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THE STUDY ON NEUROPROTECTIVE AGAINST ALCL3 INDUCED TOXICITY. ENHANCED LEARNING AND MEMORY WAS ALLIED TO INGESTION OF EXTRACT IN RATS.

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Abstract:

Objective: The current study aimed at the investigation of the effectiveness of ethanolic and methanolic extract of *Polygonum glabrum* in aluminum chloride-induced Alzheimer's disease in experimental rats.

Methods: The behavioral parameters evaluated by following methods such as Morris water maze test, radial arm maze test, and active avoidance test. Biochemical parameters were also estimated such as acetylcholine and acetylcholine esterase.

Results: *Polygonum glabrum* extract was instituted to be neuroprotective against AlCl3-induced toxicity. Enhanced learning and memory were allied to the ingestion of extract in rats. Al overload, acetylcholinesterase enzyme hyperactivity is responsible for Alzheimer's disease which is neutralized or reduced with treatment of extract, which might be due to the synergistic action of its active constituents. Ethanolic extract was shown slightly higher efficacy as compared to methanolic extract.

Conclusion: Based on these current findings, it is suggested that lowering Aβ is an unproven strategy, and it may be time to refocus on other targets for the treatment of this disease, includingpathological forms of tau.

Introduction:

Neurogenerative Disorders:

Neurodegenerative diseases are heterogeneous grouping of genetic disorders that are designated by means of loss of neuronal function, structure and in general direct to neuronal loss. These diseases may perhaps consequence directly from specific degeneration of neuronal population or not directly from changes in support iveglial cells. These types of diseases are characterized by means of an abnormal proteins buildup or other biological materials build up outside or within the neurons. These aggregations take diverse structures and consequence in neurofabrillary tangles in Alzheimer's disease, glycogen and polyglucosan bodies in Lafora disease, Lewy bodies in Parkinson's disease.

Alzheimer's Disease:

Alzheimer's disease is consideration to be in responsible of around 60% of all mental disorder in older adults or moderately aged [1] and influence in more than of 5 million Americans, a number assessed to augmentation to 7.7million by means of 2030.

Alzheimer's disease is caused because of aggregation of misfolded proteins build up of deposits of fibrillary amyloid in selective areas of central nervous system. Alzheimer's disease leads in memory loss,unusual behavior,personality changes, and loss of the capability to thinking. Early disease exhibits short term memory loss, fail to retain information names and addresses, not able to learn novel information, mood swings, as the circumstance develops, transform become more prominent and persons even forgets way to home.

Frustration, hostility and irritability are typical emotional features exhibited by means of AD patients. Genetic factors are responsible for70% of Alzheimer's disease and the remaining is environmental factor. Most of cases of Alzheimer's disease are late age onset; progresses post to an age of 60.[2]currently, most established treatment strategy of Alzheimer's disease is inhibitors of cholinesterase, inactivate acetylcholinesterase enzyme (AChE) in order to augment the acetylcholine levels in brain. Inhibitors of acetylcholinesterase comprise drugs like rivastigmine, tacrine, galantamine ,donepezil, and memantine. Yet, there is no perfect drug for Alzheimer's disease treatment, besides only relieve the disease symptoms.[3] Herbal medicine gives a substitute option to alter symptoms and development of AD.

1) Collection of plant material:

The aerial parts of plant *Polygonum glabrum* employed for the current in quest was collected from Acharya University, Guntur, India. The plant was authenticated by Dr.v.Satya naryana, Department of Botany. Preparation of Ethanolic and Methanolic Extracts:

The aerial parts of fresh and new medicinal plants collected. To get relieve of adhereddirt; aerial parts were rinsed and cleaned by means of distilled water subsequently blotted thoroughly and dehydrated by means of shade in its consign of sun light. The shadily dried aerial parts were crushed by means of a commercially available mixer. The obtained medicinal plant powder was auxiliary filter to get fine powder and engaged for extraction bymeans of solvents. Almost 100 g of the crushed plant medicinal aerial parts

was kept for Soxhlet extraction by means of 1000 ml solvents, Ethanol and Methanol.

This accuratecycle was repetitive again and again, for hours to a hardly many a days, till the color of the solvent washing out away in the siphon of the soxhlet. The extract was resolute under condensed pressure (P) and stock up in refrigerator proceeding to commencing for advancedutilizations.

2) EXPERIMENTAL ANIMALS:

Rats of Adult swiss Albino were acquired from A.M Reddy memorial college of pharmacy.. The rats were sort out into 6groups at random way, constitutes of 6 rats for each and every set of group. Each rat that weighed in in the midst of 180-200 gm was kept back disconnectedly. The animals were just kept back for 2 days to 7 days to get make use of to the conditions of animal area. They were handling in prescribed laboratory setting of temperature 22±2^{o}c, 70% humidity and cycles of 12 hours light and dark. And animals fed with standard diet of pellet and adequate valve water.

I. Acute Toxicity

Prior to commencing animal study, the acute toxicity study investigations were done to establish effective dose of test compounds. Based on acute toxicity results, the lead extracts were tested in appropriate animal models.[130]

II. In-Vivo Study

The behavioral screening was done by following methods[131-138]

1. Morris water maze test

Morris water maze test was performed for assessment of the retention of working (as a reference) and spatial memory in wistar rats. The water maze contains of a circular tank (150 cm in diameter and 40 cm in height). Water pool was alienated into 4 equally spaced quadrants all along the circumference of the pool. A flee platform (10 cm in diameter) submerged 2 cm beneath the water surface was positioned in NW quadrant. Rats were trained to situate the hidden platform at a fixed spot in NW quadrant. All rats were kept to 1 session of 4 trials per day. During each trial, the animal was positioned in each quadrant to remove quadrant effects. All rats were left in the platform for 30 seconds and then removed and dried by using towel[139]. Rats failing to locate the platform within 60 s were directed to the platform. 24 h after previous training, escape platform was taken away and probe trial was conducted. The cutoff time for animal to swim was set to at 60 s prior to the finish of session. Time elapsed in escaping to the NW quadrant, i.e. escape latency time (ELT) was measured all through the trials of retention.

Fig 1: **Morris water maze test**

1. **Radial arm maze test**

Radial arm maze is a significant tool for study of spatial memory in rats. It was employed asbeing described by Olton (1976) with minor modifications to assess spatial memory deficit in rats. The maze employed is 122 cm in diameter. It contains of 8 chambers and each chamber is 46 cm in length from the center, 16.5 cm in wide and its walls is 37.5 cm in height. The inner arena is 31 cm in diameter. Animals were kept overnight fasting prior to the test. At the start of the test each animal was free in the center of the maze facing the baited arm and was permitted to explore the maze liberally in the first day; not a single record was taken[140]. On the week basis, rats are released in the center of the maze facing the baited arm and set a maximum 6 minutes to locate the food. If 1 animal found the food priorto the finish of time then the watch was stopped and elapsed time is registered. Numbers of entry to the right arm and the wrong arms was as well recorded for week basis.

Fig 2: **Radial arm maze test**

1. **Active avoidance test**

Measurements of Active Avoidance responses were achieved by means of utilizing spaced trials behavioral procedural methods (20-trial sessions daily for every week). A conventional 2-way AA schedule was employed with trials starting at 30 sec intervals time. Each trial begins with a accustomed signal (CS) (broad band noise of 68 dB lasting 7 seconds), followed by an un-conditioned stimulus (US) (foot shock of1.5 mA, 3 seconds time duration) distributed through the floor grids. passage responses through the conditioned stimulus (AA response) ended the conditioned stimulus and not permittedthe beginning of unconditioned stimuli[136]. A reply after the onset of an escape response (unconditioned stimulus)ended both conditioned and unconditioned stimuli.

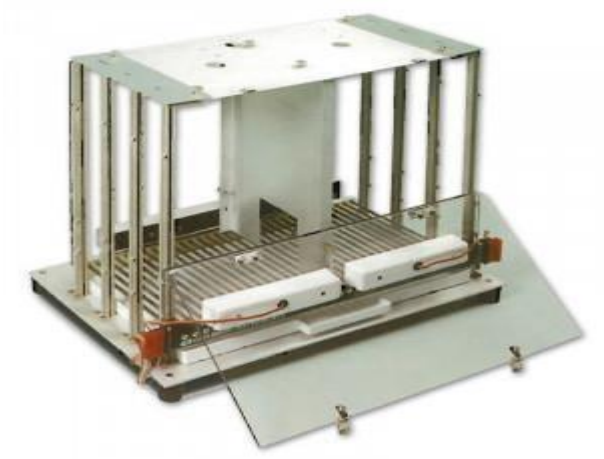

fig 3: **Active avoidance test**

For each behavioral screening model, the animals were divided into 6 groups. Each group constitutes six animals.

All the 3 models carried out for ethanol and methanol extracts separately.

I. Table 5: For ethanol extract grouping is as follows:

Group 1: Normal Group (Tween 80)
Group 2: Disease Control Group-aluminum chloride (300 mg/kg, P.O.)
Group 3: Standard- rivastigmine (0.3mg/kg, I.P.) + aluminum chloride (300 mg/kg, P.O.)
Group 4: Test-I-*Polygonum glabrum* 100 mg/kg + aluminum chloride (300mg/kg, P.O.)
Group 5: Test II-*Polygonum glabrum*200 mg/kg + aluminum chloride (300mg/kg, P.O.)
Group 6: Test III-*Polygonum glabrum*400 mg/kg + aluminum chloride (300mg/kg, P.O.)

The study Duration is 20 day

II. Table 6: For methanol extract grouping is as follows:

Group 1: Normal Group (Tween 80)
Group 2: Disease Control Group-aluminum chloride (300 mg/kg, P.O.)
Group 3: Standard- rivastigmine (0.3mg/kg, I.P.) + aluminum chloride (300 mg/kg, P.O.)
Group 4: Test-I-*Polygonum glabrum* 100 mg/kg + aluminum chloride (300mg/kg, P.O.)
Group 5: Test II-*Polygonum glabrum*200 mg/kg + aluminum chloride (300mg/kg, P.O.)
Group 6: Test III-*Polygonum glabrum*400 mg/kg + aluminum chloride (300mg/kg, P.O.)

The study Duration is 20 days

1. Biochemical analysis

The brain extract of both models were assayed for Acetylcholine, Acetylcholine esterase using standard protocol methods. Forebrain cortex and striatum were dissected by means of bilaterally from each frozen brain and crude mitochondrial portion was prepared from each region as previously illustrated methods. The determination of acetylcholine esteraseactivity was based on degradation of acetyl thiocholine iodide by action of AchE into a subsequent product ultimately binds to5, 5-dithiobis-2-nitrobezoic acid (DTNB), resulting ina yellow color[141]. Kinetics of the enzymatic reactions was followed over 3-5 minutes time at 412 nm wavelength. Values of AchE activity were deduced from the linear portion of the reaction curve and were expressed as units mmol acetyl thiocholine/min/g prot. The protein amount in the rat brain homogenates (forebrain cortex and striatum, ipsi- and contra lateral regions) was measured by the Lowry method by means of bovine serum albumin as reference standard.

2. Statistical analysis of data:

Results were characterized as mean ± S.E.M. The statistical variation amid thegroups was computed in characteristic of ANOVA with mean ± S.E.M. The discrepancy was considered significant if $P< 0.05$.

Results

1) **Percentage yield of ethanolic and methanolic extract of *Polygonum glabrum***

Table 7: Percentage yields of extracts

S no	Solvent	Percentage Yield
1.	Ethanol	12.4%
2.	Methanol	10.5%

2) Phytochemical component observed in ethanolic and methanolic extract of *Polygonum glabrum*

Table 8: Particulars of qualitative phytochemical assessment

S. No.	Test	Methanolic Extract	Ethanolic Extract
1	**Alkaloids**		
	Mayer's test	+	+
	Dragondraffs Test	+	+
	Hager's Test	+	+
	Wagner's test	+	+
2	**Carbohydrates**		
	Mohlish's test	+	+
3	**Reducing Sugars**		
	Fehling's test	+	+
	Benedicts Test	+	+
4	**Saponins**		
	Foam test	-	-
	Forth Test	-	-
5	**Phytosterols**		
	Salkowski Test	+	+
	Liberman Burchard's Test	+	+
6	**Phenolics**		
	Ferric chloride test	-	-
	Lead acetate test	-	-
7	**Tannins**		
	Ferric chloride test	+	+
8	**Flavones and Flavonoids**		
	Lead Acetate Test	+	+
	Alkaline Reagent Test	-	+
9	**Glycosides**		
	Keller killliani test	+	+
10	**Proteins and amino Acids**		
	Ninhydrintest	+	+
	Biuret test	+	+
11	**Terpenoids**		
	Salkowskis Test	-	-
12	**Fixed oils and fats**		
	Spot test	-	-
	Saponification Test	-	-
13	**Gum and Mucilages**		
	Ruthenium Red Solution	+	+

(+)POSITIVE (-) NEGATIVE

3) ACUTE TOXICITY TESTING

The Acute toxicity valuation performed on animals exposed that the *Polygonum glabrum* Methanolic and ethanolic extract was in safe and sound even at amount of 2 gram/kgb.w. The reasonably accurate and precise LD_{50} is may possibly is>2 gram/kg b.w. And hitherto supplementary not any lethality or any class of toxic retort and or moribund class of state was observed till the finish of the extent of investigational research.

Table 9: Acute Toxicity Assessment

S.no.	Code	Toxicity		Time of Death	Observation										
		Onset	Stop		Skin Color	Eyes	Resp	CNS	Tre	Con	Sali	Diah	Sleep	Leth	
1.	MCG	x	X	x	X	x	x	X	x	x	x	X	X	X	
2.	MCG	x	X	x	X	x	x	X	x	x	x	X	X	X	

(TRE-Tremor, CON-Convulsions, SALI- Salivation, Diah - Diarrhea, LET-Lethargy)

× = Negetive Ø = Positive

4) Effect of ethanolic and methanolic Extract of *Polygonum glabrum* OnBehavioral activity by morris water maze test.

In relevant case of the of ethanolic and methanolic extract of *Polygonum glabrum* effectiveness on escape latency time made by means of morris water maze test, the ethanolic and methanolic extract exposed considerably decline in escape latency time. Ethanolic extract is more effective as comparison with methanolic extract.

Table 10: Effect of ethanolic extract of Polygonum glabrum effectiveness on escape latencytime made by means of morris water maze test

GROUPS	Escape Latency Time (Sec)		
	7th day	14th day	21st day
Normal	4.85 ± 0.37	5.23 ± 0.29	5.34 ± 0.68
Disease Control ($AlCl_3$ 300mg/kg)	5.14 ± 0.19[a]	15.86 ± 0.76[a]	22.18 ± 0.72[a]
Standard (Rivastigmine 0.3 mg/kg I.P.)	4.87 ± 0.39	11.72 ± 0.48	7.39 ± 0.64***
EPG (100mg/kg)	4.97 ± 0.60	13.54 ± 0.32	10.22 ± 0.89***
EPG (200 mg/kg)	4.91 ± 0.34	12.98± 0.38	9.43 ± 0.63***
EPG (400 mg/kg)	4.89± 0.29	12.12± 0.27	7.84 ± 0.57***

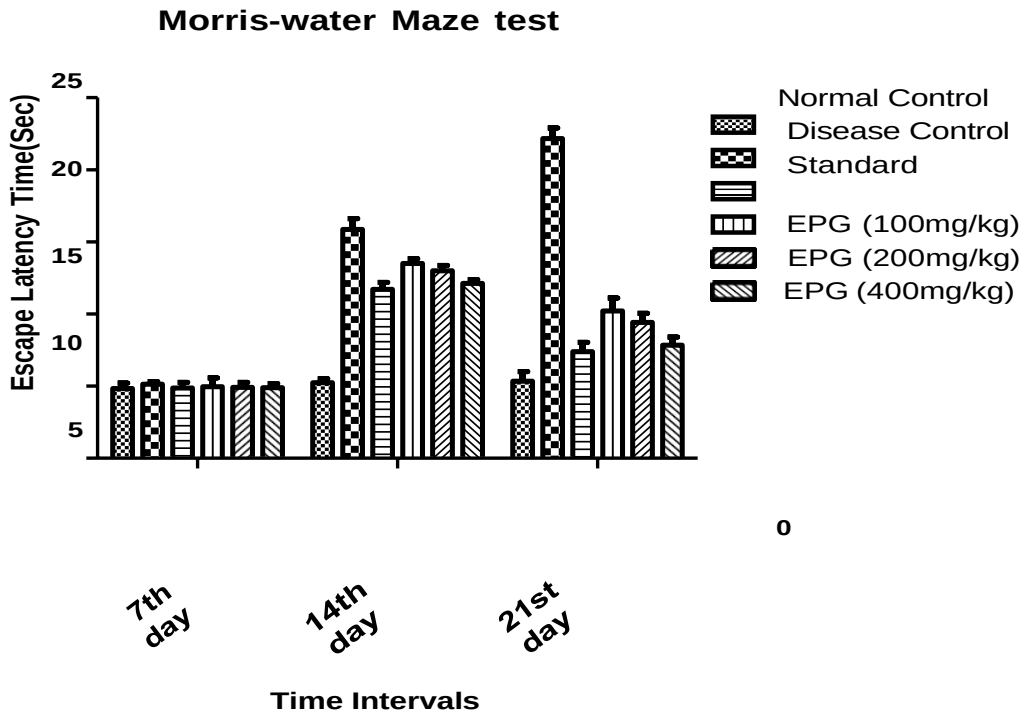

Fig 42: **Effect of ethanolic extract of Polygonum glabrum effectiveness on escape latency time made by means of morris water maze test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test);control was compared with extract and standard treated groups were compared

Table 11: Effect of methanolic extract of Polygonum glabrum effectiveness on escapelatency time made by means of morris water maze test

GROUPS	Escape Latency Time (Sec)		
	7th day	14th day	21st day
Normal	4.87 ± 0.34	5.12 ± 0.27	5.47 ± 0.63
Disease Control ($AlCl_3$ 300mg/kg)	5.32 ± 0.21[a]	16.01 ± 0.79[a]	22.18 ± 0.66[a]
Standard(Rivastigmine 0.3 mg/kg I.P.)	4.89 ± 0.43	12.67 ± 0.48	7.43 ± 0.61***
MPG (100mg/kg)	5.12 ± 0.65	14.72 ± 0.39	11.37 ± 0.77***
MPG (200 mg/kg)	4.93 ± 0.39	13.59± 0.37	10.12 ± 0.54***
MPG (400 mg/kg)	4.91± 0.34	12.82± 0.52	8.45 ± 0.68***

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

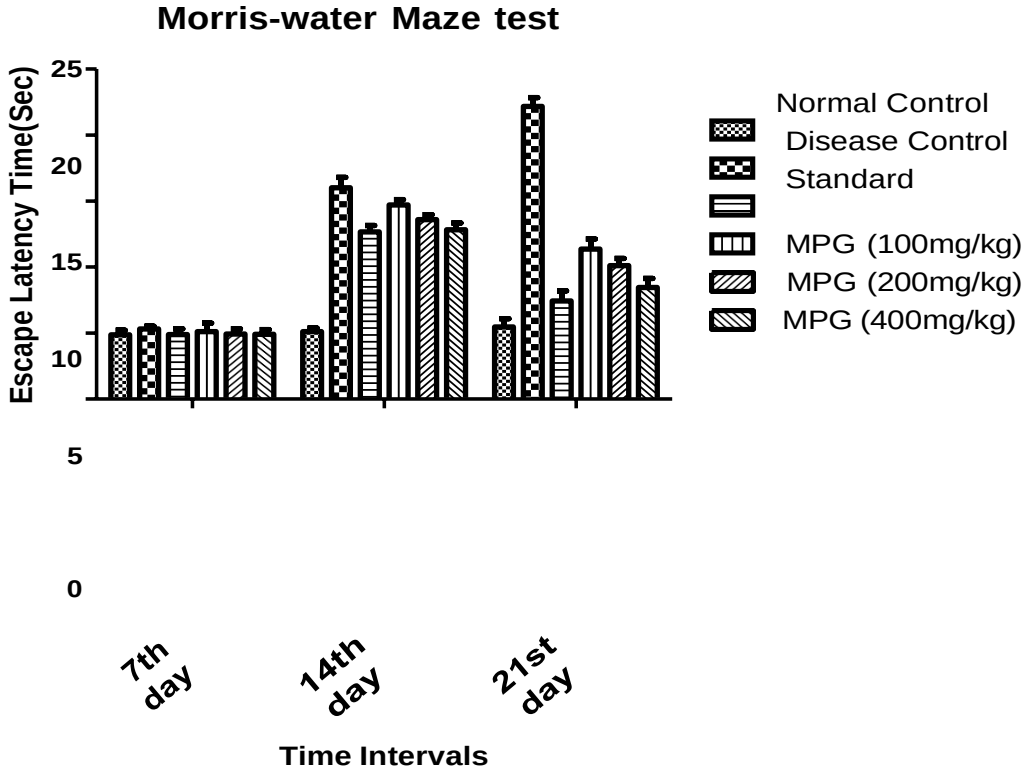

Fig 43: **Effect of methanolic extract of Polygonum glabrum effectiveness on escape latency time made by means of morris water maze test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

In relevant case of the of ethanolic and methanolic extract of Polygonum glabrum effectiveness on time lapse by means of radial arm maze test, the ethanolic and methanolic extract exposed considerably decline in time lapse. Ethanolic extract is more effective as comparison with methanolic extract.

Table 12: Effect of ethanolic extract of Polygonum glabrum effectiveness on Time lapse made by means of Radial arm maze test

GROUPS	Time lapse (Sec)		
	7th day	**14th day**	**21st day**
Normal	112 ± 1.42	120 ± 1.36	124 ± 1.66
Disease Control ($AlCl_3$ 300mg/kg)	185 ± 1.36	224 ± 1.21	273 ± 1.52
Standard(Rivastigmine 0.3 mg/kg I.P.)	145± 1.47	132 ± 1.32	128 ± 1.41***
EPG (100mg/kg)	161 ± 1.57	154 ± 1.83	143 ± 1.67***
EPG (200 mg/kg)	152 ± 1.29	145± 1.75	136 ± 1.84***
EPG (400 mg/kg)	149± 1.22	138± 1.59	129 ± 1.87***

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

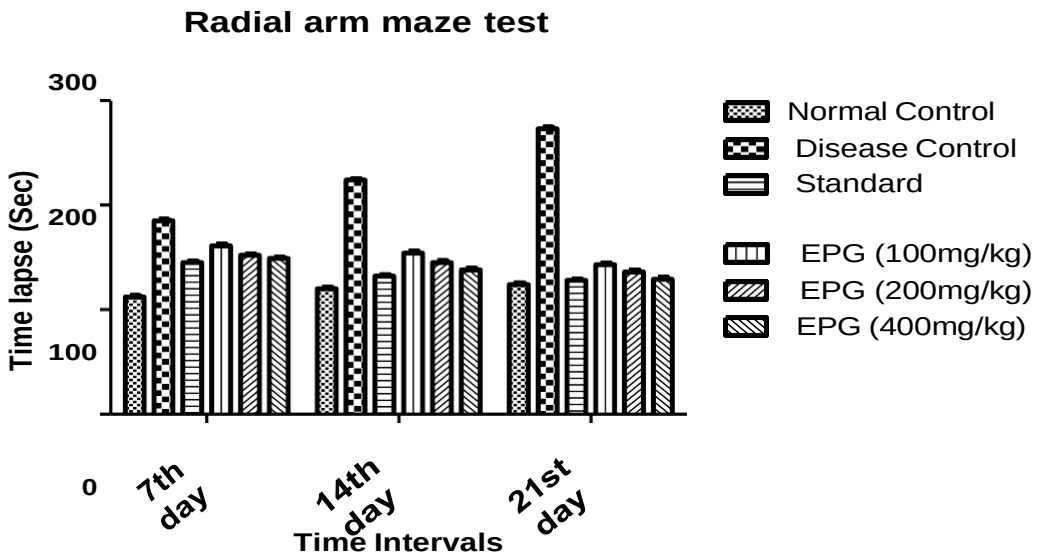

Fig 44: **Effect of ethanolic extract of Polygonum glabrum effectiveness on Time lapse made by means of Radial arm maze test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

Table 13: Effect of methanolic extract of Polygonum glabrum effectiveness on Time lapse made by means of Radial arm maze test

GROUPS	Time lapse (Sec)		
	7th day	14th day	21st day
Normal	114 ± 1.23	118 ± 1.42	128± 1.57
Disease Control ($AlCl_3$ 300mg/kg)	191 ± 1.45	232 ± 1.37	281 ± 1.49
Standard(Rivastigmine 0.3 mg/kg I.P.)	151± 1.52	137 ± 1.41	130 ± 1.55***
MPG (100mg/kg)	167 ± 1.63	160 ± 1.77	151 ± 1.59***
MPG (200 mg/kg)	114 ± 1.23	118 ± 1.42	128± 1.57
MPG (400 mg/kg)	191 ± 1.45	232 ± 1.37	281 ± 1.49

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

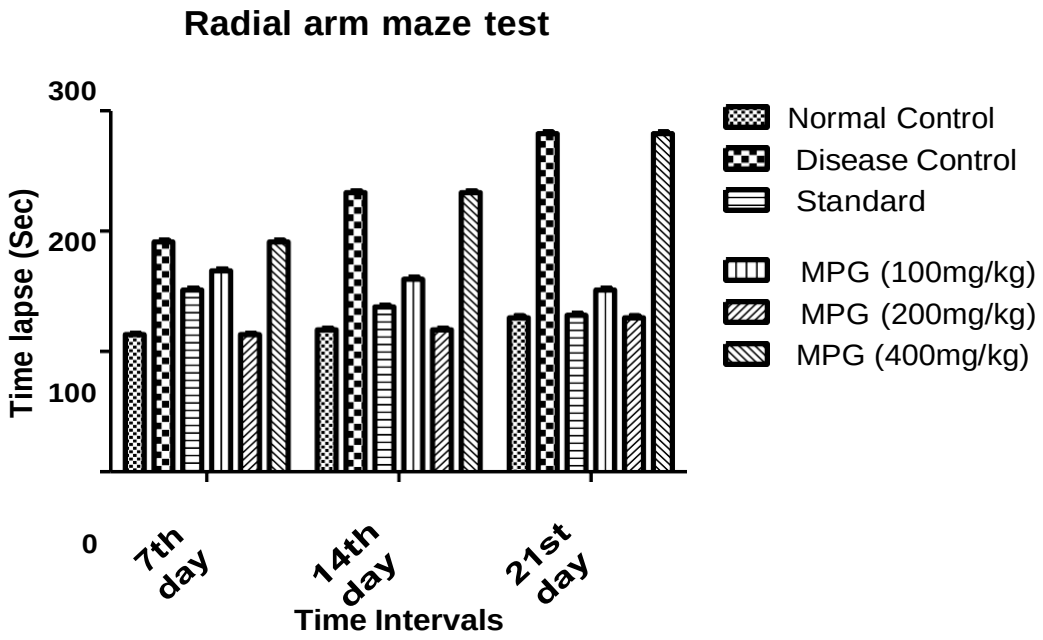

Fig 45: **Effect of methanolic extract of *Polygonum glabrum* effectiveness on Time lapse made by means of Radial arm maze test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.In relevant case of the of ethanolic and methanolic extract of *Polygonum glabrum* effectiveness on crossing responses made by means of active avoidance test, the ethanolic and methanolic extract exposed considerably increase in crossing responses. Ethanolic extract is more effective as comparison with methanolic extract.

Table 14: Effect of ethanolic extract of *Polygonum glabrum* effectiveness made by means of active avoidance test

GROUPS	Active avoidance		
	7th day	**14th day**	**21st day**
Normal	25 ± 0.31	30 ± 0.43	32± 0.59
Disease Control ($AlCl_3$ 300mg/kg)	16± 0.27	12 ± 0.36	7 ± 0.39
Standard(Rivastigmine 0.3 mg/kg I.P.)	23± 0.44	26 ± 0.61	30± 0.72***

EPG (100mg/kg)	18 ± 0.48	20 ± 0.65	23 ± 0.51
EPG (200 mg/kg)	20 ± 0.33	22± 0.49	26 ± 0.46
EPG (400 mg/kg)	22± 0.57	24± 0.59	28 ± 0.63

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

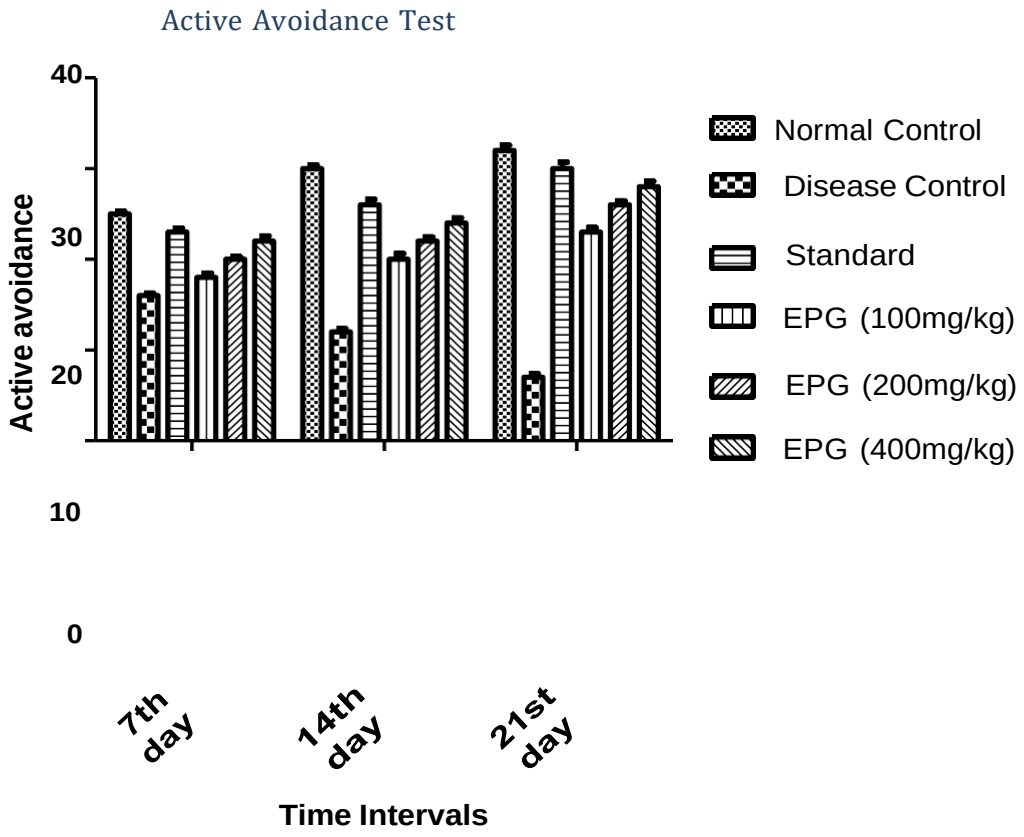

Fig 46: **Effect of ethanolic extract of *Polygonum glabrum* effectiveness made by means of active avoidance test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

Table 15: Effect of methanolic extract of *Polygonum glabrum* effectiveness made by means of active avoidance test

GROUPS	Active avoidance		
	7th day	14th day	21st day
Normal	24 ± 0.46	28 ± 0.39	30± 0.61
Disease Control ($AlCl_3$ 300mg/kg)	15± 0.24	11 ± 0.41	6 ± 0.32
Standard(Rivastigmine 0.3 mg/kg I.P.)	21± 0.42	23 ± 0.66	28± 0.48***
MPG (100mg/kg)	16 ± 0.56	18 ± 0.72	21 ± 0.49
MPG (200 mg/kg)	18 ± 0.66	20± 0.51	24 ± 0.57
MPG (400 mg/kg)	20± 0.63	22± 0.54	26 ± 0.61

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

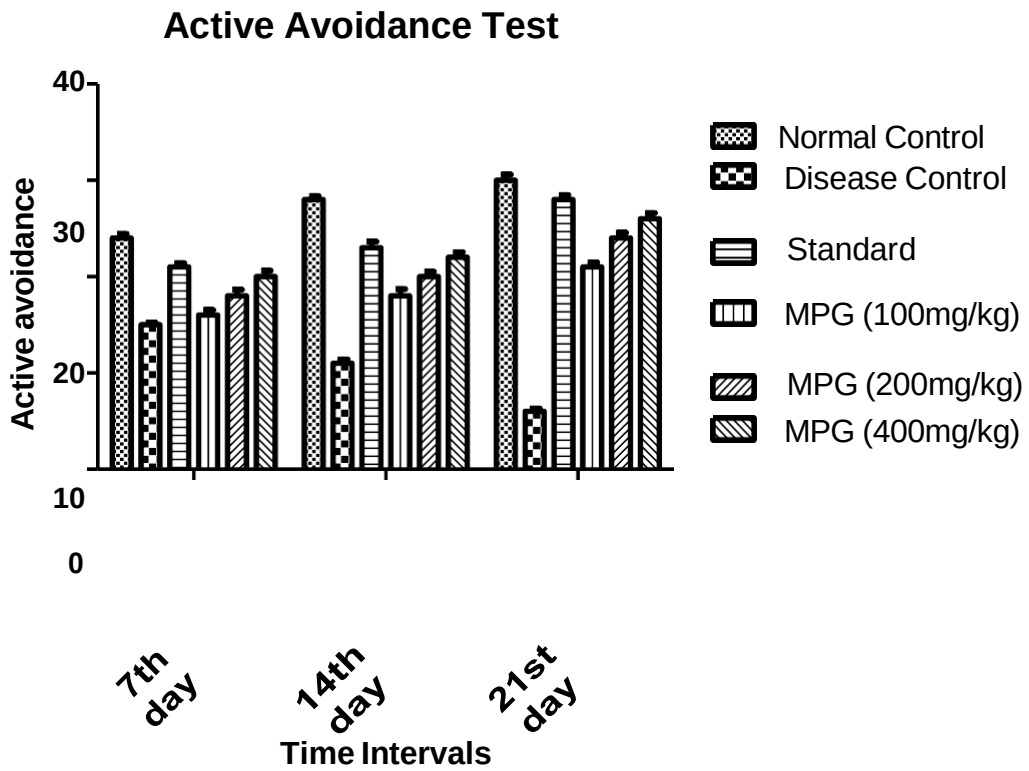

Fig 47: **Effect of methanolic extract of Polygonum glabrum effectiveness made by means of active avoidance test**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared.

In relevant case of the of ethanolic and methanolic extract of Polygonum glabrum effectiveness on levels of Ach and AchE made by means of biochemical estimations, the ethanolic

and methanolic extract exposed considerably increase in Ach and decline in AchE. Ethanolic extract is more effective as comparison with methanolic extract.

Table 16: Effect of ethanolic extract of Polygonum glabrum effectiveness acetylcholine and acetylcholineestersase levels

GROUPS	Ach (µmol/mg protein)	AchE(unit/mg protein)
Normal	5.65 ± 0.15	0.54 ± 0.04
Disease Control	0.87± 0.05	0.82 ± 0.02
($AlCl_3$ 300mg/kg)		
Standard (Rivastigmine 0.3 mg/kg I.P.)	5.4± 0.17	0.56 ± 0.03
EPG (100mg/kg)	2.7 ± 0.23	0.75 ± 0.05
EPG (200 mg/kg)	3.4 ± 0.21	0.63± 0.04
EPG (400 mg/kg)	4.9± 0.29	0.59± 0.06

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared

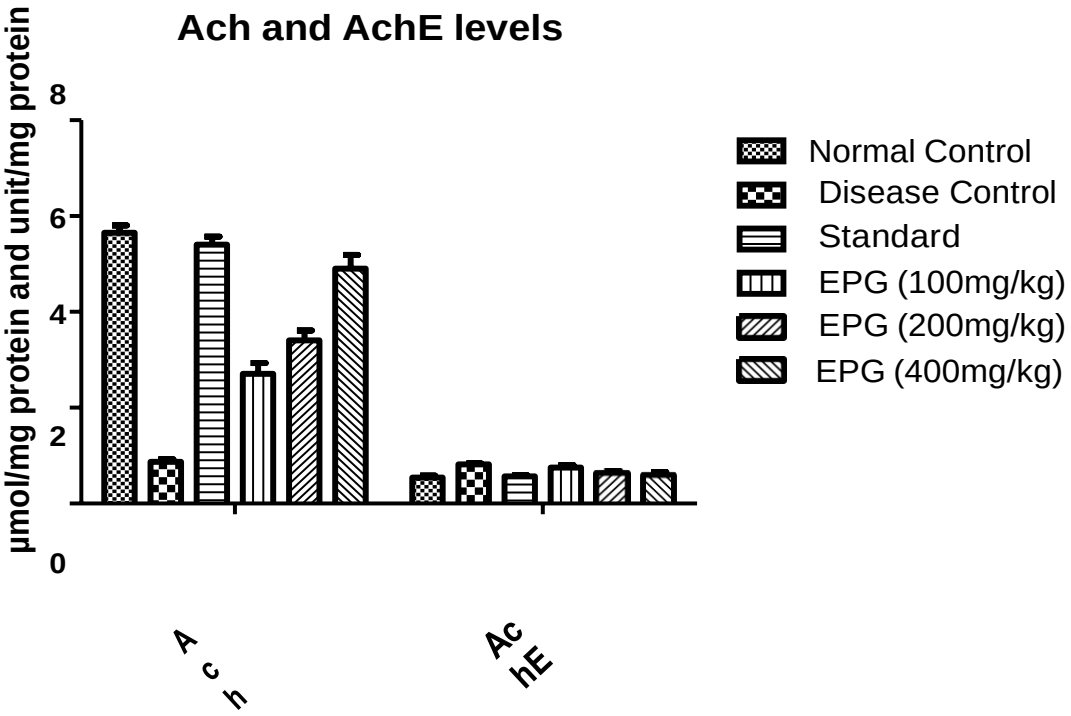

Fig 48: **Effect of ethanolic extract of Polygonum glabrum effectiveness acetyl choline and acetyl choline estersase levels**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated groups were compared

Table 17: Effect of methanolic extract of Polygonum glabrum effectiveness acetylcholine and acetylcholine estersase levels

GROUPS	Ach (µmol/mg protein)	AchE(unit/mg protein)
Normal	5.59 ± 0.12	0.57 ± 0.05
Disease Control ($AlCl_3$ 300mg/kg)	0.85± 0.03	0.85 ± 0.03
Standard (Rivastigmine 0.3 mg/kg I.P.)	5.37± 0.17	0.58± 0.02
MPG (100mg/kg)	2.5 ± 0.2	0.77 ± 0.06
MPG (200 mg/kg)	3.2 ± 0.18	0.66± 0.03
MPG (400 mg/kg)	4.7± 0.25	0.61± 0.05

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test); control was compared with extract and standard treated

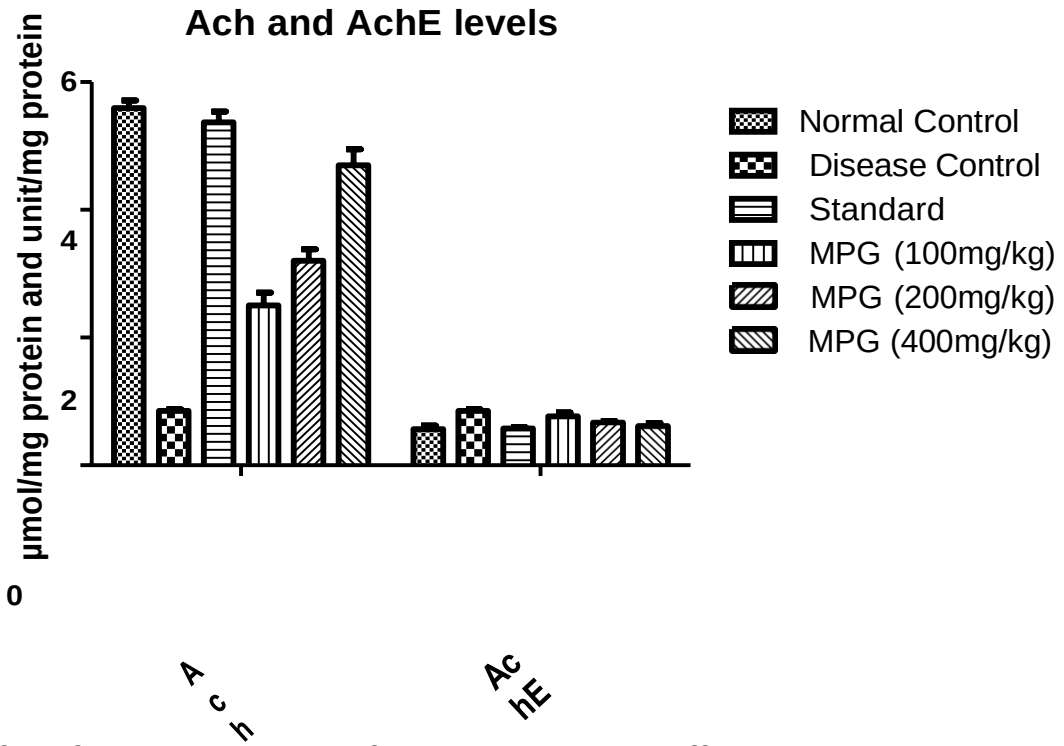

Fig 49: **Effect of methanolic extract of Polygonum glabrum effectiveness acetylcholine and acetylcholine estersase levels**

Data represented as mean ± S.E.M values of 6 animals each. *p<0.05, **p<0.01 (Dunnett t-test);control was compared with extract and standard treated.

Discussions:

Results obtained from water maze test demonstrated dependable lessen in the time required to find the platform. The aluminum treated rats showed high fluctuation in the time required toreach the platform from one day to another. The declining rate of the time needed to reach the platform was relatively steady for the control, standard and group treated with extracts. These outcomes guide us to guesstimate that extract may exert its effect by means of managing the lessening rate of time. The fluctuation in the time required to find the platform showed by means of AlCl3 treated rats was lessened by means of the ingestion of PG. Suggesting that, although theeffect of PG was not revealed by means of monitoring the time needed to find the platform, yet,it was demonstrated that PG effect was resulted to the waning rate in the time and reverting the fluctuation produced by means of AlCl3. A high correlation was found between the radial maze test and the avoidance response in PG treated groups. The correlations specify that both radial arm maze and active avoidance test possibly will assess memory dispensation in a definite regionof rat's brain. As a part of model of active avoidance (AA), demonstrated 2-fold lessening correct reactions from the 7th to the 21st day of assessment in AlCl3-treated animals as compared with the group of control.

Aluminium provoke stable and reproducible depression of AA response, meaning, Al damages rat cognitive functioning. These consequences, all along with the obtained decreased AchE activity suggest that Al exerts its toxic effects by altering transmission of cholinergic eventually imitated in neurobehavioral deficits[139]. Aluminium is not only a selective cholinergic neurotoxin and possibly will also affect non cholinergic neurons concerned in spatial learning. Earlier studies have exposed that attention and spatial learning were disturb inthe Al-treated rats[139-141].

The AD rats as well shown a significant lessen in Ach levels along with an elevation in AchE activity. Rivastigmine was used as standardized drug as it is the only proven pharmacological therapy for the symptomatic treatment of AD[142]. Treatment of AD rats with rivastigmine as a protective or therapeutic agent led to an improvement in the oxidative stress status, as represented by a significant increase in the levels of activity in the activity cages and brain Ach levels as well as a significant decrease in the results of the Radial arm maze and brain AchE levels when compared with the AD-induced groups of rats.

The efficacy of rivastigmine in the treatment of dementia has also been studied in patients with moderate-to-severe AD living in long-term care facilities. Treatment with Rivastigmine enhancescognition, behavior of daily living, and global function[143]. Rivastigmine binds to the AChE receptor in a pseudo irreversible way; the acetylmoiety of AChE is dissociated quickly but the carbamyl moiety remains binds for a few times longer. Rivastigmineis metabolized by means of the synapse rather than by means of hepaticcytochrome enzymes[144]. The investigation by Andinet al.[145]offers the first proof that the system of glutamatergic is altered after AChE inhibition by means of rivastigmine, adiscovery probable to be of significance for the clinicaleffects. Rivastigmine may act through the glutameric mechanism, diminishing the oxidative stress

and restoring brain antioxidant protection[146-148].

Rivastigmine protects behavioral alteration; reinstate antioxidant defense enzymes and advances mitochondrial enzyme effect induced neurotocixity[149]. It was found that EPG was associated with lessened anxiety in rats.

Conclusion:

Polygonum glabrum extract was instituted to be neuroprotective against $AlCl_3$ induced toxicity. Enhanced learning and memory was allied to ingestion of extract in rats. Al overload, AChE hyperactivity are responsible for alzheimers disease which are neutralized or reduced withtreatment of extract, which might be due to the synergistic action of its active constituents. Ethanolic extract was shown slightly higher efficacy as compared to methanolic extract. However extensive research is needed to validate the anti-alzheimeric effect of extract active components against a variety of models of AD, prior to entering into the clinical trials.

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