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AN EXPERIMENTAL STUDY TO ASSESS THE MEMORY-ENHANCING PROPERTY OF PITAVASTATIN AND GEMFIBROZIL IN MICE USING THE MORRIS-WATER MAZE MODEL. EVIDENCE TO CATEGORIZE THEM AS SMART DRUGS

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Keywords:

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ABSTRACT: Introduction: Discovery of smart drugs is part of advancing the science of molecular and biochemical mechanisms of memory. Smart drugs are not just memory boosters; they also act as memory enhancers that help quick decision-making. Pitavastatin and gemfibrozil both cause lipid-lowering effects by different mechanisms of action. A few studies show they can act on CREB (c-AMP response elemental binding protein), a known transcription factor. CREB performs an essential role in long-term memory restoration. **Aim and Objectives:** To evaluate the memory enhancer effect of pitavastatin and gemfibrozil compared to piracetam using Balb-c mice. **Material and Methods:** The escape latency period and time spent in the target quadrant were compared among four groups. Observations were analyzed by using paired t-tests, ANOVA, and post hoc Tukey's test. **Results:** Pitavastatin (30mg/kg) and gemfibrozil (60mg/kg) significantly decline in the escape latency period. pitavastatin increased the total time spent in the target quadrant as compared to vehicle control in the Morris-water maze test ($p< 0.01$). However, gemfibrozil fails to show any increment in spending time in the target quadrant. **Conclusion:** In the present study, we concluded that pitavastatin and gemfibrozil possess memory-enhancer properties and can define them as "smart drugs". However, further studies are needed to confirm that hypothesis.

INTRODUCTION: Psychopharmacology mainly focuses on the neurochemical basis of different behavioral tasks such as memory, attention, psychomotor performance, mood, and addiction [1]. The psychomotor performance of an individual depends upon the learning behavior and recalling power. Learning and memory are cognitive functions that encircle various subcomponents that primarily interact and overlap with each other [2].

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This complex mechanism cannot be fully understood individually by neuropsychological or neurobiological models. Advancement in the science of molecular and biochemical mechanisms of memory provides opportunities to make pharmacological tools for memory-enhancing drugs. The Discovery of smart drugs is part of these advancements.

The smart drug in the Greek dictionary means "to bend or shape the mind." Pieces of evidence say that Smart drugs work differently compared to Nootropics. Nootropics nourish long-term memory by enhancing the blood flow and oxygenation in various brain regions without side effects, like vitamins and herbs [3]. Smart drugs are not just memory boosters.

They are also memory enhancers that help in quick decision-making. This quality makes it the essential drug for technical works [4]. Based on their pharmacological actions, smart drugs are classified into four different classes. Drugs like modafinil work by making the person awake, alert and energetic and are known as "Stimulants". Piracetam-like drugs, classified under the "Racetams" group, improve chemical exchange between the brain cells. "Cholinergic" can be used with racetams. L-deprenyl-like drugs are classified under the "Dopaminergic" class and work by releasing dopamine.

Pitavastatin, first discovered by Nissan chemical industries, limited to Japan and flourish further by Kowa pharmaceuticals Tokyo, as a hypolipidemic drug belongs to 3-hydroxy3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin) family. The main action of pitavastatin is to decrease serum triglycerides and total cholesterol by enhancing the over expression of hepatocellular LDL (low-density lipoprotein) receptor.

Simultaneously it also inhibits hepatocellular VLDL (very low-density lipoprotein) release. It was found in a few studies that low to moderate doses of pitavastatin did not activate cascade, resulting in a reduction in total and phosphorylated tau levels by inhibiting of the Rho/ROCK family. Inhibition of the rho/ROCK pathway by rho inhibitors potentiates the prevention of neurodegeneration and stimulates neuro-regeneration in various neurological disorders.

Gemfibrozil is an FDA-approved drug that causes a decrease in serum triglyceride and total cholesterol levels and increases high-density lipoprotein. Peroxisome proliferator-activated receptor-alpha (PPARα) activator, gemfibrozil promotes the clearance of lipids and is essential in the metabolism of fats.

Besides those, it also regulates oxidative stress, promoting signal transduction, increasing myelination, and decreasing inflammation [5]. Morris's water maze is one of the "gold standard" tests for behavioral neuroscience and was introduced by Richard G. Morris in 1984. MWM is widely used to evaluate spatial learning and memory in mice, which is related to hippocampal synaptic plasticity [6].

MATERIAL AND METHODS:

Animal: Our research was done in the Department of Pharmacology & therapeutics, King George's medical university, Lucknow. Ethical clearance was procured from the Institutional Animal Ethics Committee (IAEC). (Ethical approval number-150/IAEC/2021)

24 adult healthy male Balb/c mice weighing 17-24 gm were utilized in the present study. Mice were purchased from the Indian Institute of Toxicology Research [IITR] Lucknow. IITR is one of the certified centers by the Committee for Control and Supervision of Experiments on Animals (CPCSEA) for the breeding and housing of animals. They were housed in appropriate-sized cages in an Institutional animal house maintaining a specific temperature-controlled environment [25±2°C], humidity (60% ± 10%) with 12 hours light / 12 hours dark cycle. Animals were fed with a regular pellet diet with water *ad libitum*. The regular pellet diet was purchased from Bharat Science Solution Company, Lok Nagar, Unnao, Uttar Pradesh. All animals were allowed to acclimatize in a new environment for two weeks before the experiments in the institutional animal house of King George Medical University. Present validated models of rodents were used to assess the memory enhancer properties of pitavastatin and gemfibrozil. Mice will be randomly divided into 4different groups, each group containing 6 mice.

Drug Treatment: Drug tests were solubilized in 0.5% carboxy-methylcellulose (CMC), dissolved in normal saline, and then given orally (p.o.) by a feeding gavage. The doses were selected based on previous studies on memory enhancement. Pitavastatin and gemfibrozil were administered to individual mice in group 1,2,3,4. None of the mice was dead due to treatment till the end of the observation period.

Drugs: Pitavastatin, gemfibrozil, and piracetam were purchased from Gyan Scientific Traders Pvt. Ltd. Authorized Company.

Vehicle: Pitavastatin and gemfibrozil were dissolved in 0.5%w/v CMC (carboxy-methylcellulose) and administered orally in mice. Piracetam was dissolved in normal saline and injected i.p.

Behavioral Model:

Morris-water Maze: The MWM task is one of the "gold standard" tests and is preferably used to test spatial memory and to learn in rodents. The present study was conducted using a 1.3 mt diameter circular tub with a depth of 0.5 mt. In this, tap water was filled up to 0.3mt at 21°C. The tub was divided into four equal vertical quadrants (Q1, Q2, Q3 and Q4). A rescue platform (10 cm in diameter, 29 cm in height) was put in the tank just below the water surface, usually in the center of a Quadrant. The platform was invisible. The maximum cut-off time for learning and memory is 120s [7]. Mice were trained to acquire spatial memory for 5 days with 4 trials/day, each trial for a 120-sec cut-off, mice, were permitted to stay on the platform for 20sec, then back to their home cage. If mice didn't find the platform, it was guided manually toward the platform & allowed to stay on it for 20 sec before returning to their home cage. The platform was kept in the same position throughout the training session. 24 mice were separated into 4 groups and each group had 6 mice. Separate animals were used for each experiment.

TABLE 1: ANIMAL GROUPING

Activity to be tested	Groups	Treatment
Larning and memory	Group 1	Normal Saline
	Group 2	TAB Pitavastatin 30 mg/kg BW
	Group 3	TAB Gemfibrozil 60 mg/kg BW
	Group 4	INJ Piracetam 200 mg/kg BW

Measurement of Memory-enhancing Effect: Escape Latency time (seconds); Time taken by the animal in finding the escape platform after it's been placed in MWM and total duration spent in the target quadrant (in seconds) were calculated. Post-training, Basal readings were taken on the first day after drug administration then the test was conducted for three continuous days (starting from the 7th day up to the 9th day).

Escape latency (EL) is the time taken by the animal to locomote from the starting point to the platform in the target quadrant. 10th day, the platform was removed and mice were placed in any of the three quadrants and allowed to search the target quadrant for 300s. After each swim mice dried with towels & heated for 15 min before returning to their home cages.

Statistical Analysis: The calculated data were expressed as MEAN ± SD from 6 animals. Final results were subjected to statistical analysis using one-way ANOVA followed by post hoc Tukey's test to calculate the significant difference among the groups. $P<0.05$ was considered significant. Paired t-test used for calculating intragroup comparison.

RESULTS:

Assessment of Effect on Learning and Memory (Escape Latency): Learning and memory were assessed by estimating the time to reach the platform (escape latency). [group 1: control, group 2: pitavastatin (test 1), group 3: gemfibrozil (test 2), group 4: standard (piracetam)]. Intergroup Comparison was done by ANOVA and has been summarized in **Table 2** and graphically in **Fig. 1**.

TABLE 2: INTERGROUP COMPARISON OF MEAN TIME TO REACH THE PLATFORM IN SECONDS (± SD)

Group	Day 1		Day 7		Day 8		Day 9	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Group 1 (NS)	97.66	9.04	95.16	6.11	92.33	9.99	96.16	10.53
Group 2 (test 1)	90.5	5.20	80.33	9.85	76.33	10.46	73.16	7.54
Group 3 (test 2)	91.83	15.94	90.66	7.86	90.5	5.82	87.83	6.24
Group 4 (Standard)	91.0	12.31	64.66	5.81	63.66	10.63	62.66	10.70
ANOVA	F = 0.51 p = 0.67		F = 19.10 p =<0.0001*		F = 12.13 p = 0.0001*		F = 16.66 p = <0.0001*	

Statistically significant N=24, n=6 in each group. Values are expressed as Mean±SD post-hoc Tukey's test was applied to find the significant difference after application of one-way ANOVA. F = 0.51; P =0.67 (1st day), F = 19.10; P =0.0001 (7th day), F = 12.13; P =0.0001* (8th day), F = 16.66; P =0.0001* (9th day).

TABLE 2: BETWEEN-GROUP COMPARISON OF MEAN TIME TO REACH THE PLATFORM (TUKEY HSD TEST)

Group	Day 1			Day 7			Day 8			Day 9		
	Mn diff	SE	'p'	Mn diff	SE	'p'	Mn diff	SE	'p'	Mn diff	SE	'p'
1 vs 2	7.16	5.34	0.78	14.83	3.09	0.01*	16	3.85	0.03*	23	3.66	0.001*
1 vs 3	5.83	5.34	0.86	4.5	3.09	0.73	1.83	3.85	0.98	8.33	3.66	0.39

1 vs 4	6.66	5.34	0.81	30.5	3.09	0.00001*	28.66	3.85	0.0002*	33.5	3.66	0.00001*
2 vs 3	-1.33	5.34	0.99	-10.33	3.09	0.11	-14.16	3.85	0.07	-14.66	3.66	0.04*
2 vs 4	-0.5	5.34	0.99	15.66	3.09	0.009*	12.66	3.85	0.12	10.5	3.66	0.21
3 vs 4	0.83	5.34	0.99	26	3.09	0.00005*	26.83	3.85	0.0004*	25.16	3.66	0.0005*

*Statistically significant.

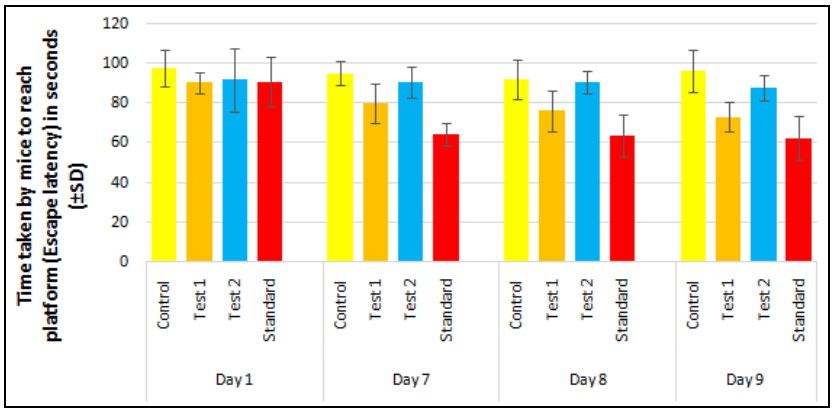

FIG. 1: TIME TAKEN BY MICE TO REACH THE PLATFORM (ESCAPE LATENCY) IN SECONDS (±SD)

Intergroup Comparison: On day 1, the time taken to reach the platform in Morris's water maze of group 1 (97.66±9.04), group 2 (90.5±5.20), group 3 (91.83±15.94) and group 4 (91.0±12.31) was found to be comparable. On day 7, the time taken to reach the platform in Morris's water maze is comparatively lower in group 4 (64.66±5.81) followed by group 2 (80.33±9.85) and group 3 (90.66±7.86) while higher in group 1 (95.16±6.11). On exploring between-group differences, a significant difference was found between all groups except groups 1 vs group 3 and group 2 vs group 3. On day 8, the time taken to reach the platform in Morris's water maze is comparatively lower in group 4 (63.66±10.63) followed by group 2 (76.33±10.46) and group 3 (90.5±5.82) while higher in group 1 (92.33±9.99). On exploring between-group differences, a significant difference was found between groups 1 vs group 2; group 1 vs group 4, and group 3 vs group 4.

On day 9, the time taken to reach the platform in Morris's water maze is comparatively lower in group 4 (62.66±10.70) followed by group 2 (73.16±7.54) and group 3 (87.83±6.24) while higher in group 1 (96.16±10.53). On exploring between-group differences, a significant difference was noticed between all groups except groups 1 vs group 3 and group 2 vs group 4.

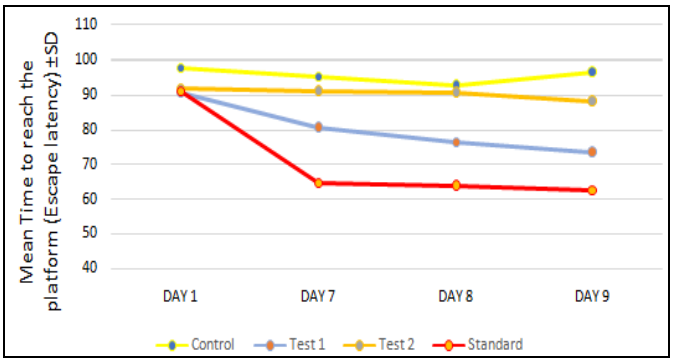

FIG. 2: TREND OF ESCAPE LATENCY OF DIFFERENT GROUP

TABLE 3: INTRAGROUP CHANGE IN BASELINE (DAY 1) ESCAPE LATENCY (PAIRED 'T-TEST)

Group	DAY	Mean change	SD	% BL change	t'	p'
Group 1	DAY 7	-2.5	11.96	-2.62	0.51	0.63
	DAY 8	-5.33	13.89	-5.77	0.94	0.39
	DAY 9	-1.5	18.27	-1.55	0.2	0.84
Group 2	DAY 7	-10.16	6.4	-12.65	3.89	0.01
	DAY 8	-14.16	10.66	-18.55	3.25	0.02
	DAY 9	-17.33	7.91	-23.69	5.36	0.003
Group 3	DAY 7	-1.16	13.67	-1.28	0.2	0.84
	DAY 8	-1.33	17.21	-1.47	0.18	0.85
	DAY 9	-4	14.77	-4.55	0.66	0.53
Group 4	DAY 7	-26.33	16.2	-40.72	3.97	0.01
	DAY 8	-27.33	11.46	-42.93	5.83	0.002
	DAY 9	-28.33	18.52	-45.21	3.74	0.01

*Statistically significant.

Intragroup Comparison: All above groups show a decline from the baseline (Day 1) in escape latency. In group 1 the range of percentage change in the baseline escape latency (1.55% to 5.77%) was observed. At all periods of observation, escape latency was lower than baseline, and change was not found to be significant. In group 2, the period of immobility on days 7, 8 and 9 was lower than on day 1. Percentage changes in the baseline period of immobility on days 10, 20 and 30 were (12.65, 18.55 & 23.69 %) and all values were found to be significant. In group 3, the period of immobility on days 7, 8 and 9 was found to be slightly lower than on day1. Percentage changes in the baseline period of immobility on days 7, 8 and 9 were (1.28, 1.47 & 4.55%) and values were not found to be significant. In group 4, the period of immobility on days 7, 8 and 9 were found to be lower than on day 1. Percentage changes in the baseline period of immobility on day 7, day 8 and day 9 were (40.72, 42.93, & 45.21%) and values were found to be significant.

Assessment of Effect on Learning and Memory (Duration Spent in Target Quadrant): Learning and memory were assessed by estimating time spent in the target quadrant. [group 1: control, group 2: pitavastatin (test 1), group 3: gemfibrozil (test 2), group 4: standard (piracetam)]. Intergroup comparison was done by ANOVA and encapsulated in **Table 4** and graphically in **Fig. 3.**

TABLE 4: INTERGROUP COMPARISON OF MEAN TIME SPENT IN THE TARGET QUADRANT IN SECONDS (± SD)

Group	Day 1		Day 10	
	Mean	SD	Mean	SD
Group 1 (NS)	173.5	9.75	171.33	12.53
Group 2 (test 1)	183.5	12.69	195	10.37
Group 3 (test 2)	176.16	10.34	174.16	174.16
Group 4 (standard)	204.66	7.22	217.5	8.80
ANOVA	F = 11.51 p = 0.0001*		F = 23.22 p =<0.0001*	

Statistically significant N=24, n=6 in each group. Values are expressed as Mean±SD post-hoc Tukey's test was applied to find the significant difference after the application of one-way ANOVA. F = 11.51; P =0.0001 (1st day), F = 23.22; P =0.0001* (10th day).

TABLE 5: BETWEEN-GROUP COMPARISON OF MEAN TIME SPENT IN THE TARGET QUADRANT (TUKEY HSD TEST)

Group	Day 1			Day 10		
	Mn diff	SE	'p'	Mn diff	SE	'p'
1 vs 2	-10	4.16	0.35	-23.66	4.78	0.01*
1 vs 3	-2.66	4.16	0.96	-2.83	4.78	0.97
1 vs 4	-31.16	4.16	0.0001*	-46.16	4.78	0.00001*
2 vs 3	7.33	4.16	0.6	20.83	4.78	0.02*
2 vs 4	-21.16	4.16	0.009*	-22.5	4.78	0.01*
3 vs 4	-28.5	4.16	0.0005*	-43.33	4.78	0.00002*

*Statistically significant

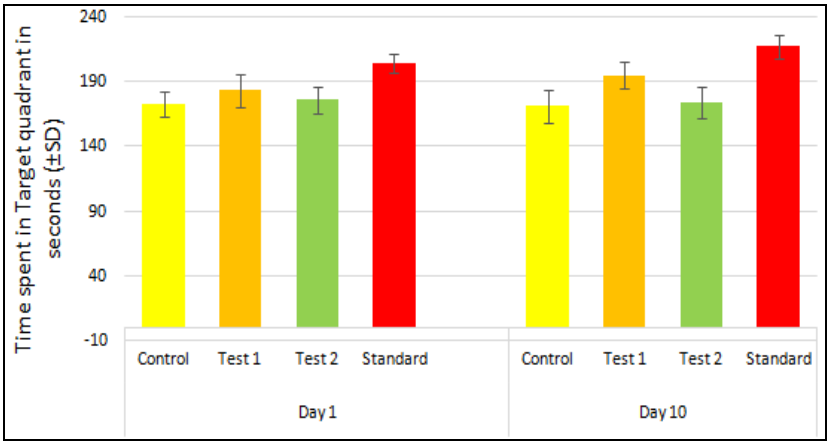

FIG. 3: TIME SPENT IN THE TARGET QUADRANT IN SECONDS (±SD)

Intergroup Comparison: On day 1, time was taken in the target quadrant in Morris's water maze of group 1 (173.5±9.75), group 2 (183.5±12.69), group 3 (176.16±10.34), and group 4 (204.66±7.22) were found to be comparable. On day 10, time spent in the target quadrant in Morris's water maze is comparatively higher in group 4 (217.5±8.80) followed by group 2 (195±10.37) and group 3 (174.16±174.16) while lower in group 1 (171.33±12.53). On exploring between-group differences, a significant difference was observed between all groups except group 1 vs. group 3.

TABLE 6: INTRAGROUP CHANGE IN BASELINE (DAY 1) TIME SPENT IN THE TARGET QUADRANT (PAIRED 'T-TEST)

Group	DAY	Mean change	SD	% BL change	t'	p'
Group 1	DAY 10	-2.16	7.98	-1.26	0.66	0.53
Group 2	DAY 10	11.5	4.46	5.89	6.31	0.001*
Group 3	DAY 10	-2	19.5	-1.14	0.25	0.81
Group 4	DAY 10	12.83	3.31	5.90	9.49	0.0002*

*Statistically significant

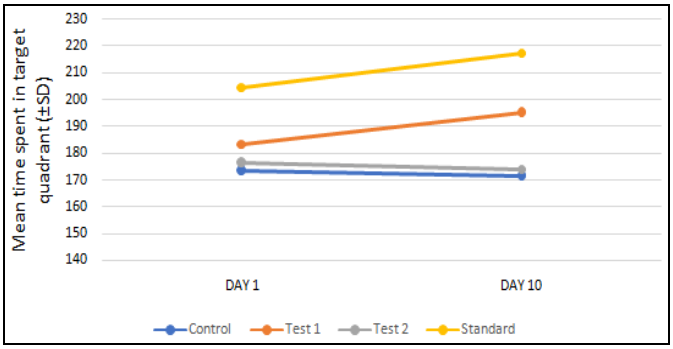

FIG. 4: TREND OF TIME SPENT IN TARGET QUADRANT OF DIFFERENT GROUP

Intragroup Comparison: Group 2 and group 4 show an increment from the baseline (Day 1) in time spent in the target quadrant, while group 1 and group 3 do not show any remarkable change.

In group 1 the total duration spent in the target quadrant on day 10 was found to be lower than on day 1. The percentage change on day 10 was (5.89 %), and values were found to be significant. In group 2, the duration spent in the target quadrant on day 10 was found to be higher than on day 1. The percentage change on day 10 was (1.14 %), and values were not found to be significant. In group 3, the duration spent in the target quadrant on day 10 was lower than on day 1. The percentage change on day 10 was (1.26 %), and values were not found to be significant. In group 4, the time spent in the target quadrant on day 10 was higher than on day 1. The percentage change on day 10 was (5.90 %), and values were found to be significant.

DISCUSSION: The development of novel drugs in the field of neuropsychology can significantly impact society to reduce the economic burden on the healthcare system [8]. Drug repurposing is a different approach to recognizing the new indications for already approved drugs [9]. In this process, hidden therapeutic functions of the drugs are uncovered using different approaches [10]. Pitavastatin and gemfibrozil are known for their hypolipidemic actions. There are research-based shreds of evidence that beyond their lipid-lowering effect, pitavastatin has several additional beneficial properties [11]. Learning is "'the act of acquiring information or skill such that knowledge and/or behavior change". Memory is generally referred to as a 'mental storage device' in which information is stored. The concept of episodic medicine also refers to a putative 'capacity of mind'. Episodic memory, also known as declarative memory, is referred to by day-to-day functions. Cognitive functions define under procedural memory or non-declarative memory. The ability to learn from the environment and others' experiences and store them in memory is essential to survival [12]. In our study, both the test drug pitavastatin and gemfibrozil have shown a decline in the escape latency period on days 7, 8, 9 as compared with baseline (day 1), with significant data. These findings show a memory enhancer effect. Memory-enhancer effect in the standard group (piracetam) was better than both test drugs.

During the intergroup comparison, a significant difference was found between group control vs pitavastatin; control vs piracetam; pitavastatin vs gemfibrozil, and gemfibrozil vs piracetam. On day 7, the percentage change in baseline was observed maximum in group 4 (40.72%) followed by group 2 (12.65%) and group 1 (2.62%) while the least change was observed in group 3 (1.28).

On day 8, the percentage change in baseline was observed maximum in group 4 (42.93%) followed by group 2 (18.55%) and group 1 (5.77%) while the least change was observed in group 3 (1.47%).

On day 9, the percentage change in baseline was observed maximum in group 4 (45.21%) followed by group 2 (23.69 %) and group 3 (4.55%) while the least change was observed in group 1 (1.55%). And the significant baseline change was found in group 2 and group 4 on all 3 days.

In our study, the test drug, pitavastatin, and the standard piracetam have shown an increment in the total time spent in the target quadrant on day 10 as compared with baseline (day 1), with a significant effect seen on day 10, showing memory enhancer effect of pitavastatin, while gemfibrozil did not show increment in the time spent in the target quadrant. The effect in the standard group (piracetam) was better than both test drugs.

During the intergroup comparison, a significant difference was found between all except the control vs Gemfibrozil Group. On day 10, the percentage change in baseline was observed maximum in Group 4 (5.90 %) followed by Group 2 (5.89 %) and Group 1 (1.26 %) while the least change was observed in Group 3 (1.14 %). And the significant baseline change was found in Group 2 and Group 4.

Most probably, this action of pitavastatin is due to the inactivation of the cascade, resulting in a reduction in total and phosphorylated tau levels via blocking of Rho/ROCK family [13]. It is found in recent studies that neurodegeneration is initiated by the aggregation of phosphorylated tau (pτ), a principal component of NFTs. The memory-enhancing increment with gemfibrozil may be due to mechanisms that regulate oxidative stress, promoting signal transduction, increasing myelination, and decreasing inflammation. Few studies explain that PPARα mainly acts on hippocampal neurons, controls calcium influx, and directly regulates CREB *via* the expression of various plasticity-related genes [14], which has a key role in memory enhancement.

CONCLUSION: Both Pitavastatin and Gemfibrozil at their respective dose 30 mg/kg and 60 mg/kg showed a reduction in the escape latency period. Which indicates the memory-enhancing effect of both drugs. During the estimation of total time spent in the target quadrant, gemfibrozil fails to show any changes/increments. Hence, it can be concluded that pitavastatin and gemfibrozil possess memory enhancer properties but the effect was less than Piracetam; however, inconclusive results were found with gemfibrozil concerning time spent in the target quadrant. Furthermore, research is needed to determine the exact role of these hypolipidemic drugs on learning and memory.

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CONFLICTS OF INTEREST: There are no conflicts of interest.

REFERENCES:

1. Faculty of psychology and neuroscience [Internet]. Available from: https://www.maastrichtuniversity.nl/research/neuropsychology-and-psychopharmacology
2. Chai WJ, Ismafairus A, Hamid A, Abdullah JM and Elliott EM: Working Memory From the Psychological and Neurosciences Perspectives : A Review 2018; 9(3): 1–16.
3. Soni S, Srivastava R and Bhandari A: Smart Drugs : A Review 2020; (11): 1–13.
4. Esposito M, Cocimano G, Ministrieri F, Rosi GL, Nunno N Di and Messina G: Smart drugs and neuroenhancement. What do We Know 2021; 26(6): 347–59.
5. Kim K, Kleinman HK, Lee H and Pahan K: Safety and potential efficacy of gemfibrozil as a supportive treatment for children with late infantile neuronal ceroid lipofuscinosis and other lipid storage disorders 2017; 1–9.
6. Hernández-mercado K and Zepeda A: Morris Water Maze and Contextual Fear Conditioning Tasks to Evaluate Cognitive Functions Associated With Adult Hippocampal Neurogenesis 2022; 15(1): 1–16.
7. Weitzner DS, Engler-Chiurazzi EB, Kotilinek LA, Ashe KH and Reed MN: Morris water maze test: Optimization for mouse strain and testing environment. J Vis Exp 2015; 2015(100): 1–11.
8. Altimus CM, Marlin BJ, Charalambakis NE, Colo A, Glover EJ and Izbicki XP: The Next 50 Years of Neuroscience 2020; 40(1): 101–6.
9. Huang F, Zhang C, Id QL, Zhao Y and Zhang Y: Identification of amitriptyline HCl, flavin adenine dinucleotide, azacitidine and calcitriol as repurposing drugs for influenza A H5N1 virus-induced lung injury. 2020; 1–16. Available from: http://dx.doi.org/10.1371/journal.ppat.1008341
10. Masoudi-sobhanzadeh Y, Omidi Y, Amanlou M and Masoudi-nejad A: Genomics Drug databases and their contributions to drug repurposing. Genomics [Internet]. 2020; 112(2): 1087–95. Available from: https://doi.org/10.1016/j.ygeno.2019.06.021

11. Sahebkar A, Kiaie N, Gorabi AM, Mannarino MR, Bainaconi V and Pirro M: Jo l P re of [Internet]. Progress in Lipid Research. Progress in Lipid Research 2021; 101127 Available from: https://doi.org/10.1016/j.plipres.2021.101127
12. Leblanc H and Ramirez S: Linking Social Cognition to Learning and Memory 2020; 40(46): 8782–98.
13. Repository C and Shu-Hui Yen: 1–25.
14. Gonzalez FJ and Pahan K: NIH Public Access. 2013; 4(4): 724–37.

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