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Research Article
Improvement of Learning and Memory by Morin, A Flavonoid in Young and Aged Mice

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Abstract

Background and Objectives: Flavonoids have been reported to possess neuroprotective effects. The present study was designed to evaluate the effect of morin, a flavonoid, on learning and memory of Swiss albino young and aged male mice. **Methodology:** Morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine salicylate (0.1 mg kg^{-1}, i.p.) were administered for 15 successive days to separate groups of young and aged mice. Morris water maze was employed to study the effect of the drugs on the learning and memory of mice. In addition, brain acetylcholinesterase activity was estimated. To explore the possible mechanisms of action, effect of morin on scopolamine and sodium nitrite-induced amnesia in young mice were investigated. **Results:** Morin (10, 20 and 40 mg kg^{-1}) and physostigmine per se significantly decreased escape latency during training and increased time spent in target quadrant during retrieval, indicating significant improvement in learning and memory of young and aged mice as compared to their respective controls. The drug treatments have no significant effect on locomotor activity of the mice. Memory-enhancing activity of morin (20 mg kg^{-1}, p.o.) was comparable to physostigmine. Morin significantly reversed scopolamine and sodium nitrite- induced amnesia in young mice. Morin and physostigmine also significantly reduced brain acetylcholinesterase activity of young and aged mice as compared to their respective controls. **Conclusion:** Morin administered for 15 successive days showed significant improvement of learning and memory of young and aged mice probably by inhibiting brain acetylcholinesterase activity. In addition, memory improving effect of morin in young mice might also be through facilitation of anti-hypoxic pathway leading to augmentation of cholinergic system.

Key words: Acetylcholinesterase, learning, memory, morin, Morris water maze, nootropic

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Learning is the process of acquiring new knowledge while memory is the process of encoding, storage and retrieval of the acquired knowledge. Dementia is a general term that describes a wide range of symptoms associated with a decline in memory or other thinking skills, severe enough to reduce a person's ability to perform everyday activities. Alzheimer's disease, a neurodegenerative disorder, is the major cause of dementia[1]. The number of people living with dementia worldwide in 2015 was estimated to be 47.47 million[2]. The cognitive deficits may be due to (i) Degeneration of the cholinergic neurons[3] and leading to decreased cholinergic activity, (ii) Aging-induced oxidative stress[4] and (iii) Hypoxia[5]. Further, acetylcholinesterase (AChE) plays a key role in metabolism of acetylcholine and hence, inhibition of AChE has emerged as one of the most promising strategy for the treatment of cognitive deficits[6]. In addition, oxidative stress and impaired cholinergic functions lead to cognitive impairments in the aged brain[7]. On the other hand, hypoxia reduces incorporation of choline into acetylcholine, thus decreases the synthesis of acetylcholine and hence lead to cognitive deficits[5].

A number of cholinesterase inhibitors like donepezil, rivastigmine, tacrine and rivastigmine etc., are in practice for the treatment of various cognitive disorders[8]. However, the adverse effects associated with anti-cholinesterase drugs (rivastigmine, galantamine, donepezil) include anorexia, nausea, vomiting, diarrhoea and insomnia[9]. Physostigmine, a cholinesterase inhibitor, improved memory of alzheimer's disease patients[10]. But this drug has a short half-life and requires complex forms of administration[11]. So there is a need to discover new drugs with better efficacy and having less adverse effects. Plants have been used since ancient times in traditional medicinal systems for the treatment of memory dysfunction. *Bacopa monniera*, also called as "Brahmi" has been used in the ayurvedic system of medicine for centuries for treatment of cognitive dysfunction. Traditionally, it was used as a brain tonic to enhance memory development, learning and concentration[12]. *Bacopa monniera* has been proven to be clinically effective in treatment of cognitive disorders[13]. The bioactive compounds isolated from plants such as galantamine[14], huperzine alpha[15], curcumin[16] have been reported to be effective for treatment of cognitive deficits in patients of dementia.

Morin is a polyphenolic flavonoid present in white mulberry (*Morus alba* L., Family-Moraceae), almond (*Prunus dulcis*, Family-Rosaceae), sweet chestnut (*Castanea sativa*, Family- Fagaceae)[17], etc. It is also one of the components of red wine[18]. It has been reported to possess a number of pharmacological activities such as anti-amyloid[19,20], anti-anxiety[21], anti-tardive dyskinesic[22], antiparkinsonian[23], antioxidant[24], anti-hyperlipidemic[25], anti-diabetic[26], hepatoprotective[27], cardioprotective[28], nephroportective[29], anticancer[30], antihypertensive[31], antiosteoarthritic[32] and antibacterial[33].

Moreover, morin has been proven to be a neuroprotective agent against excitotoxicity[34]. It has also been reported to alleviate oxidative stress and inflammation and also increased the levels of neurotrophic factors such as brain-derived neurotrophic factor, insulin growth factor-1 and nerve growth factor in the brain of streptozotocin-induced diabetic rats[35]. Furthermore, as per the molecular modeling and docking studies, morin has good binding affinity and inhibitory action on human acteylcholinesterase enzyme[36]. Thus, morin might possess the potential of improving learning and memory. Therefore, the aim of the present study was to explore the effect of morin on learning and memory of young and aged mice and also to investigate the possible mechanisms of action for its nootropic activity.

MATERIALS AND METHODS

Experimental animals: Swiss albino male young mice (Age: 2-3 months, weight: 16-24 g) and aged mice (Age: 7-9 months, weight: 28-38 g) were purchased from Disease Free Small Animal House, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar (Haryana). Female mice were not employed in the present study, since estrogens (female sex hormones) have been reported to improve memory[37]. Animals were housed separately in groups of 6 per cage (Polycarbonate cage size: 29×22×14 cm) under laboratory conditions with alternate light and dark cycle of 12 h each. The animals had free access to food and water. The animals were kept fasted 2 h before and 2 h after drug administration. The animals were acclimatized for at least five days before behavioural experiments which were carried out between 09:00 and 17:00 h. The experimental protocol was approved by Institutional Animals Ethics Committee (IAEC) on 17th December, 2014 and animal care was taken as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), ministry of environment and forests, Government of India (Registration no. 0436).

Drugs and chemicals: Morin hydrate and scopolamine hydrobromide (Sigma-Aldrich, St. Louis, USA), physostigmine salicylate, acetylthiocholine iodide and 5, 5-dithiobis-2-nitrobenzoic acid (Hi-Media Laboratories, Mumbai), Carboxy

Methyl Cellulose (CMC) and Sodium Nitrite (SD Fine Chem Ltd., Mumbai) were used in the present study.

Vehicle: Morin was suspended in 1% w/v CMC solution in distilled water and administered orally. Scopolamine hydrobromide and sodium nitirite were dissolved in normal saline.

Behavioural model employed for evaluation of learning and memory

Morris water maze: The procedure and parameters for testing of learning and memory using Morris water maze were followed as reported in the literature[38]. This Maze consisted of a circular pool (60 cm in diameter, 25 cm in height) filled to a depth of 20 cm with water maintained at 25°C. The water was made opaque with nontoxic white dye. The tank was divided into four equal quadrants with the help of two threads, fixed at right angle to each other on the rim of the pool. A submerged platform (with top surface 6×6 cm and painted in white) was placed inside the target quadrants (Q4 in present study) of this pool 1 cm below surface of water. The position of platform was kept unaltered throughout the training session. Each animal was subjected to 4 consecutive trials each day with a gap of 5 min for 4 consecutive days (starting from 11th day of drug administration to 14th day), during which they were allowed to escape on to the hidden platform and to remain there for 20 sec. During the training session, the mouse was gently placed in water between the quadrants, facing the wall of pool with drop location changing for each trial and allowed 120 sec to locate submerged platform. If the mouse failed to find the platform within 120 sec, it was guided gently on to the platform and allowed to remain there for 20 sec. Escape Latency (EL) is the time taken by the animal to move from the starting quadrant to find the hidden platform in the target quadrant. The EL was recorded on the 11-14th day for each animal. Each animal was subjected to training trials for 4 consecutive days, the starting position was changed with each exposure as mentioned below and target quadrant (Q4 in the present study) remained constant throughout the training period:

- Day 1 Q1 Q2 Q3 Q4
- Day 2 Q2 Q3 Q4 Q1
- Day 3 Q3 Q4 Q1 Q2
- Day 4 Q4 Q1 Q2 Q3

On the fifth day (i.e., 15th day of drug administration) the platform was removed and mouse was placed in any of the three quadrants and allowed to explore the target quadrant for 300 sec. Time spent in target quadrant (TSTQ) in search of the missing platform was noted as index of retrieval of memory. The observer always stood at the same position. Care was taken not to disturb the relative location of water maze with respect to other objects in the laboratory.

Measurement of locomotor activity: To rule out the effects of various drug treatments on locomotor activity, horizontal locomotor activities of control and test animals were recorded for a period of 5 min using photoactometer (INCO, Ambala, India). The procedure was followed as reported earlier[39].

Biochemical estimation: All the animals were sacrificed by cervical dislocation under light anaesthesia with diethylether. The whole brain was carefully removed from the skull. For preparation of brain homogenate, the fresh whole brain was weighed and transferred to a glass homogenizer and homogenized in an ice bath after adding 10 V of phosphate buffer (pH 8, 0.1 M). The homogenate was centrifuged using refrigerated centrifuge (Remi, Mumbai, India) at 3000 rpm for 10 min at 4°C and the resultant cloudy supernatant liquid was used for the estimation of brain acetylcholinesterase activity.

Brain acetylcholinesterase activity: Brain acetylcholinesterase was estimated using the method of Ellman *et al.*[40]. Briefly, 0.4 mL of brain homogenate was added to a test tube containing 2.6 mL of phosphate buffer. About 0.1 mL 5, 5-dithiobis-2-nitrobenzoic acid reagent was added to the above mixture and absorbance was noted at 412 nm. When absorbance had stopped increasing, the photometer slit was opened so that the absorbance was set to zero. About 0.02 mL of acetylthiocholine iodide solution was added and again absorbance was noted 15 min thereafter. Change in absorbance per min was calculated. The rate of hydrolysis of substrate was calculated using following formula:

$$R = 5.74\ (10^{-4})\ A/C_0$$

where, R is rate of hydrolysis of acetylthiocholine iodide in mmol min^{-1} g^{-1} of tissue,

A = Change in absorbance per min
C_0 = Weight of tissue homogenate in mg mL^{-1}

Experimental protocol

Groups for Morris water maze:

- **Groups 1-5 (n = 6 each):** Vehicle (1% CMC), morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine (0.1 mg kg^{-1}, i.p.), respectively were administered for 15 successive

days in young mice. Escape Latency (EL) was recorded 45 min after administration of vehicle or morin from 11-14th day. On 15th day, time spent in target quadrant (TSTQ) was noted 45 min after administration of the vehicle/drug

- **Groups 6 and 7 (n = 6 each):** Vehicle (1% CMC) and morin (20 mg kg^{-1}, p.o.) respectively, were injected for 14 successive days in young mice. The EL was recorded 45 min after drug administration from 11-14th day. On 15th day, scopolamine (0.4 mg kg^{-1}, i.p.) was injected 30 min after administration of vehicle or morin and TSTQ was noted 45 min after the injection of scopolamine
- **Groups 8 and 9 (n = 6 each):** The details of these groups are same as mentioned under groups 6-7, except sodium nitrite (75 mg kg^{-1}, i.p.) was used in place of scopolamine
- **Groups 10-14 (n = 6 each):** The details of these groups are same as mentioned under groups 1-5, except aged mice were used

Groups for locomotor activity:

- **Groups 15-19 (n = 6 each):** Vehicle (1% w/v CMC), morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine (0.1 mg kg^{-1}, i.p.) respectively, were administered for 15 successive days to young mice and after 30 min of drug adminsitration on 15th day, mice were subjected to testing of locomtor activity using actophotometer
- **Groups 20-24 (n = 6 each):** The details of these groups are same as mentioned under groups 15-19, except aged mice were used

Groups for biochemical estimations:

- **Groups 25-29 (n = 6 each):** Vehicle (1% CMC), morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine (0.1 mg kg^{-1}, i.p.), respectively were administered for 15 successive days to young mice and after 30 min of drug adminsitration on 15th day, mice were sacrificed to carry out estimation of brain acetylcholinesterase activity

After testing locomotor activity of aged mice (groups 20-24), these were sacrificed for estimation of brain acetylcholinesterase activity on 15th day.

Statistical analysis: Data were presented as Means±SEM and analyzed by using one-way ANOVA followed by Tukey-kramer multiple comparison test/Dunnett's test using Graph pad Instat version 3.10. The $p<0.05$ was considered as statistically significant.

RESULTS

Effect of morin and other drugs on Escape Latency (EL) and time spent in target quadrant (TSTQ) by young and aged mice using Morris water maze: Morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine (0.1 mg kg^{-1}, i.p.) per se significantly decreased EL of young mice on 14th day and increased TSTQ on 15th day as compared to the control group, indicating significant improvement of learning and memory of young mice. However, on 13th day, the lowest dose (10 mg kg^{-1}) and middle dose (20 mg kg^{-1}) of morin significantly reduced EL as compared to control. Administration of single dose of scopolamine (0.4 mg kg^{-1}, i.p.) and sodium nitrite (75 mg kg^{-1}, i.p.) per se 30 min prior to recording TSTQ on 15th day significantly decreased TSTQ by young mice in Morris water maze, indicating their amnesic effects. Morin (20 mg kg^{-1}, p.o.) treatment for 15 successive days significantly reversed scopolamine and sodium nitrite-induced decrease in TSTQ by young mice, indicating reversal of scopolamine and sodium nitrite-induced amnesia (Table 1).

Table 1: Effect of morin and other drugs on Escape Latency (EL) and time spent in target quadrant (TSTQ) of young mice using Morris water maze

Treatments (15 days)	Dose per killogram	EL (sec) on 11th day	EL (sec) on 12th day	EL (sec) on 13th day	EL (sec) on 14th day	TSTQ (sec) on 15th day
Vehicle (1% w/v CMC)	1 (mL, p.o.)	107.00±3.50	105.50±3.53	98.83±7.04	91.00±4.01	80.33±10.07
Physostigmine	0.1 (mg, i.p.)	94.00±6.00	80.03±4.37	64.67±4.61**	48.33±2.97***	115.50±6.32*
Morin	10 (mg, p.o.)	106.00±9.80	78.83±3.90	63.33±5.12**	49.33±2.72***	111.67±7.20*
Morin	20 (mg, p.o.)	97.00±5.22	86.33±7.59	69.33±5.13*	55.83±3.29***	115.50±8.86*
Morin	40 (mg, p.o.)	103.30±3.88	84.83±5.12	79.16±5.40	53.00±3.89***	114.33±7.69*
Scopolamine	0.4 (mg, i.p.)	105.02±4.50	100.67±4.38	88.67±4.61	90.00±4.09	49.30±6.31*
Sodium nitrite	75 (mg kg^{-1}, i.p.)	96.33±6.27	93.83±8.20	87.00±8.38	91.50±5.66	49.67±6.02**
Morin+scopolamine	20 (mg, p.o.+0.4 mg, i.p.)	97.17±5.30	78.16±6.15	73.17±4.45	64.00±4.69***	83.33±5.64[a]
Morin+sodium nitrite	20 (mg, p.o.+75 mg, i.p.)	99.00±5.28	82.83±8.28	74.50±5.09	58.50±3.16***	80.50±7.40[b]
p value		0.2908	0.0452	0.0014	<0.0001	<0.0001
F (8, 45)		1.255	2.201	3.916	16.990	16.414

Value n = 6 in each group. Values are expressed as Mean±SEM. Data were analyzed by one-way ANOVA followed by Tukey-kramer multiple comparison test, *p<0.05, **p<0.01, ***p<0.001 as compared to vehicle treated control group, [a]p<0.05 as compared to scopolamine treated group, [b]p<0.01 as compared to sodium nitrite treated group and CMC: Carboxy methyl cellulose

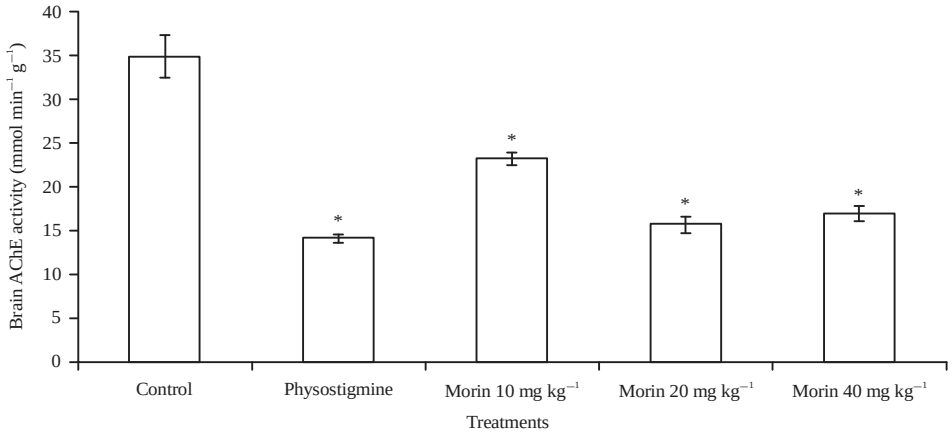

Fig. 1: Effect of morin and physostigmine on brain acetylcholinesterase (AChE) activity of young mice, n = 6 in each group. Values are expressed as Mean±SEM. Data were analyzed by one-way ANOVA followed by Tukey-kramer multiple comparison test, F (4, 25) = 44.52, p<0.0001, *p<0.001, as compared to vehicle treated young mice

Table 2: Effect of morin and physostigmine on Escape Latency (EL) and time spent in target quadrant (TSTQ) of aged mice using Morris water maze

Treatments (15 days)	Young/aged mice	Dose per kilogram	EL (sec) on 11th day	EL (sec) on 12th day	EL (sec) on 13th day	EL (sec) on 14th day	TSTQ (sec) on 15th day
Vehicle (1% w/v CMC)	Young	1 (mL, p.o.)	107.00±3.50	105.50±3.53	98.83±7.04	91.00±4.01	80.33±10.07
Vehicle (1% w/v CMC)		1 (mL, p.o.)	113.33±3.70	98.66±5.00	98.50±5.47	95.83±3.37	48.83±6.40*
Physostigmine	Aged	0.1 (mg, i.p.)	110.33±5.20	92.86±6.60	76.67±6.01	55.00±4.02***	93.16±4.01***
Morin		10 (mg, p.o.)	109.50±4.60	95.00±6.81	79.50±5.93**	59.00±5.33***	80.50±5.77**
Morin		20 (mg, p.o.)	107.60±5.18	90.83±3.36	79.67±3.36	61.66±4.33***	90.67±3.54***
Morin		40 (mg, p.o.)	105.12±5.67	92.67±9.26	67.67±9.97**	65.00±5.61***	93.67±5.18***
p-value			= 0.8576	= 0.9515	= 0.0137	<0.0001	<0.0001
F (5, 30)			0.3813	2.192	3.463	17.541	11.746

Value n = 6 in each group. Values are expressed as Mean±SEM. Data were analyzed by one-way ANOVA followed by Tukey-kramer multiple comparison test, *p<0.05, as compared to vehicle treated young mice, **p<0.05, ***p<0.001 as compared to vehicle treated aged mice, CMC: Carboxy methyl cellulose

Vehicle treated aged mice significantly decreased TSTQ on 15th day, as compared to vehicle treated young mice, indicating significant impairment of memory. There was no significant effect on EL (11-14th day) of aged mice as compared to young mice, indicating that learning was not significantly impaired in aged mice. However, morin and physostigmine per se significantly decreased EL on 14th day in aged mice, similar to that in young mice, indicating significant improvement of learning. Morin (10, 20 and 40 mg kg^{-1}) and physostigmine per se administered for 15 successive days significantly increased TSTQ on 15th day, as compared to vehicle treated aged mice, indicating significant improvement of memory (Table 2).

Effect of morin on brain acetylcholinesterase activity of mice: Morin (10, 20 and 40 mg kg^{-1}, p.o.) and physostigmine per se significantly decreased brain acetylcholinesterase activity of young mice as compared to its vehicle treated control (Fig. 1). Brain acetylcholinesterase activity was significantly increased in aged mice as compared to vehicle treated young mice. Administration of morin (10, 20 and 40 mg kg^{-1}, p.o.) as well as physostigmine per se for 15 successive days significantly decreased brain acetylcholinesterase activity of aged mice as compared to its vehicle treated control (Fig. 2).

Effect of morin on locomotor activity of mice using actophotometer: Morin (10, 20 and 40 mg kg^{-1}, p.o.) as well as physostigmine administered for 15 successive days did not significantly affect the spontaneous locomotor activities of young as well as aged mice as compared to respective vehicle treated controls (Table 3 and 4).

DISCUSSION

In present study, morin (10, 20 and 40 mg kg^{-1}, p.o.) administered for 15 successive days showed significant nootropic effect in both young and aged mice. Morris water maze was employed as a behavioral model for evaluation of learning and memory of mice. This model is widely employed for assessing the effect of drugs on learning and memory[38]. Decrease in escape latency during training period and increase in time spent in target quadrant during retrieval indicates improvement of learning and memory, respectively. Morin did not show any significant effect on locomotor functions of mice as compared to the vehicle treated control.

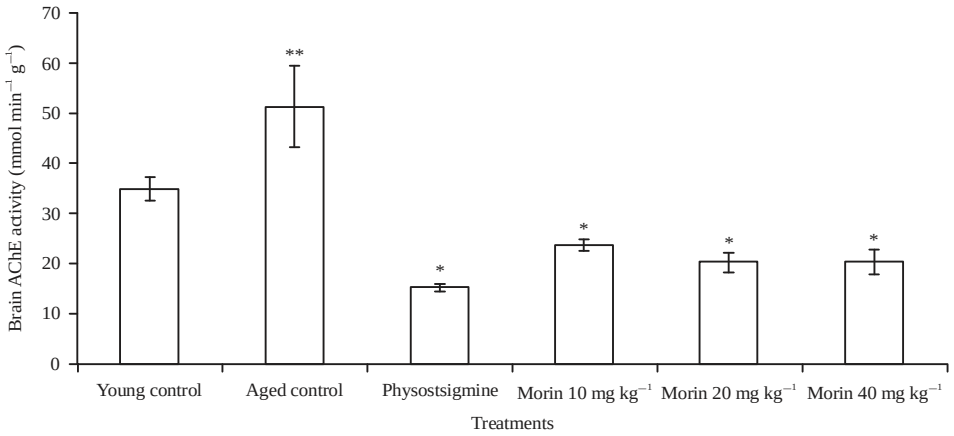

Fig. 2: Effect of morin and physostigmine on brain acetylcholinesterase (AChE) activity of aged mice, n = 6 in each group. Values are expressed as Mean±SEM. Data were analyzed by one-way ANOVA followed by Tukey-kramer multiple comparison test, F (5, 30) = 12.711, p<0.0001, *p<0.001 as compared to vehicle treated aged mice, **p<0.05 as compared to vehicle treated young mice

Table 3: Effect of morin and physostigmine on locomotor activity of young mice using actophotometer

Treatments (15 days)	Dose per kilogram	Locomotor activity score (sec)
Vehicle (1% w/v CMC)	1 (mL)	280.67±6.09
Physostigmine (1 mg kg^{-1}, i.p.)	0.1 (mg, i.p.)	284.00±14.38
Morin	10 (mg, p.o.)	286.00±9.37
Morin	20 (mg, p.o.)	283.50±11.72
Morin	40 (mg, p.o.)	285.16±11.72

n = 6 each group. Data were analysed by using one-way ANOVA followed by Dunett's test, F (4, 25) = 0.045, p-value = 0.9967 and CMC: Carboxy methyl cellulose

Table 4: Effect of morin and physostigmine on locomotor activity of aged mice using actophotometer

Treatments (15 days)	Dose per killogram	Locomotor activity score (sec)
Vehicle (1% w/v CMC)	1 (mL)	279.83±6.49
Physostigmine (1 mg kg^{-1}, i.p.)	0.1 (mg, i.p.)	288.56±7.15
Morin	10 (mg, p.o.)	294.67±7.23
Morin	20 (mg, p.o.)	290.00±5.57
Morin	40 (mg, p.o.)	289.16±5.85

n = 6 each group. Data were analysed by using one-way ANOVA followed by Dunett's test, F (4, 25) = 0.045, p-value = 0.6926

Thus, memory enhancing effect of morin is specific and not false positive. Out of three doses of morin, 20 mg kg^{-1} was found to be most effective dose, hence this dose was employed for elucidating its probable mechanisms of memory improving effect in young mice.

Acetylcholine is considered as the most important neurotransmitter involved in the regulation of cognitive functions. Selective loss of cholinergic neurons was reported to be a characteristic feature of alzheimer's disease[41]. Drugs that reduce cholinergic function such as muscarinic receptor antagonist, scopolamine produced profound memory impairments in animals[42]. In the present study, morin (20 mg kg^{-1}, p.o.) significantly reversed scopolamine-induced amnesia in young mice, indicating facilitation of the cholinergic pathway. Moreover, morin treatment also significantly inhibited brain acetylcholinesterase activity as compared to control. Physostigmine (0.1 mg kg^{-1}, i.p.) injected for 15 successive days significantly improved learning and memory of young and aged mice and significantly inhibited brain acetylcholinesterase activity. The memory enhancing effect of physostigmine is in line with the earlier studies[43]. Memory improving effect of morin observed in the present study was comparable to physostigmine.

Sodium nitrite significantly impaired memory of mice, which is also supported by the earlier study[44]. Hypoxia induced with sodium nitrite reduces incorporation of choline into acetylcholine, thus decreases the synthesis of acetylcholine[5]. Morin (20 mg kg^{-1}, p.o.) significantly reversed sodium nitrite-induced amnesia probably through facilitated cholinergic transmission.

Normal aging is known to deteriorate memory in human beings. Aged mice showed significant impairment of memory as compared to young mice. This is also supported by an earlier study[45]. Cholinergic degeneration has been reported to be involved in geriatric memory dysfunctions[46]. In the present study, morin (10, 20 and 40 mg kg^{-1}, p.o.) significantly improved memory of aged mice and also significantly inhibited brain acetylcholinesterase activity. Thus, memory

improving effect of morin in aged mice might be through involvement of cholinergic pathway.

Beta-amyloid proteins and tau proteins are patho-physiological characteristic of alzheimer's disease[47]. Morin has been reported to possess *in vitro* anti-amyloid activity[48] as well as inhibitor of tau protein phosphorylation[49], which might be responsible for its memory improving effect.

CONCLUSION

Morin administered for 15 successive days showed significant memory enhancing activity in young and aged mice probably through inhibition of brain acetylcholinesterase activity. In addition, memory improving effect of morin in young mice might also be through facilitation of anti-hypoxic pathway leading to augmentation of cholinergic system. Hence, further studies can be carried out to explore the other possible mechanisms for memory improving effect of morin and its usefulness in the management of cognitive disorders.

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