured variables. Data were statistically analyzed by using one-way ANOVA followed by Bonferroni post hoc test in SPSS version 25.0, where $p<0.05$ was considered as statistically significant.

Results

Effect of PE on memory impairment induced by hippocampal colchicine:

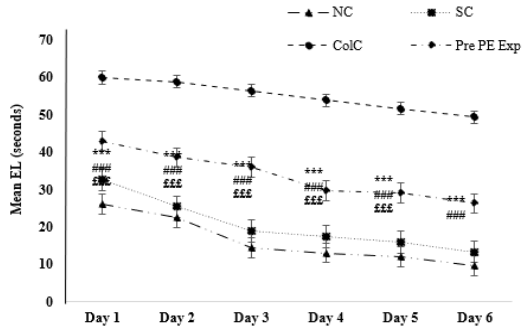

Figure-1: Mean escape latency (EL, seconds) during the acquisition phase of the Morris Water Maze test across different rat groups

Each day represents mean ± SEM of 4 trials of 6 rats in that day. Statistical analysis was performed using ANOVA for comparisons among groups, followed by Bonferroni's post hoc test for pairwise group comparisons. *=SC vs ColC, # = ColC vs Pre PE Exp. In the interpretation of results, $p<0.05$ was considered as significant. ***/###/£££ = $p<0.001$.

As shown in Figure-1, ColC rats showed significantly ($p<0.001$) higher mean EL in all acquisition days in comparison to those of SC rats. However, EEPE improved our rats 'learning ability performance, as evidenced by statistically significant ($p<0.001$) differences in mean EL of our ColC and experimental (Pre PE Exp) rats. Strikingly, the differences of this variable between experimental (Pre PE Exp) and NC rats were found statistically non-significant in the last acquisition day. These results indicate that colchicine impaired reference memory learning, and systemic administration of PE nearly restored this ability to normal levels.

In our study, ColC rats showed retrieval impairment, as evidenced by significantly ($p<0.001$) lower target crossings (TC) and time spent in target (TT) than those of SC rats. This PE carried out significantly ($p<0.001$) higher TC and TT in our experimental (Pre PE Exp) rats than that of ColC rats. Statistical analysis revealed that the differences in these variables between NC vs Pre PE Exp rats were not significant (Figure-2). This data indicated that the learning strength (retrieval) was hampered by colchicine and prevented almost to normal by i.p EEPE.

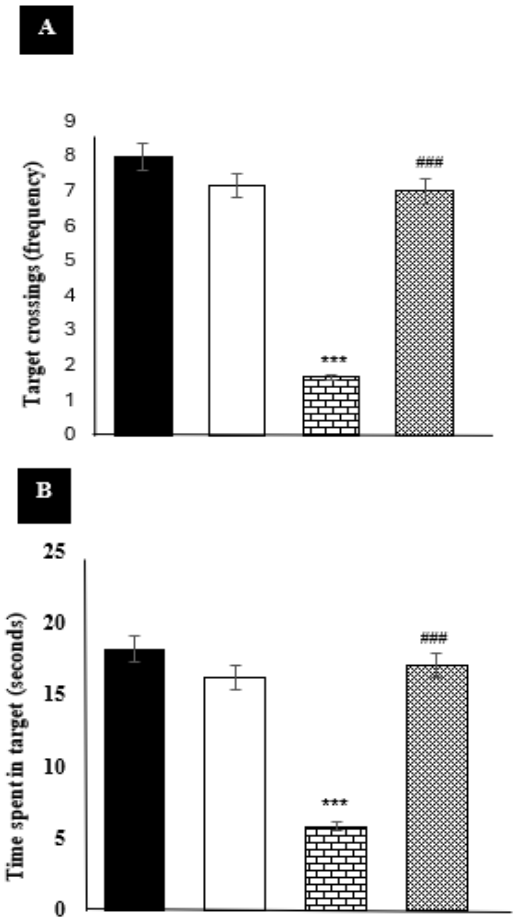

Figure-2: (A) Target crossings (TC, in frequency/minute) and (B) Time spent in target (TT, in seconds/minute) in probe trial of Morris water maze test in different groups of rats. Each bar symbolizes mean ± SEM for 6 rats. Statistical analysis was performed using ANOVA for comparisons among groups, followed by Bonferroni's post hoc test for pairwise group comparisons. *= SC vs ColC, #= ColC vs Pre PE Exp. In the interpretation of results, $p<0.05$ was considered as significant. ***/### = $p<0.001$.

OPEN ACCESS

Hippocampal malondialdehyde (MDA), to assess oxidation:

In this study, the mean values of MDA were significantly ($p<0.001$) higher in ColC group in comparison to that of SC groups of rats. However, the mean values of this variable were significantly ($p<0.01$) lower in Pre PE Exp group in comparison to that of ColC groups of rats. On the contrary, the differences of mean hippocampal MDA between the NC group and experimental group (Pre PE Exp) were statistically non-significant (Table-I).

Hippocampal glutathione peroxidase (GPx), to assess antioxidation:

In this study, the mean values of GPx were significantly ($p<0.001$) lower in ColC group in comparison to that of SC rats. Moreover, the mean values of this variable were significantly higher ($p<0.05$) in experimental group (Pre PE Exp) in comparison to that of ColC rats. On the contrary, the differences of mean hippocampal GPx between the group NC vs Pre PE Exp were statistically non-significant (Table-I).

Table-I: Hippocampal levels of malondialdehyde (MDA, ng/mg protein) and glutathione peroxidase (GPx, pg/mg protein) across different rat groups

Hippocampal oxidative stress markers	Groups			
	NC	SC	ColC	Pre PE Expe
MDA	8.04±1.43	8.32±0.59	17.34±1.97***	9.74±1.43##
GPx	316.19±28.93	252.12±15.19	121.79±6.35**	243.13±7.43#

Each column symbolizes mean ± SEM for 6 rats. Values in parenthesis indicate ranges. Statistical analysis was performed using ANOVA for comparisons among groups, followed by Bonferroni's post hoc test for pairwise group comparisons. * = SC vs ColC, # = ColC vs Pre PE Exp. In the interpretation of results, $p<0.05$ was considered as significant. */# =$p<0.05$; **/## = $p<0.01$; ***/### = $p<0.001$.

Discussion

Oxidative stress plays a significant role in the onset and advancement of numerous diseases. According to Halliwell and Gutteridge[28], the brain utilizes oxygen at a higher rate per unit of tissue mass. It also contains high levels of peroxidizable lipids, excitotoxic amino acids and low levels of antioxidants. Therefore, the brain is more prone to oxidative damage compared to other organs[28]. In this study, colchicine is infused to hippocampus by stereotaxic surgery which might bind with microtubule binding protein (tubulin)[29], might depolymerize microtubules[30], causes decreased cellular growth, differentiation[31] and hippocampal cholinergic neurons damage[32,33] which causes memory deficit. It might induce direct nitric oxide (NO) production[34] by activation of inducible nitric oxide synthase (iNOS)[35]. This NO might react with superoxide anions ($O_2^{\cdot-}$) (a reactive oxygen species, ROS) rapidly and form peroxynitrite ($ONOO^{\cdot}$) (a reactive nitrogen species, RNS), resulted in oxidative stress in our colchicine treated rats. In addition, this neurotoxic agent might elevate glutamate binding site α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and N-Methyl-D-aspartate (NMDA) receptors in hippocampal neurons causing excess Ca^{2+} influx[31].

This process might be responsible for mitochondrial stress, ROS production, oxidative stress and neuronal death in hippocampus[36]. However, markedly increased ROS and RNS might affect double bond of polyunsaturated fatty acid in cell membrane (lipid peroxidation) and might elevate hippocampal MDA level[37]. In addition, increment of oxidants might cause increased consumption of GPx for oxidative balance and decreased the GPx concentration in hippocampal neurons[37,38].

In reference memory paradigm, ColC rats showed lower learning ability as evidenced by significantly higher mean EL in all acquisition days of acquisition phase in comparison to those of SC rats (Figure-1). However, EEPE improved this learning disability, as evidenced by statistically significant differences in mean EL of our ColC and experimental (Pre PE Exp) rats. Strikingly, the differences of this variable between our experimental (Pre PE Exp) and NC rats showed no statistically significant differences on the final day of the acquisition phase. Moreover, our ColC rats showed retrieval disability, as evidenced by significantly lower target crossings (TC) and time spent in target (TT) than those of SC rats (Figure-2).

In addition, EEPE showed significantly higher TC and TT in experimental rats (Pre PE Exp) than that of ColC rats. However, the differences of these variables between our experimental (Pre PE Exp) and NC rats were found statistically non-significant. Humans and animals are largely dependent on plants not only for food but also for cures from disease or enhancing health and wellbeing. Herbal plants with medicinal property are a blessing for humans. According to WHO, more than 80% of people worldwide depend on medicinal plants for their primary healthcare needs[19]. In Bengali *Phyllanthus emblica* (PE) locally called 'Amloki' is native to tropical regions of southeast asia, particularly in central and southern India, Nepal, Pakistan, Bangladesh, Bhutan and Srilanka. It also grows in

OPEN ACCESS

Uzbekistan, Malaysia, Ceylon, Indonesia and some other countries over the world. Round the year from October to December, it is ripened.

In this study, Ethanolic extract of *Phyllanthus emblica* (EEPE) reduced oxidative stress in our experimental groups as evidenced by decrement of MDA and increment of GPx when compared to colchicine treated rats in the hippocampus. However, PE might inhibit lipid peroxidation and protect neuronal cell membrane resulting in decrement of MDA[39]. Besides that, Amloki is one of the richest source of vitamin C, which is an antioxidant vitamin, might increase antioxidant storage of our experimental rats after supplementation. In addition, *Phyllanthus emblica* (PE) fruits also contain large quantity of tannin along with polyphenol compounds, both of which have marked antioxidant property[18]. Thus, a 7-day intraperitoneal administration of a high dose of EEPE may protect against oxidative stress by activating the nuclear erythroid 2-related factor 2/antioxidant response element (Nrf2/ARE) signaling pathway in the hippocampus[40] and enhancing the expression of various antioxidant enzymes, including GPx in our experimental rats[19,41].

The elevated GPx levels may have helped reduce the heightened MDA load in the experimental rats pre-treated with PE. As a whole, it is evident that our 7-day EEPE could improve colchicine induced reference memory impairment as well as oxidative stress near to normal.

Conclusion

Phyllanthus emblica (Amloki) demonstrates a protective effect against intrahippocampal colchicine-induced memory dysfunction in male Long-Evans rats. In addition to improving cognitive performance, it also alleviates oxidative stress in the hippocampus, suggesting its potential as a neuroprotective agent.

Conflict of Interest

The authors declared that they have no conflicts of interest.

Acknowledgements

Authors would like to thank Bangladesh Medical University (BMU) for financing this research partially by a grant. We would like to express thanks to Dr. Birendra Nath Mallick, Professor and Director, Amity Institute of Neuropsychology and Neurosciences, Gautam Budh Nagar, Uttar Pradesh, India, for his valuable suggestions and helping us in proper conduction of stereotaxic surgery. We would also like to thank the Incepta Pharmaceuticals Ltd, Bangladesh, for providing us colchicine powder.

References

1. Gupta YK, Gupta M, Kohli K. Neuroprotective role of melatonin in oxidative stress vulnerable brain. Indian J Physio Pharmacol. 2003; 47 (4): 373-86.
2. Praticò D. Oxidative stress hypothesis in Alzheimer's disease: a reappraisal. Trends Pharmacol Sci. 2008; 29 (12): 609-15. doi: 10.1016/j.tips.2008.09.001.
3. Deavall DG, Martin EA, Horner JM, Roberts R. Drug-induced oxidative stress and toxicity. J Toxicol. 2012; 2012: 645460. doi: 10.1155/2012/645460.
4. Michel P, Granica S, Rosińska K, Glige M, Rojek J, Poraj Ł, et al. The effect of standardised leaf extracts of gaultheria procumbens on multiple oxidants, inflammation-related enzymes, and pro-oxidant and pro-inflammatory functions of human neutrophils. Mol. 2022; 27 (10): 3357. doi: 10.3390/molecules27103357.
5. García-Mesa Y, Colie S, Corpas R, Cristòfol R, Comellas F, Nebreda AR, et al. Oxidative stress is a central target for physical exercise neuroprotection against pathological brain aging. J Gerontol A Biol Sci. 2015; 71 (1): 40-9. doi: 10.1093/gerona/glv005.
6. Crothers SD, McCluer RH. Effect of colchicine on the delayed appearance of labelled protein into synaptosomal soluble proteins. J Neurochem. 1975; 24 (2): 209-14. doi: 10.1111/j.14714159.1975.tb11866.x
7. Yu Z, Cheng G, Hu B. Mechanism of colchicine impairment on learning and memory, and protective effect of CGP36742 in mice. Brain Res. 1997; 750 (1-2): 53-8. doi: 10.1016/S00068993(96)01158-4.
8. Jose JK, Kuttan R. Hepatoprotective activity of Emblica officinalis and Chyavanaprash. J Ethnopharmacol. 2000; 72 (1-2): 135-40. doi: 10.1016/S03788741(00)00219-1.
9. Nosal'ova G, Mokrý J, Hassan KT. Antitussive activity of the fruit extract of Emblica officinalis Gaertn.(Euphorbiaceae). Int J Phytomedicine. 2003; 10 (6-7): 583-9. doi: 10.1078/094471103322331872.
10. Perianayagam JB, Sharma SK, Joseph A, Christina AJM. Evaluation of anti-pyretic and analgesic activity of Emblica officinalis Gaertn. J Ethnopharmacol. 2004; 95 (1): 83-5. doi: 10.1016/j.jep.2004.06.020.
11. Patel SS, Goyal RK, Shah RS, Tirgar PR, Jadav PD. Experimental study on effect of hydroalcoholic extract of Emblica officinalis fruits on glucose homeostasis and metabolic parameters. AYU. 2013; 34 (4): 440-4. doi: 10.4103/0974-8520.127731.
12. Liu AX, Zhao BM, Wua K, Chai AX, Yu AH, Tao AZ, et al. Immunomodulatory and anticancer activities of phenolics from emblica

fruit (Phyllanthus emblica L.). Food Chem. 2011; 131 (2): 685-90. doi: 10.1016/j.foodchem.2011.09.063.
13. Pinmai K, Hiriote W, Soonthornchareonnon N, Jongsakul K, Sireeratawong S, Tor-Udom S. In vitro and in vivo antiplasmodial activity and cytotoxicity of water extracts of Phyllanthus emblica, Terminalia chebula, and Terminalia bellerica. J Med Assoc Thai. 2011; 93 (12): 120-6.
14. Santoshkumar J, Devarmani MS, Sajjanar M, Pranavakumar MS, Dass P. A study of anti-inflammatory activity of fruit of Emblica officinalis (Amla) in Albino rats. Medica Innovatica. 2013; 2 (1): 17-26.
15. Santoshkumar J, Manjunath S, Pranavakumar MS. A study of anti-hyperlipidemia, hypolipedimic and anti-atherogenic activity of fruit of Emblica officinalis (Amla) in high fat fed Albino rats. Int J Med Res Health Sci. 2013; 2 (1):70-7.
16. Malik S, Suchal1 K, Bhatia1 J, Khan SI, Vasisth S, Tomar A, et al. Therapeutic potential and molecular mechanisms of Emblica officinalis Gaertn in countering nephrotoxicity in rats induced by the chemotherapeutic agent cisplatin. Front Pharmacol. 2016; 7: 350. doi: 10.3389/fphar.2016.00350.
17. Al-Gbouri NM, Hamzah AM. Evaluation of Phyllanthus emblica extract as antibacterial and antibiofilm against biofilm formation bacteria. Iraqi J Agric Sci. 2018; 49 (1): 142-51. doi: 10.36103/ijas.v49i1.217.
18. Shukla V, Vashistha M, Singh SN. Evaluation of antioxidant profile and activity of amalaki (Emblica officinalis), spirulina and wheat grass. Indian J of Clin Biochem. 2009; 24 (1): 70-5. doi: 10.1007/s12291-009-0012-3.
19. Uddin MS, Al Mamun A, Hossain MS, Akter F, Iqbal MA, Asaduzzaman M. Exploring the effect of Phyllanthus emblica L. on cognitive performance, brain antioxidant markers and acetylcholinesterase activity in rats: promising natural gift for the mitigation of Alzheimer's disease. Ann.Neurosci. 2016; 23 (4): 21829. doi: org/10.1159/000449482.
20. Wren-Dail MA, Dauchy RT, Ooms TG, Baker KC, Blask DE, Hill SM, et al. Effects of colored enrichment devices on circadian metabolism and physiology in male Sprague-Dawley rats. Comp Med. 2016; 66 (5): 384-91.
21. Fischer AW, Cannon B, Nedergaard J. Optimal housing temperatures for mice to mimic the thermal environment of humans: an experimental study. Mol Metab. 2018; 7: 161-70. doi: 10.1016/j.molmet.2017.10.009.
22. Islam KN, Rahman ASMH, Al-Mahmud KA. Manual for care and use of laboratory animals. Animal resources branch. International Centre for Diarrheal Disease Research, Bangladesh (iccdr,b), 2023.
23. Deboer T. Sleep homeostasis and the circadian clock: do the circadian pacemaker and the sleep homeostat influence each other's functioning? Neurobiol Sleep Circadian Rhythms. 2018; 5: 68-77. doi: 10.1016/j.nbscr.2018.02.003.
24. Paxinos G, Watson C. The rat brain in stereotaxic coordinates. 6th ed. Paris, Armstredium: Elsevier; 2007. pp XII-XXIX.
25. Kumar A, Dogra S, Prakash A. Protective effect of naringin, a citrus flavonoid, against colchicine-induced cognitive dysfunction and oxidative damage in rats. J Med Food. 2010; 13 (4): 976-84. doi: 10.1089/jmf.2009.1251.
26. Sarihi A, Motamedi F, Naghdi N, Pour AR. Lidocaine reversible inactivation of the median raphe nucleus has no effect on reference memory but enhances working memory versions of the Morris water maze task. Behav Brain Res. 2000; 114 (1-2): 1-9. doi: 10.1016/S01664328(00)00176-5.
27. Topuz RD, Gunduz O, Tastekin E, Karadag CH. Effects of hippocampal histone acetylation and HDAC inhibition on spatial learning and memory in the Morris water maze in rats. Fundam Clin Pharmacol. 2020; 34 (2): 222-8. doi: 10.1111/fcp.12512.
28. Halliwell B, Gutteridge JM. Free radicals in biology and medicine. 5th ed. USA: Oxford University Press; 2015. pp 600-3.
29. Margolis RL, Rauch CT, Wilson L. Mechanism of colchicine-dimer addition to microtubule ends: implications for the microtubule polymerization mechanism. Biochemistry. 1980; 19 (24): 5550-7. doi: 10.1021/bi00565a014.
30. Osborn M, Weber K. Cytoplasmic microtubules in tissue culture cells appear to grow from an organizing structure towards the plasma membrane. Proc Natl Acad Sci USA. 1976; 73 (3): 867-71. doi: 10.1073/pnas.73.3.867.
31. Nakagawa Y, Nakamura S, Kaśe Y, Noguchi T, Ishihara T. Colchicine lesions in the rat hippocampus mimic the alterations of several markers in Alzheimer's disease. Brain Res. 1987; 408 (1-2): 57-64. doi: 10.1016/0006-8993(87)90358-1.
32. Emerich DF, Walsh TJ. Selective working memory impairments following intradentate injection of colchicine: attenuation of the behavioral but not the neuropathological effects by gangliosides GM1 and AGF2. Physiol Behav. 1989; 45 (1): 93-101. doi: 10.1016/00319384(89)90170-4.
33. Emerich DF, Walsh TJ. Cholinergic cell loss and cognitive impairments following intraventricular or intradentate injection of colchicine. Brain Res. 1990; 517 (1-2): 157-67. doi: 10.1016/0006-8993(90)91021-8.

34. Dufourny L, Leroy D, Warembourg M. Differential effects of colchicine on the induction of nitric oxide synthase in neurons containing progesterone receptors of the guinea pig hypothalamus. Brain Res Bull. 2000; 52 (5): 435-43.
35. Sil S, Ghosh T, Ghosh R, Gupta P. Nitric oxide synthase inhibitor, aminoguanidine reduces intracerebroventricular colchicine induced neurodegeneration, memory impairments and changes of systemic immune responses in rats. J Neuroimmunol. 2016; 303: 51-61. doi: 10.1016/j.jneuroim.2016.12.007.
36. Coyle JT, Puttfarcken P. Oxidative stress, glutamate, and neurodegenerative disorders. Sci. 1993; 262 (5134): 689-95. doi: 10.1126/science.7901908.
37. Pourkhodadad S, Alirezaei M, Moghaddasi M, Ahmadvand H, Karami M, Delfan B, et al. Neuroprotective effects of oleuropein against cognitive dysfunction induced by colchicine in hippocampal CA1 area in rats. J Physiol Sci. 2016; 66 (5): 397-405. doi: 10.1007/s12576-016-0437-4.
38. Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10th ed. Philadelphia, PA: Elsevier; 2018. pp 31-56.
39. Golechha M, Bhatia J, Arya DS. Studies on effects of Emblica officinalis (Amla) on oxidative stress and cholinergic function in scopolamine induced amnesia in mice. J Environ Biol. 2012; 33 (1): 95-100.
40. Li C, Long P, He M, Han F, Jiang W, Li Y, et al. Phyllanthus emblica Linn. fruit polyphenols improve acute paradoxical sleep deprivation-induced cognitive impairment and anxiety via Nrf2 pathway. J Funct Foods. 2023; 110 (2023): 105884. doi: 10.1016/j.jff.2023.105884.
41. Ma YF, Wu ZH, Gao M, Loor JJ. Nuclear factor erythroid 2-related factor 2 antioxidant response element pathways protect bovine mammary epithelial cells against H2O2-induced oxidative damage in vitro. J Dairy Sci. 2018; 101 (6): 5329-44. doi: 10.3168/jds.2017-14128.

Citation of this article
Akter F, Mostafa MB, Basak P, Amin RB. Analysis of the Effects of *Phyllanthus emblica* (Amloki) Fruit on Colchicine Induced Memory Deficit and Hippocampal Oxidative Stress in Male Long-Evans Rats. Eastern Med Coll J. 2026; 11 (1): 47-54.
doi https://doi.org/10.3329/emcj.v11i1.90000