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A STUDY ON NOOTROPIC ACTIVITY OF WHOLE PLANT EXTRACT OF *PERGULARIA DAEMIA* IN MICE AND RATS

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ABSTRACT
Nootropic activity was evaluated with the aqueous extract of whole plant of Pergularia daemia (AQEWPPD) on exteroceptive behavior & interoceptive behavior by using shock box & shuttle box. Albino mice and Rats were administered with different doses of AQEWPPD low (100mg /kg), Medium(200mg/kg) and High (400mg/kg) daily per oral. The results were compared to Piracetam (100mg/kg p.o) which served as a standard drug. The buzzer (conditioned stimulus) and an electric shock (unconditioned stimulus, 30 v and 0.5 sec) were used in the Shuttle box. The plant extracts have shown statistically significant improvement in memory retention and learning when compared to standard. The study shows that Pergularia daemia extract has dose-dependent cholinergic activity to improve memory. In light of the above, it may be worthwhile to explore the potential of Pergularia daemia in the management of Dementia patients.

KEYWORDS: Nootropics, Dementia, Pergularia daemia, Shock box, Shuttle box.

INTRODUCTION

In 1972 Corneliu Giurgea coined the term nootropic to describe a new class of molecules that selectively acted towards the higher-level integrative activity of the brain. Nootropics are cognitive enhancer drugs or supplements that improve the mental action or process of acquiring knowledge, memory, executive function, judgment, reasoning, problem solving and decision making. Nootropics can be divided into three categories: Synthetic compounds, dietary supplements and prescription drugs.

Prescription drugs like stimulants are suggested for attention deficit hyperactivity disorder (ADHD) or donepezil for Alzheimer's. Problems with memory, thinking and behaviour are caused by Alzheimer's disease. Nootropics act probably by altering the neurotransmitter, hormone and enzyme levels that are present in the brain by increasing the oxygen supply or nerve growth stimulation of brains. Herbs may increase the level of acetylcholine and also increase blood flow towards the brain. The class of drugs that's share pyrrolidone nucleus such as piracetam is a class of Racetams which is considered as nootropics.

There is a lot of research that has been done for the treatment of Alzheimer's disease and the other brain-related disease after doing the literature survey of different herbal drugs whole plant of *Pergularia daemia*.

Phytoconstituents like flavonoids, saponins, alkaloids, steroidal triterpenoid, tannins and glycosides are already reported for this nootropic activity. Some of the phytoconstituents mentioned above are present in *Pergularia daemia*. can be accounted for the observed nootropic action.

METHODOLOGY

A. Exteroceptive Behavior Model

1. Passive avoidance paradigm

Group of adult Swiss albino mice 24-32 g, each consisting of 6 animals were divided into following groups and animals were fasted overnight prior to the test but water was supplied *ablibitum*

Group I: Normal control (distilled water 10 ml/kg, p.o.)
Group II: Phenytoin alone (25 mg/kg, p.o.) once daily for 14 days.
Group III: Piracetam (200 mg/kg, p.o.) + once daily for 7 days.
Group IV: AQEWPPD (low dose, 100 mg/kg, p.o.) + once daily for 7 days
Group V: AQEWPPD (medium dose, 200 mg/kg, p.o.) + once daily for 7 days.
Group VI: AQEWPPD (high dose, 400 mg/kg, p.o.) + once daily for 7 days.

Experimental procedure

Passive avoidance task is a method widely used for screening drugs affecting learning and memory. The method described by Papazova et al. (1994) was modified as follows. An inverted petridish placed in the centre of the grid floor of a continuous avoidance apparatus (Techno, Lucknow) was used. The petridish served as the shock free zone (SFZ). Mice were placed in the SFZ and up on stepping down from the SFZ were given an electrical shock (20V) through the grid floor. Animals were trained to remain on the SFZ for at least 60 sec and mice which did not meet these criteria in five trials were rejected. Observations were made for acquisition i.e. the number of trials required to reach the learning criteria and for retention of learning for 10 min at 2 h and 24 h post training. The following retention parameters like step-down latency (SDL) in sec, step-down error (SDE) as the number of times the animal stepped down from the SFZ and the time spent in the shock zone (TSZ) in sec are noted.

Treatment schedule

The memory-impairing dose of phenytoin 25 mg/kg was administrated daily once for 14 days and the selected doses of AQEWPPD for 7 days i.e. on 8th to 14th day. On 14th day after 1 hh of administration of standard and extracts the parameters mentioned above were noted. Group I was maintained as normal control which was given with distilled water (10 ml/kg, p.o), Group II, III, IV, V, and VI group with phenytoin (25 mg/kg, p.o) daily once for 14 days. Additionally, Group III with piracetam (200 mg/kg, p.o) which served as standard, Groups IV, V, VI, Group were treated with different doses of AQEWPPPD (100, 200 and 400 mg/kg p.o) respectively once daily for 14 days as mentioned above.

Fig. No. 1: Passive avoidance paradigm (Shock Box).

2. Active avoidance paradigm (Shuttle Box)

Groups of adult male albino rats 150-180 g each consisting of 6 animals were divided into following groups and animals were fasted overnight prior to the test but water was supplied *ad libitum*

Group I: Normal control (distilled water 10 ml/kg, p.o) once daily for 14 days.

Group II: Piracetam (200 mg/kg, p.o) once daily for 14 days.

Group III: AQEWPPD (low dose, 100 mg/kg, p.o) once daily for 14 days.

Group IV: AQEWPPD (medium dose, 200 mg/kg, p.o) once daily for 14 days.

Group V: AQEWPPD (high dose, 400 mg/kg, p.o) once daily for 14 days.

Experimental procedure

All groups of rats were trained up to 100% learning criterion of active avoidance response. During the training period, each rat was placed in one of the two chambers of the Sidman box and after 5 sec the buzzer (conditioned stimulus, CS) was sounded for 2 sec, followed by an electric shock (unconditioned stimulus, UCS;30v,0.5 sec) through the grid floor. Thereafter, a rest pause of 180 sec allowed. If the rat jumped within the CS duration to the unelectrified safe box, so as to avoid the USC, it will be allowed to rest there for next 30 sec. However, if the rat did not show the avoidance response, immediately removed from the shock chamber after 180 sec and was initiated for the next trial. The rats were given 10 trials daily until they reached the 100% criterion of active avoidance response. After an interval of 15 days rats were subjected to a repeat test with treatment of different doses of the extracts in order to assess the retention of the previously learned active avoidance response. The nootropic activity of the extracts was compared with standard drug.

Treatment schedule

Group I was maintained as normal control which was given with distilled water only daily once for 14 days. Group II with Piracetam (200 mg/kg, p.o) which served as standard. Groups III, IV, V Groups were treated with different doses of AQEWPPD (100, 200 and 400 mg/kg p.o) respectively once daily for 14 days.

Fig. No. 2: Active avoidance Paradigam (Shuttle Box).

RESULT

Table No. 1: Effect of AQEWPPD on Passive avoidance learning and retention (Shock box model) in mice (mean ±SEM).

	Step Down Latency (SDL) in sec											
	Normal control		Toxicant Phenytoin 25 mg/kg		Standard (Piracetam) 200 mg/kg		AQEPD 100 mg/kg		AQEPD 200 mg/kg		AQEPD 400 mg/kg	
	Retention at		Retention at		Retention at		Retention at		Retention at		Retention at	
	2h	24h	2h	24h	2h	24h	2h	24h	2h	24h	2h	24h
H	108	187	4	47	190	385	276	430	280	550	280	600
B	17	120	79	120	250	600	161	339	219	500	210	450
T	10	154	40	200	188	500	104	280	175	480	195	429
HB	45	188	5	97	279	498	180	330	198	418	212	467
BT	60	158	30	102	180	490	195	390	180	390	180	433
HT	30	120	46	120	190	530	175	320	205	400	250	480
mean ±SEM	**45 ± 14.64**	**154.5 ± 12.34**	**34 ± 11.49**	**114.3 ± 20.32**	**212.8 ± 16.83*** **	**500.5 ± 28.42*** **	**181.83 ± 22.79*** **	**348.16 ± 21.83*** **	**209.5 ± 15.57*** **	**456.3 ± 26.00*** **	**221.6 ± 15.14*** **	**476.5 ± 25.95*** **
Number of Step Down Error (SDE)												
H	5	2	11	9	4	3	4	3	1	2	2	0
B	9	5	15	11	0	0	4	3	2	3	3	2
T	12	6	7	5	2	1	6	5	4	3	3	2
HB	6	2	15	10	3	2	4	3	4	2	2	2
BT	10	4	14	9	3	2	4	3	5	5	4	3
HT	6	2	14	11	2	1	5	4	4	3	2	2
mean ±SEM	**8 ± 1.12**	**3.5 ± 0.71**	**12.66 ± 1.28**	**9.16 ± 0.90**	**2.33 ± 0.55*** **	**1.55 ± 0.42*** **	**4.5 ± 0.34*** **	**3.5 ± 0.34*** **	**3.33 ± 0.61*** **	**3 ± 0.44*** **	**2.66 ± 0.33*** **	**1.83 ± 0.40*** **
Time Spent in Shock Zone (TSZ) in sec												
H	23	11	38	19	10	1	15	9	12	4	8	0
B	33	15	17	9	5	0	12	5	14	5	10	3
T	18	9	22	11	12	6	32	13	20	9	12	4
HB	20	9	25	12	9	2	18	6	16	6	13	5
BT	18	7	22	13	9	3	17	6	18	7	15	7
HT	22	10	19	17	6	2	23	11	14	4	9	3
mean ±SEM	**22.16 ± 2.290**	**10.16 ± 1.108**	**23.8 ± 3.04**	**13.50 ± 1.54**	**8.5 ± 1.057*** **	**2.33 ± 0.84*** **	**19.5 ± 2.90 ns**	**8.33 ± 1.30***	**15.66 ± 1.20***	**5.83 ± 0.79*** **	**11.16 ± 1.078*** **	**3.66 ± 0.95*** **

Table No. 2: Effect of AQEWPPD on Passive avoidance learning and retention (Shock box model) in mice (mean ±SEM).

Treatment	Dose ml, mg/kg	SDL Trial	Step Down Latency (SDL)		Step Down Error (SDE)		Time Spent in Shock Zone (TSZ) in sec	
			Learning	Retention	Learning	Retention	Learning	Retention
Normal control	10 ml p,o.	1.75	**45 ± 14.64**	**154.5 ± 12.34**	**8 ± 1.12**	**3.5 ± 0.71**	**22.16 ± 2.29**	**10.16 ± 1.108**
Toxicant (Phenytoin)	25 mg p.o.	2.75	**34 ± 11.49**	**114.3 ± 20.32**	**12.66 ± 1.28**	**9.16 ± 0.90**	**23.8 ± 3.04**	**13.50 ± 1.544**
Standard (Piracetam)	200 mg p.o.	2.25	**212.8 ±16.83*** **	**500.5 ± 28.42*** **	**2.33 ± 0.55*** **	**1.55 ± 0.42*** **	**8.5 ± 1.057*** **	**2.33 ± 0.8433*** **
AQEPD	100 mg p.o.	3.75	**181.83 ± 22.79*** **	**348.16 ±21.83*** **	**4.5 ± 0.34*** **	**3.5 ± 0.34*** **	**19.5 ± 2.90*** **	**8.33 ± 1.308***
AQEPD	200 mg p.o.	1.25	**209.5 ± 15.57*** **	**456.3 ± 26.00*** **	**3.33 ± 0.61*** **	**3 ± 0.44*** **	**15.66 ± 1.20***	**5.83 ± 0.7923*** **
AQEPD	400 mg p.o.	2.25	**221.6 ± 15.14*** **	**476.5 ± 25.95*** **	**2.66 ± 0.33*** **	**1.83 ± 0.40*** **	**11.16 ± 1.07*** **	**3.66 ± 0.9545*** **

n=6, Significant at P<0.05*, 0.01** and 0.001***, ns=not significant.

AQEPD - Aqueous extract of whole plant of *Pergularia daemia*

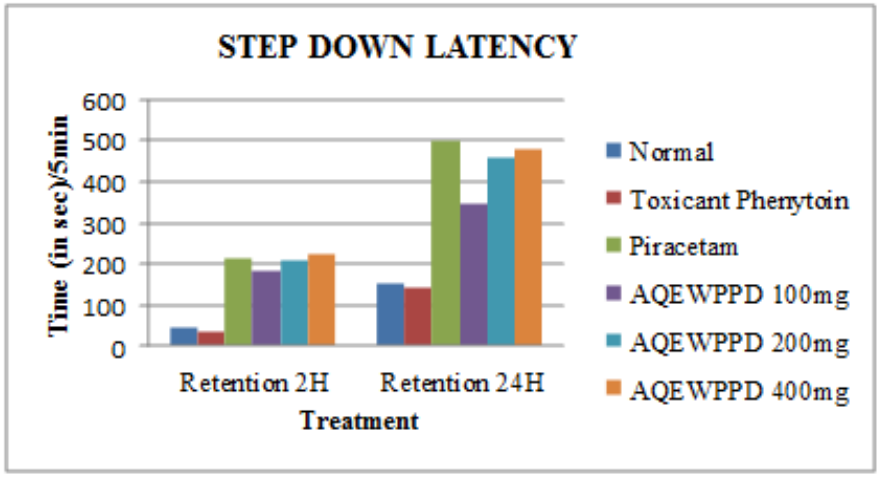

Fig. No. 3: Effect of AQEWPPD on Step- Down latency (SDL) on 15th day using shock box model in mice (mean ± SEM).

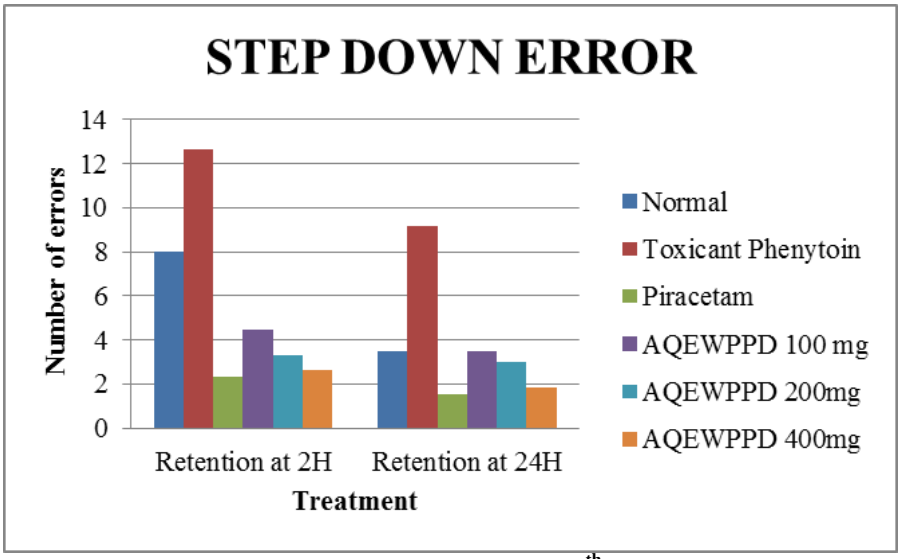

Fig. No. 4: Effect of AQEWPPD on Step – Down Error (STE) on 15th day using Shock box model in mice (mean ±SEM).

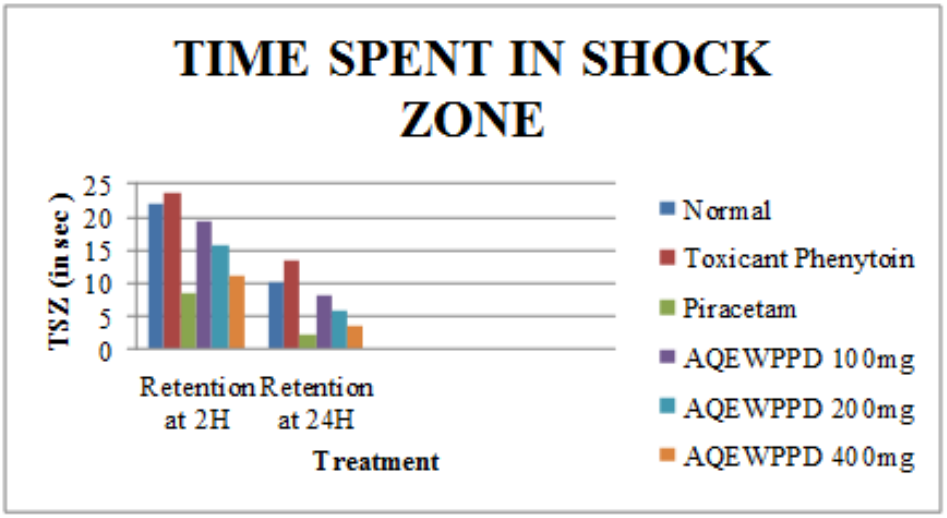

Fig. No. 5: Effect of AQEWPPD on Time spent in shock zone error (TSZ) on 15th day using Shock box model in mice (mean ±SEM).

Table No. 3: Effect of AQEWPPD on Active Avoidance learning and retention (Shuttle box) model in rats (mean ±SEM)

Animals	Learning on 1st day									
	Normal		Standard (Piracetam) 200 mg/kg		AQEWPPD 100 mg/kg		AQEWPPD 200 mg/kg		AQEWPPD 400 mg/kg	
	No. of Shocks	TSZ (sec)	No. of Shocks	TSZ (sec)	No. of Shocks	TSZ (sec)	No. of Shocks	TSZ (sec)	No. of Shocks	TSZ (sec)
H	5	25	3	15	4	22	3	15	4	15
B	6	27	2	14	5	24	5	21	3	1
T	4	24	4	16	6	25	4	18	2	210
HB	5	26	5	12	3	16	6	23	5	19
BT	6	23	4	13	5	18	3	17	3	13
HT	5	28	3	12	6	28	4	19	4	18
mean ±SEM	**5.16 ± 0.307**	**25.5 ± 0.763**	**3.5 ± 0.428****	**13.66 ± 0.66*****	**4.83 ± 0.4773^{ns}**	**22.16 ± 1.833 ^{ns}**	**4.16 ± 0.477***	**18.83 ± 1.167****	**3.5 ± 0.428****	**14.5 ± 1.432*****
Learning on 15th day										
H	2	12	2	2	2	7	2	5	2	3
B	3	10	3	5	2	7	2	2	2	2
T	4	23	2	3	3	8	2	2	1	1
HB	3	23	1	1	2	8	2	2	3	5
BT	3	16	2	2	3	12	3	8	2	2
HT	2	8	1	1	2	15	1	2	1	1
mean ±SEM	**2.83 ± 0.307**	**15.33 ± 2.654**	**1.83 ± 0.307****	**2.33 ± 0.61*****	**2.33 ± 0.210 ^{ns}**	**7.83 ± 0.945****	**2 ± 0.258***	**3.5 ± 1.025 *****	**1.83 ± 0.307****	**2.5 ± 0.614*****
Learning on 16th day										
H	1	2	0	0	0	0	1	1	0	0
B	2	15	0	0	0	0	1	1	1	2
T	3	15	0	0	1	2	1	1	0	0
HB	2	12	0	0	1	3	0	0	0	0
BT	2	7	0	0	1	5	0	0	0	0
HT	1	5	0	0	1	2	0	0	0	0
mean ±SEM	**1.83 ± 0.307**	**9.33 ± 2.231**	**0 ± 0.0****	**0 ± 0.0*****	**0.66 ± 0.210***	**2 ± 0.774*****	**0.5 ± 0.223***	**0.5 ± 0.223*****	**0.16 ± 0.33****	**0.33 ± 0.333*****

n=6, Significant at P<0.05*, 0.01** and 0.001***, ns=not significant.
AQEPD-Aqueous extract of whole plant of *Pergularia daemia*

Table No. 4 Effect of AQEWPPD on Active Avoidance learning and retention (Shuttle box) model in rats (mean ±SEM)

Treatment	Dose ml, mg/kg	Number of Shocks			Time Spent In Shock Zone		
		Learning (acquisition)	Relearning	Retention	Learning (acquisition) (Sec)	Relearning (Sec)	Retention (Sec)
		1st day	15th day	16th day	1st day	15th day	16th day
Control(vehicle)	10 ml p.o	**5.16 ± 0.307**	**2.83 ± 0.307**	**1.83 ± 0.307**	**25.5 ± 0.763**	**15.33 ± 2.654**	**9.33 ± 2.231**
Piracetam	200 mg p.o	**3.5 ± 0.428****	**1.83 ± 0.307****	**0 ± 0.0****	**13.66 ± 0.66*****	**2.33 ± 0.6146*****	**0 ± 0.0*****
AQEPD	100 mg p.o	**4.83 ± 0.4773^{ns}**	**2.33 ± 0.210 ^{ns}**	**0.66 ± 0.210***	**22.16 ± 1.833 ^{ns}**	**7.83 ± 0.945****	**2 ± 0.774*****
AQEPD	200 mg p.o	**4.16 ± 0.477***	**2 ± 0.258***	**0.5 ± 0.223***	**18.83 ± 1.167****	**3.5 ± 1.025 *****	**0.5 ± 0.223*****
AQEPD	400 mg p.o	**3.5 ± 0.428****	**1.83 ± 0.307****	**0.16 ± 0.33****	**14.5 ± 1.432*****	**2.5 ± 0.614*****	**0.33 ± 0.333*****

n=6, Significant at P<0.05*, 0.01** and 0.001***, ns=not significant.
AQEPD - Aqueous extract of whole plant of *Pergularia daemia*

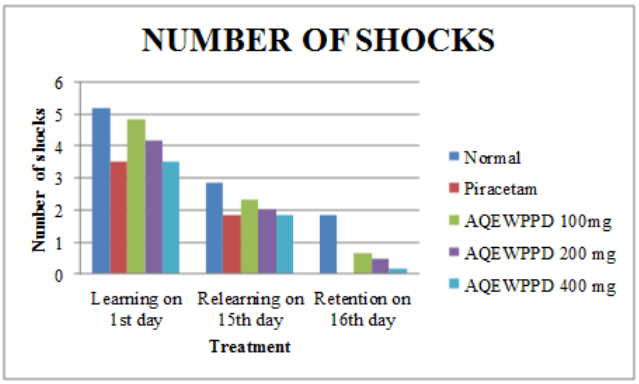

Fig. No. 6: Effect of AQEWPPD on Active Avoidance learning and retention (Shuttle box) model in rats (mean ±SEM)

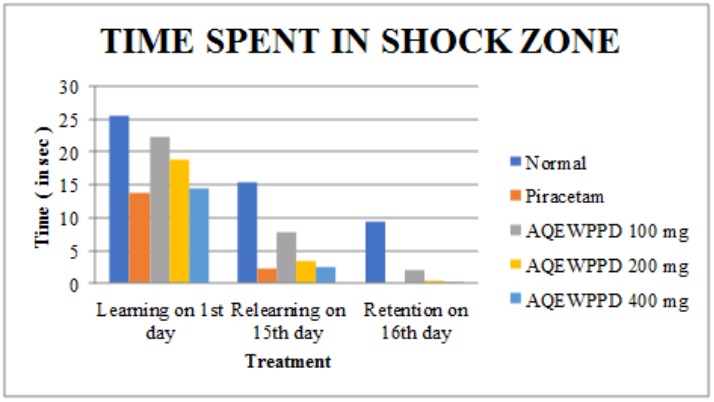

Fig. No. 7: Effect of AQEWPPD on Active Avoidance learning and retention (Shuttle box) model in rats (mean ±SEM).

CONCLUSION

- Preliminary phytochemical investigation of AQEWPPD extracts were noted with phytochemicals like flavonoids, tannins, saponins, alkaloids, carbohydrates, proteins and amino acids.
- In acute toxicity study (LD_{50}) (as per OECD Guidelines No.420) with AQEWPPD no mortality or behavioural abnormality was recorded in mice even at the highest dose tested of 2000 mg/kg, p.o.
- The nootropic activity of both the extracts was evaluated by Active avoidance model in rats, Passive avoidance model.
- In Passive avoidance paradigam model and also in Active avoidance model, nootropic activity was found in AQEPD.
- Phytochemical constituents like flavonoids, tannins, saponins, alkaloids, carbohydrates, proteins and amino acids present in AQEPD are responsible for the observed nootropic activity.

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