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Review Article

A Review on Medicinal Plants Affecting Amnesia on Scopolamine Induced Model

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ABSTRACT

Scopolamine a cholinergic antagonist may cause amnesia in human and animal models. Amnesia induced by Scopolamine has been widely used to understand the biochemical and behavioral changes in rodents. This model can be used to describe the therapeutic targets of memory impairment. In this model the Scopolamine decreases the central cholinergic neuronal activity, block muscarinic receptor and induces oxidative stress. Cholinesterase inhibitors (Donepezil, tacrine, galantamine, and rivastigmine are widely used in the treatment of amnesia. These inhibitors showed non-significant effects. Therefore, herbal medicine can be the sources for the treatment of memory loss due to their Antiacethylcholine esterase and antioxidant activities. In this paper introducing the medicinal plants and their components affecting amnesia on the scopolamine induced model are discussed.

Keywords: Amnesia, Scopolamine, Acetylcholine esterase inhibitors, Memory

INTRODUCTION

Formation and recall of memories involve complex neurological processes across multiple parts of the brain. [1] Amnesia occurs when there is a problem with the way the brain stores or retrieves memories. [2] Amnesia is the general term for a condition in which memory (either stored memories or the process of committing something to memory) is disturbed or lost, to a greater extent than simple everyday forgetting or absent-mindedness. Amnesia may result either from organic or neurological causes (damage to the brain through physical injury, neurological disease or the use of certain drugs), or from functional or psychogenic causes (psychological factors, such as mental disorder, post-traumatic stress or psychological defense mechanisms). Scopolamine is a non-selective muscarinic receptor antagonist that inhibits central cholinergic neuronal activity and impairs learning and short-term memory. [3] In addition, scopolamine also causes an increase in cognitive impairment. [4] Muscarinic M_2 auto receptor inhibitors increase the release of acetylcholine while cholinesterase inhibitors decrease the breakdown of acetylcholine. [5] Cholinesterase inhibitors are the most common pharmacotherapy for amnesia such as, Donepezil, tacrine, piracetam, galantamine, and rivastigmine. These are cholinesterase inhibitor's which are widely used in the treatment of amnesia; however, their therapeutic effects are not significant. [6] Therefore, other possibilities, including herbal medicine sources have been considered and evaluated for memory loss therapy. In this paper other than introducing the medicinal plants effects on memory loss, their probable advantages over synthetic drugs are discussed.

Medicinal plants and their derivatives

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Acori Graminei: The aqueous extract of *Acori Graminei* has been shown to reverse scopolamine induced amnesia by decreasing whole brain acetylcholine esterase activity. [7]

***Allium sativum* (Garlic):** Chronic administration of garlic extract has been shown to prevent memory impairment by scopolamine due to anti-AchE activity and anti-oxidant property of garlic. [8]

***Anacyclus pyrethrum*:** Ethanolic extract of *A.pyrethrum* has been able to improve cognitive processes by enhancing memory in different experimental paradigms in scopolamine induced amnesia model by enhancing central cholinergic neurotransmission. [9]

Angelica gigashas been able to significantly ameliorate the scopolamine-induced amnesia in passive avoidance and Morris water maze test. This activity was observed due to Decursin, a major coumarin constituent isolated from *AG*. Decursin significantly inhibited AChE activity in the hippocampus of treated mice and shown the anti-amnesic effect. [10]

***Asparagus recemosus*:** Pretreatment with methanolic extract of *A. recemosus* (50, 100 and 200 mg/kg, p.o) for 7 days significantly reversed scopolamine-induced amnesia by an increase in transfer latency on elevated plus maze. Further, MAR dose-dependently inhibited acetylcholinesterase enzyme in specific brain regions (prefrontal cortex, hippocampus and hypothalamus) indicating anti-amnesic activity. [11]

***Bacopa monniera*:** Pretreatment with *Bacopa monniera* has been shown to reverse scopolamine induced amnesia in both anterograde and retrograde amnesia by decreasing whole brain acetylcholine esterase activity. [12, 13]

Caesalpinia Crista: The aqueous extract of *Caesalpinia Crista* has been shown to ameliorate the amnesic effect of scopolamine in mice. [14]

***Canscora decussata* (Shankhpushpi):** *Shankhpushpi* is an Ayurvedic drug used for its action on the central nervous system, especially for boosting memory and to improve the intellect. Ethanolic extract of *Canscora decussata* has shown a significant effect on learning behavior and memory enhancement by reversing the amnesia induced by scopolamine (0.3 mg/kg i.p.). This activity has been attributed to the presence of various xanthones and mangiferin, a polyphenolic xanthone. [15]

Carica papaya: The ethanolic extract of seed of *papaya* fruits has been able to significantly ameliorate the scopolamine-induced amnesia by its antioxidant activity. EECP at 200 mg/ kg and 400 mg/kg showed the significant reduction in the elevated enzyme level of acetylcholine esterase. [16]

***Chong–Myung–Tang* (CMT)** is one of the traditional Korean herbal medicines, used for the therapy of learning and memory improvement. Administration of *CMT* significantly restored memory impairments induced by scopolamine in the passive avoidance test and also reduced escape latency during the trial sessions in the Morris water maze test. The increased acetyl cholinesterase activity produced by scopolamine was significantly inhibited by *CMT*. [17]

Clitoria Ternatea: The anti-amnesic activity of alcoholic extract of *C. ternatea* was shown against scopolamine induced amnesia in passive avoidance and step down type of passive avoidance task model in rats by a decrease in acetylcholine esterase activity. It has been shown that the reduction in acetylcholinesterase (AChE) activity which

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reduces the destruction of the neurotransmitter, acetylcholine (ACH), in the brain. [18]

Commiphora whighitii: *C.whighitii* extract has significantly improved learning and memory in mice and reversed the scopolamine induced amnesia. This activity was observed due to Guggul, a major resin constituent isolated from *C.whighitii*. Guggul significantly inhibited AChE activity of treated mice and shown the anti-amnesic effect. [19]

Corydalis Tuber is one of the important medicinal plants in traditional medicine. It has been shown to confer anti-amnesic activity of scopolamine-induced memory and learning impairments. This activity was observed due to Pseudocoptisine, a quaternary alkaloid with benzylisoquinoline skeleton constituent isolated from Corydalis Tuber. This effect was related partially to inhibition of acetylcholine esterase activity in a dose-dependent manner. It has been shown that the detected acetylcholine esterase inhibitory activity might be traced back to the presence of a benzylisoquinoline alkaloid. [20]

Desmodium gangeticum: The aqueous extract of *Desmodium gangeticum* has been shown to reverse scopolamine induced amnesia by decreasing whole brain acetylcholine esterase activity. [21]

Edaravone**:** Chronic treatment of *Edaravone* has shown to avert the deficit of long-term memory by scopolamine induced amnesia, measured by transfer latency using spatial cues in the elevated plus maze task by protecting against reducing the antioxidant defense activity in the areas of hippocampi and cerebral cortices. [22]

Emblica officinalis **(Anwala churna):** Pretreatment with *Anwala churna* for 15 days dose-dependently has shown of improvement in memory scores of young and aged mice in Elevated plus maze and passive avoidance apparatus. Furthermore, it reversed the amnesia induced by scopolamine (0.4 mg/kg, i.p.) by reducing the brain cholinesterase activity. [23]

Foeniculum vulgare: Methanolic extract of the whole plant of *F.vulgare Linn* has shown significantly ameliorate the amnesic effect of scopolamine (0.4 mg/kg) induced memory deficits by inhibition of acetylcholinesterase activity in mice. [24]

Geissospermum vellosii: Pretreatment with the ethanolic extract of *G. vellosi* stem barks has been shown to reduce scopolamine-induced memory loss as evidenced in Morris water maze and passive avoidance tests. *G. vellosii* has shown potent anticholinesterase activity. [25]

Glycyrrhiza glabra **(Liquorice)*:*** The aqueous extract of *liquorice* has been shown to significantly reverse the amnesia induced by scopolamine and enhance the learning and memory property due to facilitation of cholinergic-transmission in mouse brain. [26]

Hibiscus sabdariffa Linn: The aqueous extracts of calyces of *Hibiscus sabdariffa* (100 and 200 mg/kg, p.o.) had shown to significantly attenuate amnestic deficits induced by scopolamine. *HS* (100 and 200 mg/kg) decreased the transfer latencies and increased step down latencies significantly in the scopolamine induced amnesic mice as compared with Piracetam (200 mg/kg, i.p.). *H. sabdariffa* has significantly decreased acetyl cholinesterase activity in mice. [27]

Hippophae rhamnoides **(Seabuckthorn):** SBT leaf extract has shown significant potential effect against scopolamine induced cognitive impairment by regulation of cholinergic enzyme

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activity (AChE activity) and promoting the antioxidant system by reducing the brain MDA levels. [28]

Huperzia serrata: It has been reported that Huperzine A has a unique anti-acetylcholine esterase activity. Pretreatment of rats with Huperzine A (0.1-0.4 mg/kg/p.o.) before scopolamine injection resulted in improvement of reference memory and working memory, as shown in radial maze performance. [29]

***Lepidium meyenii* (Black Maca):** The aqueous and hydroalcoholic extract of *L.meyenii* was shown to improve scopolamine-induced amnesia deficits by inhibition of acetylcholinesterase activity in mice. [30]

Melissa officinalis: The ethanolic extract of *M. officials* has been able to significantly ameliorate the scopolamine-induced amnesia by inhibition of AChE activity. [31]

Mimusops elengi:*M. elengi* (100 and 200 mg/kg, p.o.) significantly attenuated amnesia deficits induced by scopolamine by decreasing transfer latencies and increases step down latencies of *M. elengi* treated group. It has been shown to decrease whole brain acetyl cholinesterase activity. [32]

Murraya koenigii: The leaves of *M. koenigii* has been able to alleviate scopolamine-induced amnesia in young (3-4 months) and aged (12-15 months) mice. Inhibited brain cholinesterase activity has been attributed to this protection. [33]

Nardostachys jatamansi: The ethanolic extract of root of *N. jatamansi* (200 mg/kg) has been shown significantly improved learning and memory in young mice and also reversed the amnesia induced scopolamine by facilitation of cholinergic transmission in the brain. [34]

Nelumbo nucifera: The aqueous extract of *N. nucifera* semen has been shown to attenuate scopolamine-induced deficit in which the acetylcholine esterase activity of the *N. nucifera* treated group decreased to 7.35 % and CHAT-positive neurons in the *N. nucifera* treated group increased by 51.02 % compared with the control group. [35]

Table 1: Anti amnesic plants and their derivatives with dose of scopolamine

S.No	Scientific Name	Family	Part used/Active ingredients	Dose of Scopolamine	Reference
1.	*Acori Graminei*	Acoraceae	Rhizome	2 mg/kg, i.p.	7
2.	*Allium sativum* (Garlic)	Amaryllidaceae	Garlic extract	0.4 mg/kg, i.p.	8
3.	*Angelica gigas*	Umbelliferae	Decursin	1 mg/kg, s.c.	10
4.	*Anacyclus pyrethrum*	Asteraceae	Roots	1 mg/kg, i.p.	9
5.	*Asparagus recemosus*	Asparagaceae	Roots	1 mg/kg, i.p.	11
6.	*Bacopa monniera*	Plantaginaceae	Whole plant	1 mg/kg, i.p. 3 mg/kg, i.p.	12 13
7.	*Caesalpinia crista*	Fabaceae	Dried seed	1 mg/kg, i.p.	14
8.	*Canscora decussate*	Gentianaceae	Whole plant	0.3 mg/kg, i.p.	15
9.	*Carica papaya*	Caricaceae	Seeds	1 mg/kg, i.p.	16
10.	*Commiphora whighitii*	Burseraceae	Whole plant	0.4 mg/kg, i.p.	19
11.	*Corydalis Tuber*	Papaveraceae	Pseudocoptisine	1 mg/kg, i.p.	20
12.	*Clitoria ternatea*	Fabaceae	Roots	1 mg/kg, s.c.	18
13.	*Desmodium*	Leguminosae	Leaves and roots	0.4 mg/kg, i.p.	21

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	gangeticum				
14.	*Emblica officinalis*	Euphorbiaceae	Fruits	0.4 mg/kg, i.p.	23
15.	*Ficus religiosa*	Moraceae	Figs	1 mg/kg, i.p.	48
16.	*Foeniculum vulgare*	Umbelliferae	Whole plant	0.4 mg/kg, i.p.	24
17.	*Glycyrrhiza glabra*	Leguminosae	Root, Rhizomes	0.4 mg/kg, i.p.	26
18.	*Geissospermum vellosii*	Apocynaceae	Stem bark	1 mg/kg, i.p.	27
19.	*Hibiscus sabdariffa*	Malvaceae	Red calyces	0.4 mg/kg, i.p.	27
20.	*Hippophae rhamnoides*	Elaeagnaceae	Leaves	2 mg/kg, i.p.	28
21.	*Huperzia serrate*	Huperziaceae	Huperzine A	0.2 mg/kg, i.p.	29
22.	*Lepidium meyenii*	Brassicaceae	Hypocotyl	1 mg/kg, i.p.	30
23.	*Melissa officinalis*	Lamiaceae	Leaves	1 mg/kg, i.p.	31
24.	*Morinda citrifolia*	Rubiaceae	Noni juice	0.3 mg/kg, i.p.	49
25.	*Murraya koenigii*	Rutaceae	Leaves	0.5 mg/kg, i.p.	33
26.	*Mimusops elengi*	Sapotaceae	Stem bark	0.4 mg/kg, i.p.	32
27.	*Nardostachys jatamansi*	Valerian	Roots	0.4 mg/kg, i.p.	34
28.	*Nelumbo nucifera*	Nelumbonaceae	Whole plant	1 mg/kg, i.p.	35
29.	*Phyllanthus amarus*	Euphorbiaceae	Leaves and Stems	0.4 mg/kg, i.p.	36
30.	*Pueraria thunbergiana*	Fabaceae	Daidzein	1 mg/kg, s.c.	37
31.	*Prunus amygdalus*	Rosaceae	Nuts	1 mg/kg, i.p.	38
32.	*Salvia miltiorrhiza*	Lamiaceae	Tanshinones (diterpenoids)	1 mg/kg, i.p.	39
33.	*Soybean*	Fabaceae	Phytoestrogens	1.4 mg/kg, i.p.	40
34.	*Scrophularia buergeriana*	Scrophulariaceae	Iridoid glycosides	1 mg/kg, s.c.	41
35.	*Teucrium polium*	Lamiaceae	Whole plant	1 mg/kg, i.p.	42
36.	*Thespesia populnea*	Malvaceae	Bark	0.4 mg/kg, i.p.	43
37.	*Vigna Radiata*	Fabeaceae	Seed	0.4 mg/kg, i.p.	44
38.	*Vitex Negundo*	Verbenaceae	Whole plant	3 mg/kg, i.p.	45
39.	*Withania somnifera*	Solanaceae	Leaf extract	3 mg/kg, i.p.	3
40.	*Zingiber officinale*	Zingiberaceae	Dried rhizomes	0.4 mg/kg, i.p.	46
41.	*Ziziphus mauritiana*	Rhamnaceae	Seeds	0.4 mg/kg, i.p.	47

Phyllanthus amarus: *PA* has shown to produce a dose-dependent significant improvement in memory scores of young and older mice in Elevated plus maze and passive avoidance. *PA* has also reversed successfully the amnesia induced by scopolamine by decreasing brain AChE activity. [36]

Pueraria thunbergiana: Daidzein isolated from *P. thunbergiana* inhibited scopolamine-induced amnesia in the Y-maze test by acting as a choline acetyltransferase activator for acetylcholine biosynthesis. [37]

Prunus amygdalus **(almond):** Pretreatment with *P. amygdalus* for a 14 day dose-dependently has shown significantly reversed scopolamine-induced amnesia by a decrease in transfer latency in elevated plus maze and step down latency in the passive avoidance task by reducing brain ChE activity. It has been also shown that the PA exhibited a remarkable

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cholesterol and triglyceride lowering property. [38]

Salvia miltiorrhiza: It has been able to significantly ameliorate the scopolamine-induced amnesia in passive avoidance test. This activity was observed due to Tanshinone, a major diterpenoids found in the roots of *Salvia miltiorrhiza* Bunge. Tanshinone has significantly shown the anti-amnesic effect due to enhancement of cholinergic signaling in the mice brain. [39]

Scrophularia buergeriana: *Scrophularia buergeriana* has shown significantly enhance in cognitive activities against scopolamine induced amnesia in the Morris water maze test in mice. This activity was observed due to E-harpagoside and MCA-Hg, an iridoid glycosides isolated from *SB.* E-harpagoside or MCA-Hg significantly decreased TBARS level, which was accompanied by an increase in the activities or contents of glutathione reductase, SOD and reduced GSH. [41]

Soybean: Pretreatment with *soybean* for 60 days has shown to protect the animal significantly from developing memory impairment against scopolamine induced memory deficits. *Soybean* administration also resulted in diminished brain AChE activity, decrease in brain TBARS and the increase in GSH levels was observed, which indicated facilitation of the cholinergic transmission, reduced free radical generation and enhanced scavenging of free radicals. Thus, *soybean* appears to be a useful remedy for improving memory and for the management of cognitive deficits owing to its pro-estrogenic, antioxidant, procholinergic, and or neuroprotective properties. [40]

Teucrium polium: An ethanolic extract of *T. populnea* reversed the scopolamine-induced amnesia through reduced brain cholinesterase activity. [42]

Thespesia populnea: Pretreatment with ethanolic extract of *T. populnea* (TPE) for 7 days has shown significantly reversed scopolamine-induced amnesia by reducing the central (brain) cholinesterase activity in mice. [43]

Vigna radiate: Aqueous and ethanolic extract of dried seeds of *Vigna radiata linn* has been shown to ameliorate the amnesic effect of Scopolamine induced memory deficit in mice using the Radial arm maze and Morris water maze models. [44]

Vitex Negundo: Pretreatment with aqueous extract of *V. negundo* has shown a significant decrease in the phenomenon of scopolamine-induced amnesia by increase in learning about memory through antioxidant effect and decreasing AChE activity. [45]

Zingiber officinale: *Z. officinale* extract has been shown significantly improved learning and memory in young mice and also reversed the amnesia induced by scopolamine. *Z.officinale* has also significantly increased whole brain acetyl cholinesterase inhibition activity. [46]

Ziziphus mauritiana: The extracts of *Z.mauritiana* seeds impaired spatial recognition of rodents, the activity of which was greatly produced by the portion extracted with ethyl acetate. Spatial memory as measured by the Y-maze test is dependent on hippocampal learning and memory function and is related to the NMDA receptor/Ca2+ influx signaling pathway. It is possible that, compounds contained in the ethyl acetate portion of the extract may inhibit this hippocampal NMDA receptor/Ca2+ signaling pathway. Seeds from *Z. Mauritania* extracted with ethyl acetate not only impair the acquisition but also consolidation and retrieval of spatial

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recognition memory in animals in the Y- maze. [47]

CONCLUSION

From this study, it is clear that the medicinal plants play a vital role against amnesia and dementia. Various above-mentioned medicinal plants and plant extracts have significant antiamnesic and antidementic activity in the scopolamine induced amnesia model. Scopolamine is a muscarinic receptor antagonist that inhibits central cholinergic neuronal activity and impairs learning and short-term memory, and it is used as a standard/reference drug for inducing cognitive deficits in healthy humans and animals. This review provides some evidence of the benefit of a wide range of herbs (included in the Indian Medicine System, Chinese Medicine System, European Medicine System, etc.) in the treatment of amnesia.

Further large-scale, multicenter studies are necessary to determine the effectiveness of these substances in the cognitive deterioration of amnesia.

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