Original Article

Invivo Study On Memory Enhancing Potential Of Azilsartan On Amnesia Rats

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Abstract

Azilsartan AT2 receptor antagonist was designed for the investigation on memory enhancing activity. Azilsartan is used to treat high blood pressure. Azilsartan belong to a class of drug called Angiotensin receptor blockers (ARBs). Scopolamine (0.4mg/kg I.P) was administered to induce amnesia. Scopolamine is muscaranic receptor antagonist with amnesia properties that have been used for decades in experimental rats to induce impairment in their performance of a variety of tasks requiring intact working and reference memory piracetam dose of (400mg/kg I.P) was used as a standard drug. The azilsartan dose (10mg/kg and 20mg/kg P.O) was prepared by mixing the suitable amount of drug in normal distilled water to make for oral administration. Azilsartan was studied for investigation of memory enhancing activity by using scopolamine induced amnesia as interoceptive model and Morris water maze (MWM) test and elevated plus maze (EPM) test as exteroceptive model. The two were selected for oral administration of azilsartan. The azilsartan (10mg/kg and 20mg/kg) for this study NO effect of memory enhancement was recorded for test drug by MWM&EPM test because azilsartan treated rats manifested increases in escape latency time (ELT) and decrease in time does not possess memory (TSTQ) in MWM test and increase in transfer latency time does not possess memory enhancing effect against scopolamine induced amnesia using both model.
The present study signalized that azilsartan does not possess memory enhancing activity.

INTRODUCTION

The brain is the ganglion of the nervous system in all vertebrates. The cerebral cortex of the human brain inset roughly 15-33 billion neurons dependent on gender and age. Every cubical millimetre of cerebral cortex inset approximate one billion synapses. [1] drugs that are in existence evolved for over three decennary and are the predominantly applied method for treating cognitive reduction they are also known as Nootropic. This has been derivative of two words, which is “noos,”pertaining “to mind” and “tropein”, signifying “to monitor”. It means any gives essence that impress is the perception capability in a positive way. [2] Spontaneous nootropics combine neurotransmitter concentration in the brain. These reportedly promote the discharge of different neurotransmitters such as dopamine as well as uptake of choline, along with cholinergic transmission, turnover of phosphatidylinositol, and functions of α-amino-3-hydroxy-5-methyl-4-isoxazole propionate receptor, and activity of phosphatise A2. Some of them positively govern the activity and expression of receptor for acetylcholine (Ach) or glutamate. Due to improved levels and activity of

neurotransmitters, these special predominance of natural nootropic directs the long-term possible and extended synaptic transmission.[3]

The “nootropic” or simply known as “smart drug”, “memory-enhancing drug “or “brain booster” is a general term given to compounds with the capability to enhance mental executions. Even though people with a history of mental conjugation may be perceptive to its adverse effects [4] By definition, nootropics are compounds that enhance mental eligibility inclusive meditation, concentration, remembrance, and provocation. [5]

There are multiple nutraceutical, supplements and function foods accessible in market which acts as the perception extend and used as nootropic agents. Herbal plants such as Prunus amygdalus, Hibiscus Sabdariffa, chtoria ternatea, Baccopa monniera and Centella asiatica, also resolution expeditious nootropic influence because it may be used as primary ingredients of several nootropic formulation; nutraceutical and supplements. This representative surplus may also offer other pharmacological activities such as the Antioxidant and neuroprotective effects [6]

1.2 MECHANISMS OF ACTION OF NOOTROPIC AGENT

- Shortage of malondialdehyde level in brains, enhancement level of antioxidant molecules namely; glutathione and superoxide dismutase.
- Interplay with dopamine-D2, serotonergic and GABA receptors.
- Shortage of MAO-A and plasma corticosterone levels.
- Shortage the concentration of noradrenalin and reduction turnover of central monoamines.
- Resistor of acetyl cholinesterase activity in brain.
- Enhancement of lipids and phospholipids in brains.
- Preserve neurons against glutamate-induced the toxicity.
- Regularize NMDA receptor activity.[7],[8]

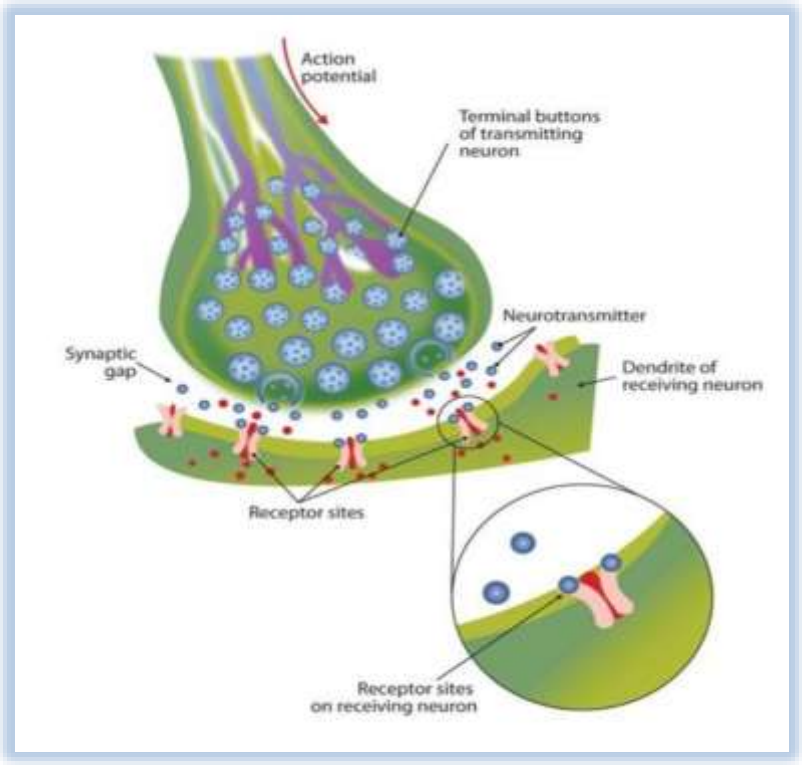


Fig.no: 1.1 Dendrite of Receiving Neuron

1.3 LEARNING AND MEMORY

Memory is one of the signification ability of specific to record events, protect information and hold in them over short and long period. In the process of learning and memory are involved the neurotransmitters. Memory is the key of clinical confirmation as well as pertaining to experiment; central cholinergic system is recognized as the most significant neurotransmission system which is contiguous in regulation of cognitive function [9]. Learning assigns too much or less enduring transfer in behavior which occurs as results of exercises is a meager good [10].Important attributes of human intelligence are learning and memory. These evolutions establish the very perspective of awareness of your own individuality [11].Learning is a transfer in experience or in potential behavior that occurs as results of experience. Learning represented by behavioral psychology is classical conditioning, operant and observational learning is the three general types [12]. In the environment objects of when people recognize (e.g. knowing that a function is a plants or animals) or when they give the answer to a genuine question, they withdraw upon stand of general intelligence about the world accumulated over time. [13]. the memory system affected is depending on the action of drug on memory is much or less specific and serious. In the process of learning and memory, acquisition, consolidation and recall of the learned task have suggested three important stages [14], [15].

TYPES OF MEMORY : Sensory memory-Sensory memory capture sensory information no more than one second after an item is understood. The capability to look at an item and recall what it looked like with just a divided second of examination or memorization is the example of sensory memory [16], [17]. Short term memory

- Long term memory
- Declarative memory
- Implicit memory

Amnesia: Amnesia is an intensive memory loss which is commonly raised up either by the ingestion of a toxin substance or by substantial harm to the brains which affects the brains. In addition to the memory loss can be generated by an injury, emotional events, concussion, morbidness or sometimes by anaesthesia. Some amnesia are operate and not reversible and some are mild can be reversible. Which part of the brain is affected by and damaged depends on types of the amnesia. Male or female can affected it. It can be occurring at any age [18], [19]

Alzheimer disease: The major features of Alzheimer disease (AD) are functions of mild cognitive imperilments [20] Alzheimer's disease is types of brain disease, just as coronary artery disease is types of hearts disease. It is also a despicable disease, meaning that it becomes worse with time. Alzheimer's disease is even thought to begin 20 years or more before symptoms arise [21],with small changes in the brain that are unwitting to the person impressed. Only after years of brain substitute do exclusive experience observable symptoms, such as memory loss and language problems. Symptoms become because nerve cells (neurons) in parts of the brain involved in both, learning and memory (cognitive function) have been defaced or destroy.[22]

2. MATERIAL AND METHOD

2.1 Experimental animal

In the investigation male experimental rats weighting from 150-200gm were used. They were housed in divided groups of six all were kept up under normal light and cloudy condition. These were adjusted for seven days before the inquiry in the Institutional animal house. The rats were put on standard feed. All the rest techniques were completed as per the CPCSEA guidelines.

2.2 Medication and chemical

Azilsartan (10mg/kg and 20mg/kg P.O), Piracetam (400mg/kg I.P), Scopolamine (0.4mg/kg I.P) were bought from Universal Pharmacy Gurgaon India.

AZILSARTAN (TEST DRUG)

(Azilsartan medoxomil),a prodrug is hydrolyzed to azilsartan in the gastrointestinal tract throughout absorption. Azilsartan is orally delivered Angiotensin 2 receptors type 1 antagonist (blocker) used in the treatment of adult with essential hypertension. It is marketed in tablets under the brand name EDARBI.[23] Azilsartan is a selective AT1 subtype Angiotensin 2 receptor antagonist. It is mechanism of action to lower blood pressure by inhibiting action of vasopressin hormones Angiotensin-II, a polypeptide that causes vasoconstriction, increased blood pressure and aldosterone liberation. **Azilsartan** is exclusively referred for the treatment of hypertension, single or in addition with other anti- hypertension agents. It is EDARBI as the prodrug Azilsartan medoxomil (INN). [24], [25] Azilsartan medoxomil is the 8^{th} sartan developed since the first ARB losartan potassium was approved by the United States food and drug administration (FDA) in 1995.Azilsartan medoxomil was approved by FDA in February 2011[26].Azilsartan (AZL) is a selective AT1 receptor antagonist that only antagonizes the AT1 but not the AT2 receptor. There by it is mediating vasodilatation, reducing aldosterone release and reducing sympathetic stimulus of vessels and kidney [27].

CLINICAL TRIALS WITH AZILSARTAN

Azilsartan medoxomil was tested in several clinical trials. In most of these trials, AZL was compared to other ARBs and placebo groups.AZL was found to be superior in its BP- lowering effects and was well tolerated with similar adverse effects to placebo or the comparative drug[28], [29], [30]

Mode Of Action: Azilsartan is a selective blocker of AT1 receptors that prevents Angiotensin 2 binding, resulting in vasodilatation and decrease in the effects of aldosterone, because of the presence of such receptor in the effects of

aldosterone, because of the presence of such receptors in the vascular smooth muscle and in the adrenal gland. Azilsartan is highly selective for the AT1 receptor and not the AT2 receptor. [31], [32]

SCOPOLAMINE (Negative Control)

Scopolamine and atropine derive the plants Atropa belladonna also called "deadly nightshade" Hyoscine, also known as scopolamine, is a medication used to treat motion sickness and postoperative nausea and vomiting. This medication function by reformation the mismatch of natural substance (acetylcholine and nor epinephrine) that can become in motion sickness. It also blocks one or two signals to the brains that can cause nausea and vomiting. [33] Scopolamine is moreover used to induce amnesia in experimental animals like rodents, rat and mice due to the reason of its anticholinergic activity at various dosage ranges from 0.4mg/kg. Reducing the impact of acetylcholine The characterization of the interplay of scopolamine with the muscaranic acetylcholine receptor in the CNS referred a two-step process with an initials binding of ligand to receptor followed by isomerisation of the receptor ligand complex to a higher affinity form.It was stipulated that scopolamine also interferes with neurotransmitter system [34] and affects the regional cerebral blood intensity during the execution of memory tasks. [35]

Adverse effect: Confusion and hallucinations are rarely reported with transdermal use. Clissold and Heel commented on the unpublished Ciba-Geigy data: "CNS adverse reactions such as disorientation, memory impairment, dizziness, restlessness, hallucinations, confusion and insomnia are rarely reported. After application of transdermal hyoscine patches.5 Three cases of presumed scopolamine-induced psychosis have been reported. [36]

PIRACETAM (STANDARD DRUG)

Piracetam is a nootropic class of drug that may extend memory and promotion cognitive function. Derivate from the amino acid gamma-amino butyric acid (GABA), piracetam was first developed in the 1960s and is touted for the prevention and treatment of age-related cognitive decline, seizers, and learning disability, Piracetam profound uses include for Alzheimer's disease. Dementia, memory dysfunction, alcoholism, Reynaud's phenomenon, deep vein thrombosis (DVT), stroke, tar dive, dyslexia, brain injury, and vertigo. The dose of piracetam is 400mg/kg. [37], [38]

Mode of action: Piracetam is a positive allosteric repair of the AMPA receptor, and It is hypothesized to act on ion channels or ion carriers, thus leads to increased neuron excitability. [39].GABA brain metabolism and GABA receptor are genuine by piracetam [40].

Piracetam renovate the function of the neurotransmitter acetylcholine via muscaranic cholinergic (Ach) receptor, piracetam may have an effects on NMDA glutamate receptors, which are involved with learning and memory processes .piracetam is thought to increase cell membrane permeability.[41].piracetam may exert its global effect on brain neurotransmission via modulation of ion channels(i.e. ,Na+ ,k+)[42].

2.2 BEHAVIOURAL TEST

1. EXTEROCEPTIVE
   a) Morris water maze test.
   b) Elevated plus maze test.

2. INTEROCEPTIVE

   a) Scopolamine induced Amnesia in rats.

MORRIS WATER MAZE (MWM) TEST

The MWM as an exteroceptive behavioural model has been used extensively to investigation spatial learning and memory in rodents. The MWM consisted of the circular pool (diameter 70 cm, height 31 cm) contain water at 25±1 ◦C to a depth 30 cm rendered opaque by the addition of power. A circular platform (diameter 10 cm) was hidden 1 cm below the surface of water and placed in a constant position. [43], [44]

ACQUISITION TRAILS

Each rats was placed in the pool for six consecutive trials on each day with an interval of five minutes, allowed 90s to find the hidden platform, and permitted to stay there for 10s (modified from Morris, 1984).[45]

During training and testing sessions, escape latency time (ELT), time to find the hidden platform was recorded. Extensive pre-training is not required in this model because animals learn rapidly to locate the hidden platform. The starting position on each day to conduct four acquisition trails was changed. [46]

RETRIEVAL TRIAL

On the next day, platform was removed, and each rats was allowed to explore the pool for 90 seconds. Mean time spent by the rats in each of four quadrants was noted. The mean time spent by the rats in target quadrant (Q4) for searching the hidden platform was noted. [47]

ELEVATED PLUS MAZE (EPM) MODEL

The EPM served as the exteroceptive behavioural model to evaluate learning and memory in rats. An elevated plus maze consisting of two open arms and two enclosed arms was used. The arms extended from a central platform and the maze was elevated to the height of 50cm from the floor. Rats were placed individually at the end of an open arm facing away from the central platform and the time they took to move from the end of open arm to either of the closed arms (transfer latency time, TLT) was recorded [48] TLT is recorded on the first day. If the rats do not enter into one of the covered arms within 90 sec, they will be gently pushed into one of the two covered arms and the TLT will be assigned as 90sec.The rat will be allowed to explore the maze for 10 sec and then return to its home cage. Memory retention will be calculated 24hr of acquisition trial on second day. [49]

Fig.No: 2.1 ELEVATED PLUS MAZE

SCOPOLAMINE INDUCED AMNESIA IN RATS

Scopolamine hydro bromide 0.4mg/kg I.P. was administered to induce amnesia. Scopolamine is muscaranic receptor antagonist with amnesic properties that have been used for decades in experimental rats to induce impairment in their performance of a variety of tasks requiring intact working and reference memory. [50] Scopolamine has also been used clinically as an adjunct to surgical or obstetric procedure to induce sedition and post-procedural amnesia. This reversible amnesic effect was induced by centrally acting muscaranic cholinergic antagonist. [51] Indeed, blockade of central muscaranic receptors could induce a pattern of cognitive impairment. Scopolamine actions are limited to the blockade of brain function mediated via cholinergic (muscaranic) receptors. [52]

2.3 EXPERIMENTAL PROTOCOL

Rats were divided into nine group and each group contains six rats (n=6).

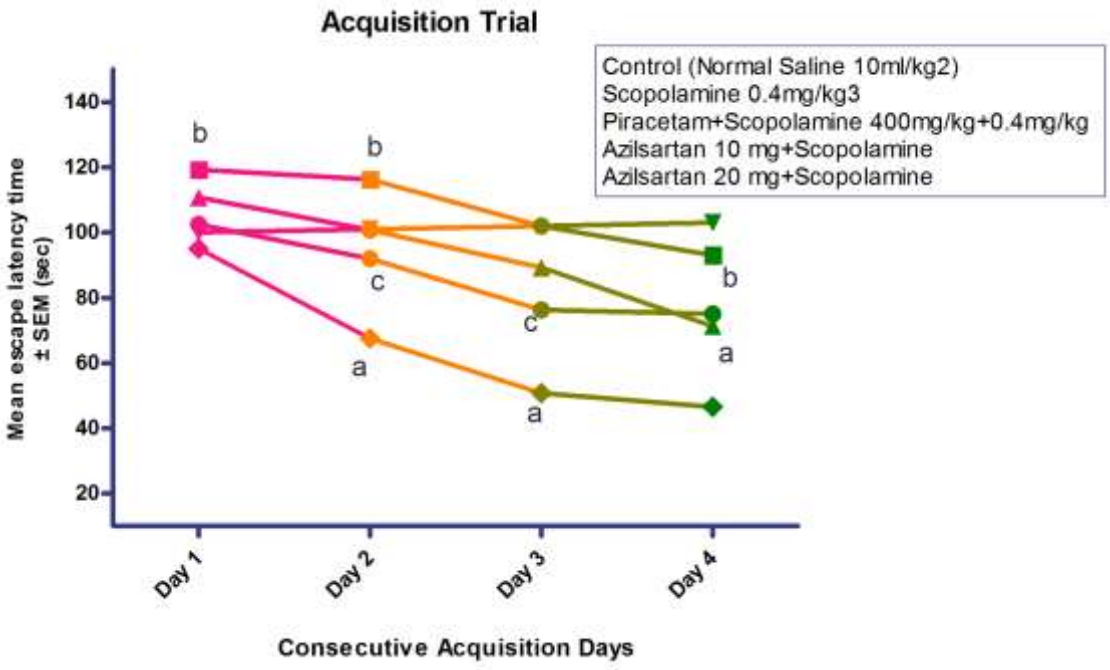
S.N	GROUPS	TREATMENT	DOSE/ROUTES OF ADMINISTRATION
1.	Control	Normal saline 0.9%NaCl	10ml/kg ,I.P
2.	Negative Control	Scopolamine	0.4mg/kg ,I.P
3.	Negative control	Sodium nitrite	75mg/kg ,I.P
4.	Standard	Piracetam +Scopolamine	400mg/kg ,I.P
5.	Standard	Piracetam +Sodium nitrite	400mg/kg ,I.P
6.	Test drug at low dose	Azilsartan +Scopolamine	10mg/kg ,P.O/I.P
7.	Test drug at high dose	Azilsartan +Scopolamine	20mg/kg ,P.O/I.P
8.	Test drug at low dose	Azilsartan +Sodium nitrite	10mg/kg ,P.O/I.P
9.	Test drug at high dose	Azilsartan +Sodium nitrite	20mg/kg ,P.O/I.P

3. RESULT AND DISCUSSION

3.1 Pharmacological screening using Morris water maze model:

3.1.1 Effect of Azilsartan on scopolamine and sodium nitrite induced changes in ELT during acquisition trials:

Azilsartan was investigated for its effect on scopolamine induced amnesia and sodium nitrite using Morris Water Maze test. Azilsartan was administered at 10mg/kg, p. o. and 20mg/kg, p. o. doses in rats. The ELT of Azilsartan conducted on four consecutive days is shown. It is noted that the scopolamine have a significantly increasing effect on ELT. Piracetam have a decreasing effect on ELT. Increase in ELT was seen due to Azilsartan



3.1.1.2 Table 1: Effect of Azilsartan on Scopolamine and Induced Changes in ELT during Acquisition Trials

S. N	Groups (n=6)	Treatments	Dose	Day 1	Day 2	Day 3	Day 4
1	Control	Normal Saline	10ml/kg2	100± 0.8	101.25± 4.47	102±4 .2	103±7.66

2	Negative control	Scopolamine	0.4mg/kg3	119.25± 0.9	116.25± 3.12	102±5.33	93±4.96
3	Standard	Piracetam+ Scopolamine	400+0.4(mg/kg)	110.75± 5.24	100.75±6.21	89.25±5.32	71.25±3.97
4	Test Drug	Azilsartan+Scopolamine	(Low dose 10 mg)	102.5± 7.54	92± 3.42	76.25±4.12	75±2.12
5	Test Drug	Azilsartan+Scopolamine	(High dose 20 mg)	95±4.8	67.5± 1.12	50.75±1.24	46.5± 1.32

3.1.1.3 Table 1: Effect of Azilsartan with Sodium Nitrite in ELT during Acquisition Trials

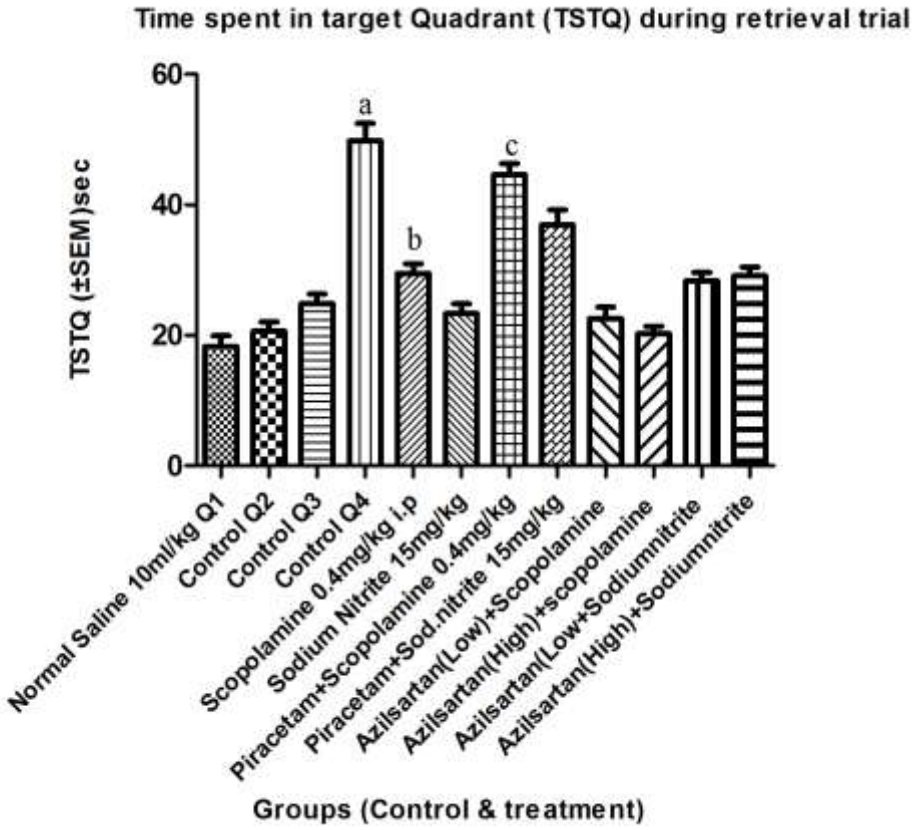
S. N	**Groups (n=6)**	**Treatments**	**Dose**	**Day 1**	**Day 2**	**Day 3**	**Day 4**
1	Control	Normal Saline	10ml/kg2	100± 0.8	95± 4.47	102±4.2	103±7.66
2	Negative control	Sodium Nitrite	75mg/kg	112.5± 1.2	103±2.23	87±5.75	69±4.26
3	Standard	Piracetam +Sodium nitrite	400+75(mg/kg)	101±4.8	97.50± 3.21	73±5.2	59± 4.32
4	Test Drug	Azilsartan+Sodium nitrite	(Low dose 10 mg)	95±3.23	63.50± 4.21	57.75±2.13	50± 7.12
5	Test Drug	Azilsartan+Sodium nitrite	(High dose 20 mg)	104.56±3.3	68.36±5.32	62.35±1.25	56.36±3.69

3.1.2 Effect of Azilsartan on scopolamine and sodium nitrite induced changes in Time spent in target Quadrant (TSTQ) during retrieval trial by Morris water maze method

Azilsartan was investigated for its effect on scopolamine induced amnesia using Morris Water Maze test. Azilsartan was administered at 10mg/kg, p. o. and 20mg/kg, p. o. doses in rats. The TSTQ of Azilsartan is shown. Note that while the scopolamine and azilsartan has a significantly decreasing effect on TSTQ but piracetam has an increasing effect.

Scopolamine treated rat's decreased time spent in target quadrant as compared to target quadrant (Q4) of control group. But piracetam increased time spent in target quadrant and showed protection against scopolamine induced amnesia. Results were expressed as mean ± S.E.M. with n=6 in each group.

a = p≤0.05 Vs time spent in target quadrant (TSTQ) in control group; b = p≤0.05 Vs time spent in target quadrant (TSTQ) in Scopolamine treated group.



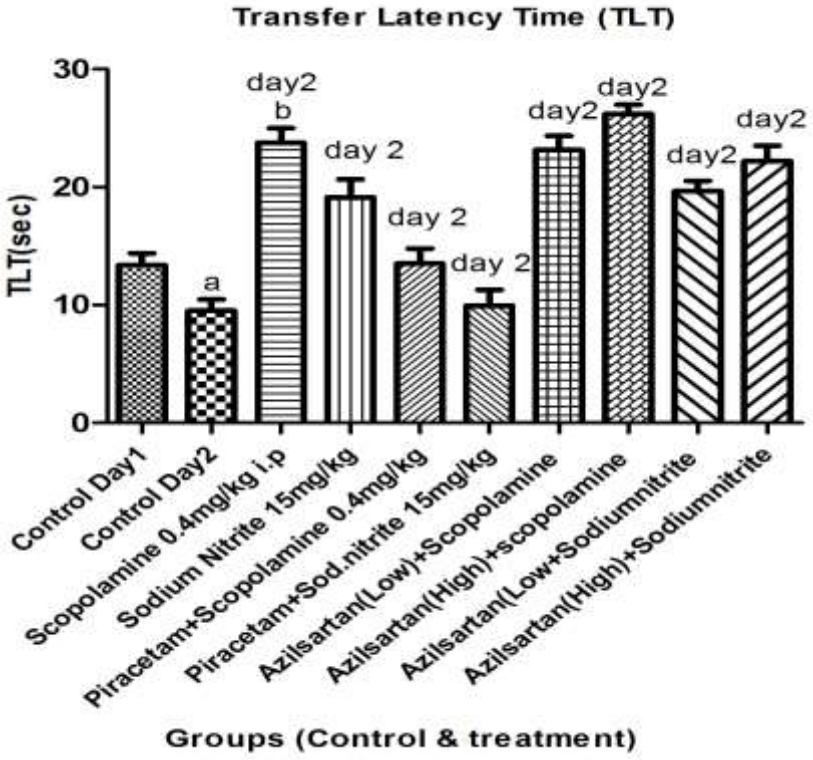
Effect of Azilsartan on scopolamine and sodium nitrite induced changes in Time spent in target Quadrant (TSTQ) during retrieval trial by Morris water maze method

Normal Saline Q1	Target quadrant Q2	Target quadrant Q3	Target quadrant Q4	Scopolamine	Sodium Nitrite	Piracetam & Scopolamine	Piracetam & Sodium nitrite	Azilsartan +Scopolamine	Azilsartan +Scopolamine	Azilsartan +Sodium nitrite	Azilsartan +Sodium nitrite
21.25 ±2.25	22.35 ±3.65	26.36 ±4.23	40.28 ±1.25	28.528 ±2.69	25.36 ±4.25	44.25 ±1.89	40.25 ±1.56	24.25 ±2.36	20.36 ±5.64	25.25 ±4.25	30.25 ±2.36
22.32 ±3.56	24.25 ±4.23	25.36 ±1.89	51.25 ±2.25	35.36 ±4.32	23.25 ±4.21	42.25 ±2.66	41.25 ±1.99	23.25 ±4.88	18.25 ±3.33	26.25 ±4.11	28.25 ±2.88
18.25 ±2.78	23.25 ±4.85	26.35 ±2.84	48.25 ±5.36	32.25 ±2.78	20.25 ±3.56	40.25 ±4.32	42.25 ±1.45	21.25 ±1.89	19.36 ±1.45	30.25 ±2.58	29.36 ±3.65
16.36 ±2.89	15.25 ±2.74	29.68 ±2.01	45.25 ±4.25	28.36 ±1.65	19.25 ±1.35	43.36 ±4.57	34.21 ±3.11	15.25 ±4.87	17.25 ±2.22	25.25 ±3.54	30.35 ±1.28
11.25 ±2.77	21.25 ±3.54	21.25 ±2.87	55.36 ±2.04	25.25 ±1.88	29.36 ±7.56	52.36 ±5.36	36.36 ±6.54	28.25 ±2.44	25.25 ±1.77	30.25 ±1.89	23.25 ±2.98
20.25 ±1.65	17.25 ±6.53	20.32 ±5.68	58.36 ±1.78	27.25 ±2.71	22.36 ±2.87	45.36 ±2.45	27.25 ±2.31	23.25 ±6.66	21.02 ±4.32	32.69 ±3.77	33.25 ±2.88

3.2.2 Effect of Azilsartan on scopolamine and sodium nitrite induced changes in Transfer Latency Time (TLT) of rats by Elevated plus-maze method:

The effect of Azilsartan on TLT at doses of 10 mg/kg, p.o. and 20 mg/kg, p.o. was observed against scopolamine induced amnesia in rats using Elevated plus maze test. Piracetam was found to decrease the TLT and restore memory function at higher dose.

In case of scopolamine treated rats, significant increase in Transfer Latency Time (TLT) was noted. Azilsartan treated group also increased TLT in Elevated plus maze. Results were expressed as mean ± S.E.M. with n=6 in each group. a = p≤0.05 Vs TLT in control group; b = p≤0.05 Vs TLT in scopolamine treated group.



3.2.2.1 Table: Effect of Azilsartan on scopolamine induced changes in Transfer Latency Time (TLT) of rats by Elevated plus-maze method:

Control Day 1	Control Day 2	Scopolamine	Sodium Nitrite	Piracetam +Scopolamine	Piracetam +Sodium Nitrite	Azilsartan (Low) +Scopolamine	Azilsartan(High) +Scopolamine	Azilsartan (Low) +Sod. nitrite	Azilsartan(High) +Sod. nitrite
15.00 ±1.25	8.25 ±2.36	24.25 ±3.56	20.00 ±3.58	13.00 ±2.65	10.00 ±3.65	22.36 ±4.32	26.55 ±2.36	18.25 ±2.58	22.25 ±4.23
10.25 ±2.58	9.36 ±4.25	26.25 ±2.36	21.25 ±3.36	12.25 ±4.25	9.36 ±2.36	25.36 ±1.99	24.25 ±2.87	16.36 ±1.87	21.25 ±2.58
16.25 ±1.87	12.25 ±2.45	28.25 ±1.65	19.25 ±2.77	11.25 ±3.55	8.36 ±2.01	24.25 ±1.87	29.25 ±1.99	19.58 ±4.25	20.35 ±3.33
12.25 ±2.25	10.25 ±4.36	22.25 ±1.22	12.25 ±1.88	14.65 ±2.66	11.25 ±4.36	18.25 ±2.34	25.25 ±2.78	21.25 ±4.66	19.25 ±3.77
11.25 ±1.35	5.68 ±1.69	21.25 ±2.47	23.35 ±3.54	19.25 ±2.44	5.26 ±1.89	22.36 ±2.45	27.36 ±3.55	20.36 ±6.47	21.98 ±2.99
15.36 ±1.22	11.25 ±7.12	20.25 ±2.88	18.69 ±3.46	10.69 ±5.32	15.36 ±2.48	26.35 ±3.88	24.58 ±4.36	22.25 ±2.81	28.25 ±1.54

3.3 DISCUSSION

All the smart drug are related to the category of psychotic drug with specific site of action on learning and memory .Piracetam was used as standard medicine to reserve memory deficit by scopolamine .Piracetam is a nootropic drug commonly used as smart drug to treat amnesia and also used for treatment of AD .Scopolamine induced amnesia test was used as an interceptive model to induce amnesia in rats and Morris water maze test and elevated plus maze model were used as exteroceptive model .In MWM test's acquisition trials animals learned to find hidden plate form to escape from water(ELT) and in Retrieval trials on 5^{th} day the highest TSTQ {Q4) shows the retrieval of memory . Scopolamine produced impairment of memory in both acquisition trials and retrieval trial by increasing the ELT and decreasing the TSTQ. The second exteroceptive model was elevated plus maze model in which the TLT was noted on first day and after 24Hrs.

CONCLUSION

Memory enhancing effect of Azilsartan was investigated against scopolamine induced amnesia in rats applying MWM test. Azilsartan was given at dose of 10 and 30 mg/kg P.o scopolamine was given at dose of 0.4 mg/kg I.p before test drug to induced amnesia. Increase in ELT during acquisition trials and decrease in TSTQ in retrieval trial show that azilsartan does not have memory enhancing property. Further examination of TLT by EPM test revealed that it had no effect on TLT. So both the screening model clarified that it does not have any kind of memory enhancing activity.

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