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Assessing the Impact of Methanolic Extract of Zea Mays Silk on Scopolamine-Induced Cognitive Impairment

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Abstract

Cognitive impairment, including dementia, is associated with aging and deficits in attention and learning power, and traumatic brain injury is a common cause of disability. The most common and important disease that affects cognitive function is Alzheimer's disease (AD), it is a progressive neurodegenerative disorder. Higher mental working areas of the brain, such as the neocortex and hippocampus, are the most influenced by Alzheimer's disease clinical symptoms. Corn silk (*Zea mays* Linn) is an essential herb used traditionally by Americans and Chinese to prevent many diseases. In this study, the effects of methanolic effects of the silk part of Zea mays on scopolamine-induced dementia were investigated. Thirty male mice were taken and divided into five groups (n=6) for a period of 21 days. Group 1 received normal saline; Group 2 received scopolamine (3mg/kg) i.p; Group 3 received Donepezil (5mg/kg) oral and scopolamine and served as standard; Group 4 was treatment group and received 400 mg/kg of methanolic extract of corn silk and scopolamine; Group 5 received treatment of 800 mg/kg with standard drug and scopolamine. For behavioral studies, escape latency, transfer latency, and errors in reference memory were measured and calculated, and then after two days, animals were sacrificed, and the brain was isolated from them. A homogenate mixture of the brain was used to estimate acetylcholinesterase, malondialdehyde, reduced glutathione, and superoxide dismutase levels. Finally, statistical data analysis was performed using the one-way ANOVA test. Accordingly, the *Zea mays* silk extract might improve mice's cognitive behavior after 21 days.

Keywords: Alzheimer's Disease, Corn Silk (*Zea mays*), Scopolamine, Cognition

INTRODUCTION

Alzheimer's disease is a neurodegenerative disorder in which the loss of neurons occurs in specific locations of the brain, particularly in the hippocampus and basal forebrain.[1] Corn silk is an essential herb used traditionally by Americans and Chinese to prevent many diseases. It is the part of the female flower of Corn (*Zea mays* Linn), also known as maize. In corn silk extract, a higher amount of polyphenolic compounds are found; most of these are flavonoids. There is now various proof to explain that fruit & vegetables obtained phytoconstituents, particularly flavonoids, are able to show useful effects on learning and memory.[2,3]

The literature survey found that corn silk is important for protecting biological cells from damage and has potent antioxidant and anti-inflammatory activity, so it will be predicted that it also protects nerves from oxidative stress and inflammation caused by Aβ plaques and tau protein in Alzheimer's Disease.[3] The study aimed to evaluate the effect of corn silk extract on scopolamineinduced cognitive impairment in mice.

MATERIALS AND METHODS

The animals were housed in regular propylene cages and monitored the temperature of the room (25±2 ° C) and 12:12 hour light and dark cycle humidity. All the animals are given proper diet and water. The organizational animal ethics committee permitted the animal experimental studies (Approval no: CPCSEA/IAEC/SBS/2018-19/008).

Thirty male mice were taken and divided into five groups (n=6) for a period of 21 days. Group 1 received normal saline; Group 2 received scopolamine (3mg/kg) i.p; Group 3 received Donepezil (5mg/kg) oral and scopolamine and served as standard; Group 4 was treatment group and received 400 mg/kg of methanolic extract of corn silk and scopolamine; Group 5 received treatment of 800 mg/kg with standard drug and scopolamine.

Corn silk was dried, crushed, and converted into powder to prepare corn silk extract. Then 100 gm Corn silk powder in 1000 ml of methanol was soaked for 72 hours. The extract is then shaken, filtered, and evaporated in the water bath, giving a semi-solid mass. This process has been repeated several times. The extract is stored in a bottle, dried and put in a desiccator which absorb the solvent from the methanolic extract.[4] The extract stock solution was ready by liquefying 25 g of extract in 50 ml of water to produce a 500 kg/ml concentration. All other treatments were formulated and administered to the animals in distilled water.

To investigate cognitive impairment two days before the treated animals were trained for evaluation by behavioral parameters like escape latency and transfer latency. Animals were sacrificed, and the brain was isolated from them. A homogenate mixture of the brain was kept in the refrigerator until used for the biochemical estimation of acetylcholinesterase, malondialdehyde, reduced glutathione, and superoxide dismutase levels.

Finally, statistical data analysis was conducted using the one-way ANOVA test

RESULTS

In the present study, behavioral models like the Radial maze and Morris's water maze were employed to estimate the memory of treated Mice. The behavioral model gives an idea of memory consolidation.

Escape latency was measured by using the Morris water maze. The scopolamine-treated group produced impaired acquisition by impairing a gradual increase in escape latency time. Administration of corn silk extract caused a decrease in the escape latency on day 6 in the

cognitively impaired Mice. However, the administration of corn silk extract and their combination with Donepezil produced a more significant reduction in escape latency time on day six compared to scopolamine Mice. The results of the present study are summarized in table no. 1 and shown in figure1.

Table 1. Escape latency measured at different intervals of time

Treatment	**Escape latency(sec.) Day 1**	**Escape latency (sec.) Day 7**	**Escape latency (sec.) Last Day**
Normal control	2.80±0.37	2.40±0.2445	4.20±0.5831
Scopolamine (3mg/kg)	3.60±0.5099	12.20±3.652	11.40±1.435
Scopolamine + Donepezil (5mg/kg)	2.40±05099	3.00±0.3162**	3.200±0.5831**
Scopolamine + Extract (400mg/kg)	2.80±0.3742	3.80±0.3742*	7.00±2.429*
Scopolamine + Donepezil + Extract (800mg/kg)	1.80±0.2000	2.20±0.2000**	3.00±0.894**

Results are characterized by Mean ±SEM. ANOVA measured the statistical value of the difference between measures, followed by t-testing for unpaired comparison. * P<0.05; * * P<0.01; * * * P<0.001.

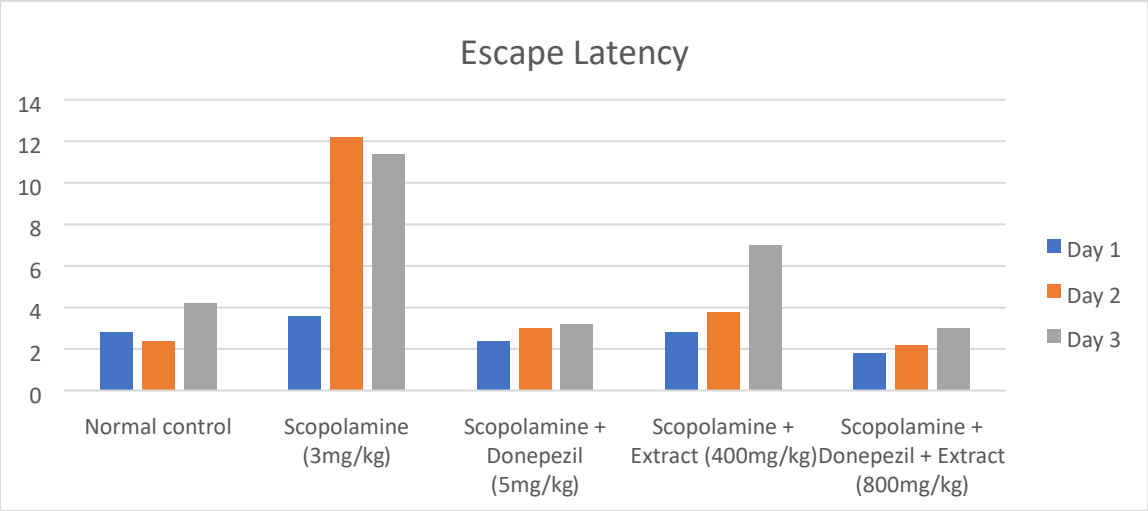

Figure 1. Escape Latency measured by Morris water Maze

Transfer latency was measured by Elevated plus maze. The treated group produced an increase in transfer latency time. Administration of corn silk extract caused a decrease in the transfer latency time on day 6 in the conatively impaired Mice. Administration of corn silk extract and their combination with Donepezil produced a more significant reduction in transfer latency time

on day six than in scopolamine-treated mice. The results of the present study are summarized in table no. 2 and shown in figure 2.

Table 2. Measurement of transfer latency at different interval of time.

Treatment	**Transfer latency(sec.) Day 1**	**Transfer latency (sec.) Day 7**	**Transfer latency (sec.) Last Day**
Normal control	5.20±1.319	6.60±1.288	6.40±0.9274
Scopolamine (3mg/kg)	9.80±1.156	14.40±2.182	16.00±1.871
Scopolamine + Donepezil (5mg/kg)	8.00±0.7071	6.60±0.678**	6.40±1.364***
Scopolamine + Extract (400mg/kg)	8.20±1.114	7.60±0.927**	4.80±1.068***
Scopolamine + Donepezil + Extract (800mg/kg)	9.20±1.881	7.20±0.969***	4.60±0.6782***

Results are characterized by Mean ±SEM. ANOVA measured the statistical value of the difference between measures, followed by t-testing for unpaired comparison. * P<0.05; * * P<0.01; * * * P<0.001.

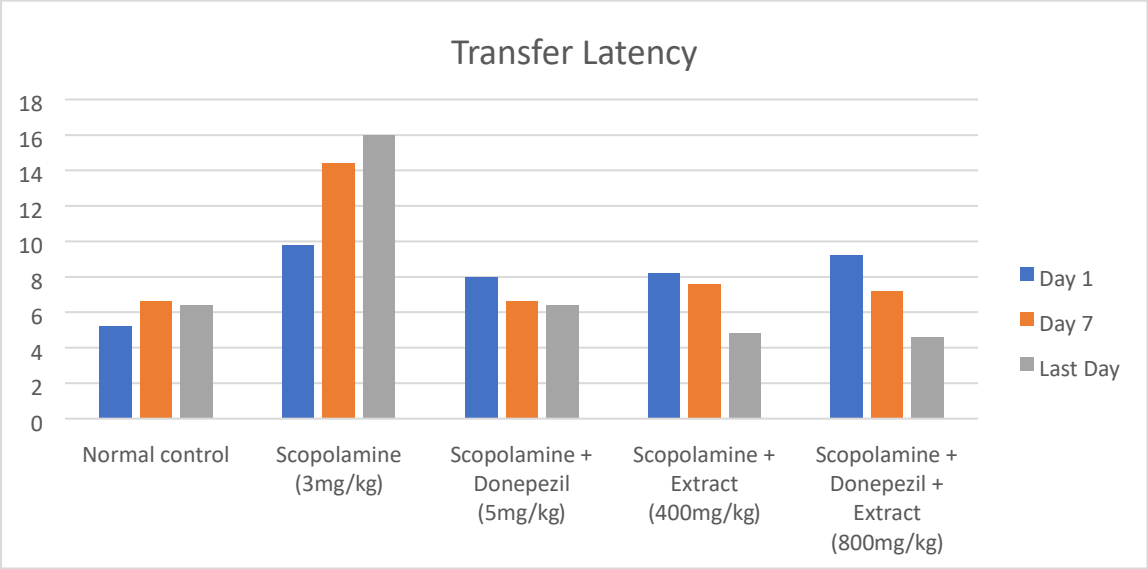

Figure 2. Transfer Latency shown by different groups in Elevated Plus Maze

The occurrence of reference memory errors was higher in the scopolamine (3mg/kg) treated group when evaluated with the control group, indicating an induction of memory impairment. Administration of corn silk extract and their combination with Donepezil demonstrate a protective effect against scopolamine-induced memory impairment summarized in table 3 and shown in figure 3**.**

Table 3. Occurrence of reference memory errors with different treated groups.

Treatment	**No. of reference memory errors**
Normal control	0.7±0.05831
Scopolamine (3mg/kg)	1.8±0.1449*
Scopolamine + Donepezil (5mg/kg)	0.8±0.03742*
Scopolamine + Extract (400mg/kg)	1.4±0.1200**
Scopolamine + Donepezil + Extract (800mg/kg)	1.4±0.1122*

Results are characterized by Mean ±SEM. ANOVA measured the statistical value of the difference between measures, followed by t-testing for unpaired comparison. * P<0.05; * * P<0.01; * * * P<0.001.

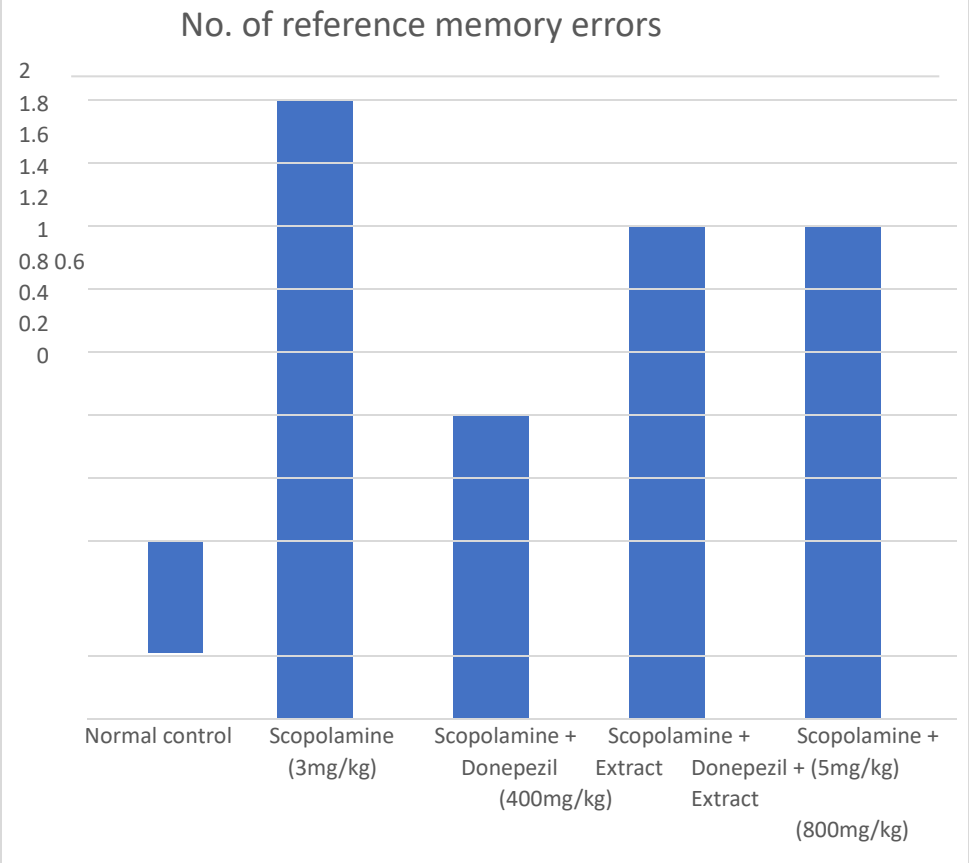

Figure 3. Graph showing reference memory errors

Effect on acetylcholinesterase level

The study revealed an elevated level of acetylcholinesterase in the control group compared to the normal group. Following the administration of Donepezil in the standard group, there was a significant decrease in the level of acetylcholinesterase compared to the control group. Moreover, both test groups, T1 and T2, demonstrated a significant reduction in acetylcholinesterase levels compared to the control group, as depicted in Table 4.

Effect on lipid peroxidation level

In this study, an elevated level of Malondialdehyde (MDA) was observed in the control group, similar to that of the normal vehicle group. However, in the standard group, following the administration of Donepezil, a notable decrease in the level of MDA was observed compared to the control group. Additionally, both test groups, T1 and T2, showed significant reductions in MDA levels after treatment. Moreover, in test group 2, among all the groups, it resulted in a statistically significant decrease in the level of MDA compared to the control group shown in table no.4.

Effect on reduced glutathione level

In the current study, a lower level of reduced glutathione was observed in the control group compared to the normal vehicle group. Following the administration of donepezil in the standard group, a significant increase in the level of reduced glutathione was noted compared to the control group. Moreover, both test groups, T1 and T2, exhibited significantly elevated levels of reduced glutathione after treatment. Moreover, in test group 2, among all the groups, it resulted in a statistically significant elevated level of reduced glutathione compared to the control group shown in table no.4.

Effect on superoxide dismutase level

The present study revealed that the control group exhibited a lower level of superoxide dismutase compared to the normal vehicle group. Following administration of Donepezil in the standard group, a notable increase in superoxide dismutase (SOD) levels was observed compared to the control group. Additionally, both test groups, T1 and T2, exhibited significantly elevated levels of superoxide dismutase post-treatment. Moreover, among all the groups, test group 2 demonstrated a statistically significant increase in reduced glutathione levels compared to the control group, as depicted in Table 4 and illustrated in Figure 4 for comparison.

Table no. 4 Level of superoxide dismutase in the control group and normal vehicle group.

Treatment	**AchE(µmol/min/mg)**	**LPO**	**GSH**	**SOD**
Normal control	0.18±0.01444	1.86±0.2135	15.4±1.77	9.4±0.87
Scopolamine (3mg/kg)	0.23±0.01077***	2.82±0.08***	9.0±0.70**	5.2±0.58**
Scopolamine + Donepezil (5mg/kg)	0.18±0.009618**	1.9±0.11**	11.O±0.70**	9.0±0.70**
Scopolamine + Extract (400mg/kg)	0.18±0.007672**	2.18±0.06**	10.40±0.92*	7.4±0.50*
Scopolamine + Donepezil + Extract (800mg/kg)	0.15±0.01228***	1.56±0.13**	11.60±1.07**	8.8±0.58*

Results are characterized by Mean ±SEM. ANOVA measured the statistical value of the difference between measures, followed by t-testing for unpaired comparison. * P<0.05; * * P<0.01; * * * P<0.001.

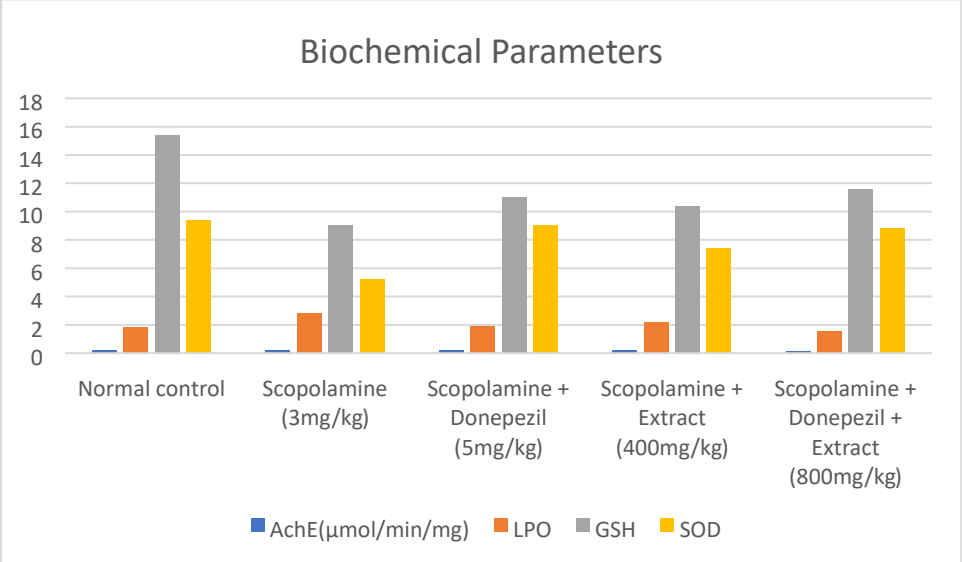

Figure 4. Graph showing different biochemical parameters

DISCUSSION

Alzheimer's is a neurodegenerative disease in which progressive neuron death happens, which affects higher mental functioning locations of the brain, for example, the neocortex and hippocampus, causing memory loss and cognitive impairment (Dementia). Pathological characteristics of AD include microscopic features, such as the extracellular deposits of βamyloid and intracellular hyperphosphorylated tau protein. Another feature observed in AD is oxidative stress and low levels of acetylcholine.

Corn silk (CS) is a female part of corn (*Zea mays*), also known as Maize, cultivated worldwide. The CS extracts have numerous biological activities such as Diuresis, Hypoglycemic, Antifatigue, nephroprotective, Antioxidant, and anti-inflammatory[5] because they have higher flavonoid content. Flavonoids are polyphenolic compounds with potent antioxidant activity. Certain studies show flavonoids have neuroprotective activity and improve memory and cognition.[6] The highest number of flavonoids was established in the methanolic extract, showing the potent free radical inhibiting activity as compared to other extracts.[7]

The present study aimed to evaluate the effect of corn silk extract on scopolamine-induced cognitive impairment in mice models. Scopolamine blocks the muscarinic receptor (M1) in the brain, decreases the amount of acetylcholine, and causes dementia. The Normal Control group received normal saline, and the control group received scopolamine (3mg/kg) through the i.p route and standard group; treatment 1 and 2 groups received Donepezil (5mg/kg), methanolic extract of corn silk (400mg/kg) and Donepezil + extract (800mg/kg) respectively through oral route for 21 days. The level of superoxide dismutase (SOD), and reduced glutathione were decreased while the amount of acetylcholinesterase (AchE), and LPO increased in the control group, and the level of SOD, GSH was increased. LPO and AchE activity was decreased in the standard and treatment groups. Confirmation was shown by behavioral activities in the Elevated plus maze, Morris's water maze, and radial arm maze.

CONCLUSION

Alzheimer's is an abnormality of the central nervous system (CNS) in which a progressive neurodegeneration will occur. It is generally characterized by dementia, and it is a most ordinary form of dementia. In this disorder, the amount of Acetylcholine is reduced in the brain, which is a most dynamic neurotransmitter of the brain. Reduced quantity of Ach in the brain is due to the degeneration of cholinergic circuits. In this study, cognitive impairment is induced by Scopolamine (3mg/kg). Scopolamine is an antimuscarinic drug that blocks the muscarinic (M2) receptor, thus causing loss of acetylcholine and producing Alzheimer-like symptoms. This dementia was treated by the methanolic extract of corn silk, which contains a higher number of flavonoids and other plant antioxidants. It was confirmed that the corn silk extract, which contains a higher number of natural antioxidants, was used to overcome the characteristics of Alzheimer's. In the present study, methanolic extract of corn silk is studied only for its effect on dementia. The complications related to neurodegenerative diseases could be studied in the future with minimum side effects. By understanding the complete activity of corn silk extract for dementia, it can be evaluated in the future with possible mechanisms of action; further clinical data may be required to support the present study, and these drugs may be used in different combinations.

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