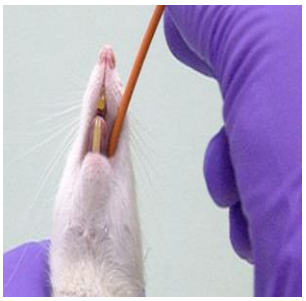

Chapter 10

Pharmacodynamic Study

Management of Dyslexia and ADHD

10.1 Introduction

Different animal models are available to evaluate efficacy of the formulation for pharmacodynamic studies. However, due to ease of administration, rat animal model is generally preferred over mice animal models, as rat nostrils are quite large compared to the mice nasal cavity. Different dynamic responses are studied after dosing of the formulation in appropriate animal model.

Dyslexia and ADHD is a heterogeneous disorder. Animal models cannot be used to study complex human behavior such as language; they do not have similar basic functions. In fact, human disorders that have animal models are better understood than disorders that do not. (1) The brain is the most complex of biochemical machines. The many technical and ethical constraints on studying its development and functioning make it unsurprising that we have no definitive causal models for any of the complex developmental psychiatric disorders. Indeed, it is impressive that we know as much as we do about the biological underpinnings of Dyslexia and ADHD. Considerable convergent, replicated evidence now supports the role of complex polygenic and environmental factors in causing alterations in neural architecture and functioning; these changes result in a range of neuropsychological performance deficits and ultimately the behavioral symptoms associated with Dyslexia and ADHD. (2) Dyslexia and ADHD patient have memory deficient; stimulant and nootropic drug improve memory in patient as well in healthy people. The relatively simple nervous systems of rodent models have enabled identification of neurological changes that underline certain aspects of Dyslexia and ADHD behavior but not all. Modafinil is used for the treatment of ADHD and various researchers have proved that modafinil is effective in enhancing learning and memory both in healthy and ADHD in human. (3, 4) Vinpocetine is used as nootropic drug, and was effective in improving memory and concentration of cognitively impaired patients and in healthy human being. (5) Therefore, in order to evaluate the influence of each of Modafinil and Vinpocetine formulation, we decided to use healthy model and analyzed formulations on rat's spatial performance. We have explored in this study the performance of Modafinil and Vinpocetine treated rats in the water maze.(6)

10.2 Animal

Sprague Dawley (350-400 g, 12-14 months old) rats of either sex, were selected for the study. The animals were housed in a group of 3 rats per cage under well-controlled conditions of temperature (22 ± 2°C), humidity (55 ± 5%) and 12hrs/12hrs light-dark cycle.(7) The animals had free access

to conventional laboratory diet and distilled water. The beddings were changed regularly. During experimental work, the animals were examined properly for infection, metabolic disorders and protected from any injury.

The experimental procedures and protocol for this study was reviewed and approved (IAEC Reg. No.: MSU/PHARM/IAEC/2011/15) by the Institutional Animal Ethics Committee (IAEC) of pharmacy Department, The M.S. University of Baroda, India. And the pharmacological work was performed according to Committee for the Purpose of Control and Supervision of Experimentation on Animals (CPCSEA) norms and Government of India and The Prevention of Cruelty to Animals act (PCA), 1960.

10.3 Experimental Method

10.3.1 Administration of Formulation

The rats were randomly divided into nine groups.

Modafinil Formulations by Oral Administration

Group I served as control and received saline (p.o) for seven days and on eighth day received Modafinil. Groups II-IV received Modafinil Suspension, Modafinil SMEDDS (Diluted), Modafinil Marketed Formulation (converted to suspension) (p.o) respectively in the dose of 10.278±0.02mg/kg (Before each drug administration, the drug preparation was thoroughly vortexes to ensure homogeneity and each oral formulation of Modafinil was administered via oral gavage). All groups received preparation for seven days from the beginning of the experiment as an oral supplementation and on eight day received saline.

Vinpocetine Formulations by Nasal Administration

Group V served as control, received saline by nasal route each day up to seven days, and on eighth day received Vinpocetine microemulsion. Groups VI-IX received Vinpocetine Microemulsion (nasal), Vinpocetine Mucoadhesive Microemulsion (nasal), Vinpocetine Solution (nasal), and Vinpocetine Suspension (p.o.) respectively in the dose of 0.514 ± 0.02 mg/kg for seven days. And on eight days in group VI, VII and VIII saline was administered nasally whereas in group IX saline was administered orally. The rats received 20 µl mucoadhesive microemulsion (10 µl in each nostril) using micropipette (10 µl) of low-density polyethylene (LDPE) micro tip, having 0.1 mm internal diameter was attached at the delivery site (8) 15 min before conducting experiment on

each day. Morris water maze (MWM) test was performed on all animals for eight consecutive days.

10.3.2 Morris Water Maze Test

The Morris water maze (MWM) is the classic, and probably most widely used test of spatial learning and memory. (6, 7, 9, 10) This test is unique in that virtually all proximal (olfactory etc.) cues are hidden (the animal swims in the water) and only the distal, landmarks outside a pool can be used to localize the platform in a cognitive map-like fashion (in the classical version). In addition, the test uses the natural ability of rats to swim while not causing a major distress. Morris Water Maze apparatus: The apparatus was designed by Richard G. Morris in 1981. It represents a circular pool (90 cm in diameter, 45 cm in height, filled to a depth of 25 cm with water at 26 ± 1°C) filled with water and made opaque with white colour. The pool was divided into 4 quadrants of equal area and a submerged platform (6 cm diameter) was centered in one of the 4 quadrants of the pool and submerged just below the water surface (hidden 1cm below water). The rats were placed into the maze such that it could escape from water onto the platform and the time (in seconds) taken by the rat was measured as escape latency.

The first experimental day was dedicated to swimming training for 60s in the presence of the platform. On the 2nd day, the rats were given three trial sessions with the platform in place. The time interval between 1st and 2nd trial sessions was 15 sec while last trial session (3rd) was performed after 30 min of 2nd trial.

For each trial sessions, rat was placed every time in the water facing the pool wall in one of the pool quadrants. The entry point was changed every day, trial lasted until rat found platform. Escape latency (indicative of Learning and Intact Reference Memory) was measured (Table 15.3) and it was permitted to remain on platform for 15 s, after 15 seconds the animals were placed back in the water (in previous position) and allowed to search for platform (retained in previous position). Escape latency (indicative of Short-Term Working Memory ie, second test) was recorded (Table 15.4). But if the rat did not locate the platform within 60s, it was placed on the platform for 20s. The rat was dried by dry towel and was returned to cage. During each trial session, the time taken to find the hidden platform (escape latency) was recorded. After the last training trial sessions, the platform was removed from the pool and rats were allowed to swim for 60s to search for it. A record was kept for the time spent in each quadrant. (6)

10.4 Result and Discussion

10.4.1 Learning and Memory Effect of Modafinil Formulations by Oral Administration

Table 10.1 Learning and Intact Reference Memory

	Escape latency (Second)			
Days	**Suspension**	**Saline**	**Marketed**	**SMEDD**
1	55.5 ± 3.45	55.00 ± 3.69	55.67 ± 3.50	56.17 ± 3.97
2	54.33 ± 4.97	53.50 ± 6.09	53.00 ± 4.94	53.50 ± 3.33
3	50.50 ± 6.09	46.83 ± 7.44	48.50 ± 5.89	46.33 ± 3.01
4	40.83 ± 4.36	39.00 ± 5.62	34.00 ± 4.86	39.00 ± 5.10
5	31.83 ± 4.71	36.83 ± 6.15	28.50 ± 6.56	24.83 ± 3.92
6	29.17 ± 3.92	25.67 ± 5.12	28.67 ± 4.63	21.17 ± 3.31
7	19.83 ± 4.07	27.17 ± 5.27	24.50 ± 5.13	18.50 ± 3.73
8	20.17 ± 3.06	24.67 ± 4.08	17.67 ± 4.76	19.67 ± 5.20

Each point represents Mean ± SEM (n=6)

One-way ANOVA followed by post hoc bonferroni test using graph pad prism 6.

*p<0.5, **p<0.01, ***p<0.001 compared to saline.

No significant difference was found in escape latency of all Modafinil formulations as compared to saline treated rat.

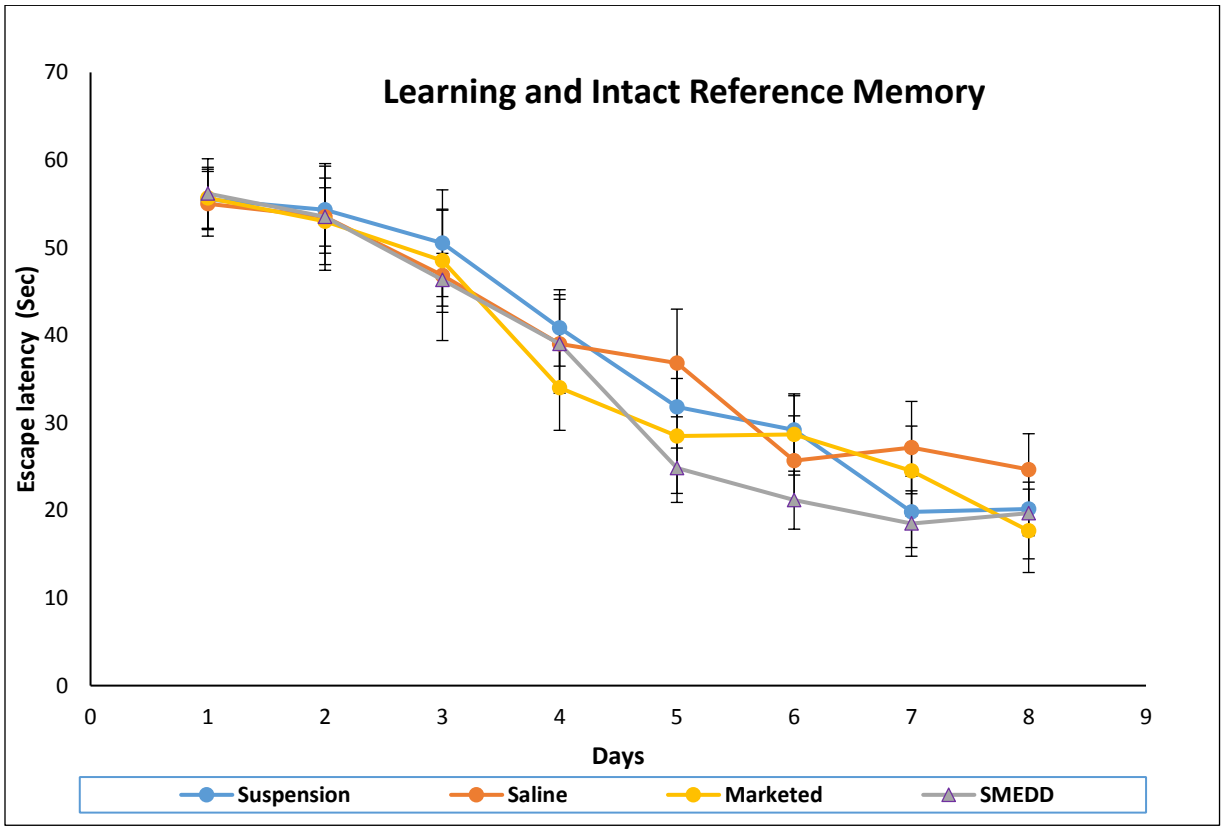

Fig. 10.1: Learning and Intact Reference Memory

Table 10.2 Short Term Working Memory

	Escape latency (Second)			
Days	**Saline**	**Suspension**	**Marketed**	**SMEDDS**
1	50.50 ± 7.12	52.67 ± 4.13	46.33 ± 3.67	49.00 ± 4.51
2	48.00 ± 6.10	47.83 ± 4.71	45.50 ± 5.89	44.33 ± 4.63
3	38.50 ± 7.42	42.50 ± 5.54	40.83 ± 6.88	42.50 ± 4.32
4	32.33 ± 7.26	34.67 ± 4.08	36.67 ± 6.35	31.67 ± 3.72
5	30.67 ± 5.50	28.50 ± 4.97	24.00 ± 4.21	25.00 ± 7.72
6	26.17 ± 4.31	24.33 ± 4.68	25.67 ± 4.41	21.83 ± 3.66
7	24.17 ± 4.71	17.50 ± 5.39	20.83 ± 3.06	21.50 ± 4.85
8	21.50 ± 4.85	16.17 ± 4.31	13.50 ± 4.97	13.00 ± 4.47

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
No significant difference was found in escape latency of all Modafinil formulations as compared to saline treated rat.

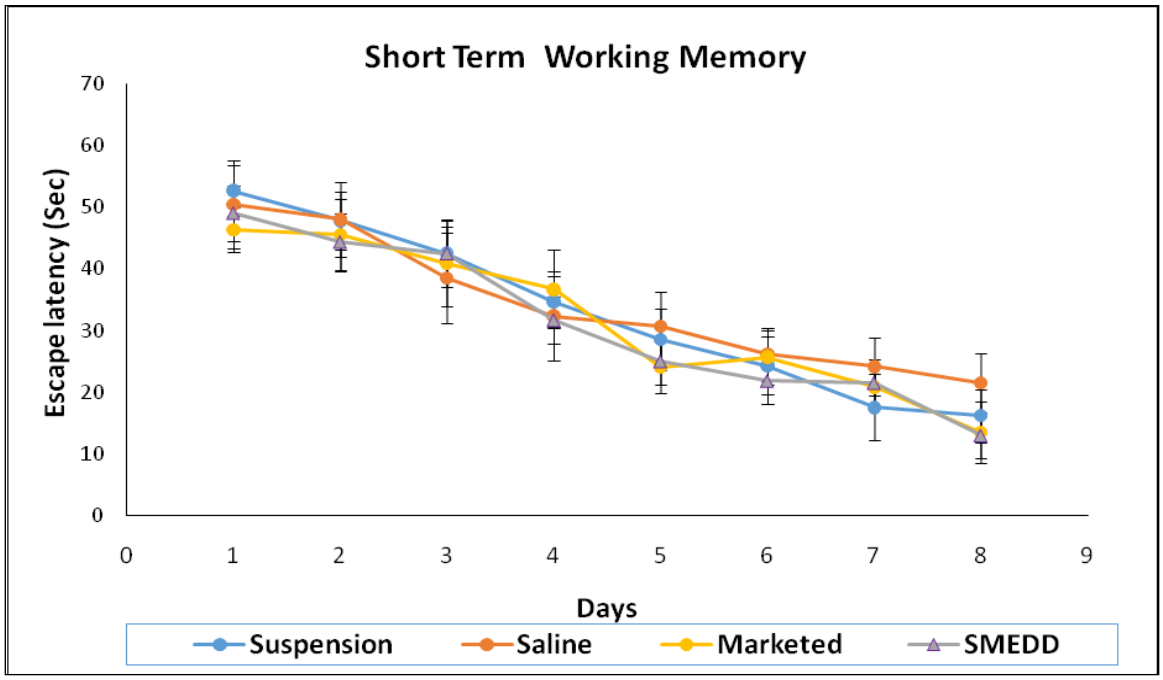

Fig. 10.2 Short Term Working Memory

Table 10.3 Percentage Time Spent in Each Quadrant on Day 6

Time(%)(day:6)				
Quadrant	Saline	Suspension	SMEDDS	Marketed
Previously place	27.5 ± 2.74	25.83 ± 2.53	26.94 ± 2.88	26.67± 2.79
Left	24.44± 2.51	22.22 ± 4.55	23.89 ± 3.93	25.83 ± 2.30
Right	22.78 ± 4.04	27.78 ± 2.72	27.50 ± 5.03	25.56 ± 2.02
Opposite	25.28 ± 2.87	24.17± 3.46	21.67 ± 3.50	21.94 ± 2.87

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
Neither modafinil nor saline rat spent significantly more time in the quadrant where platform was previously place than other quadrants

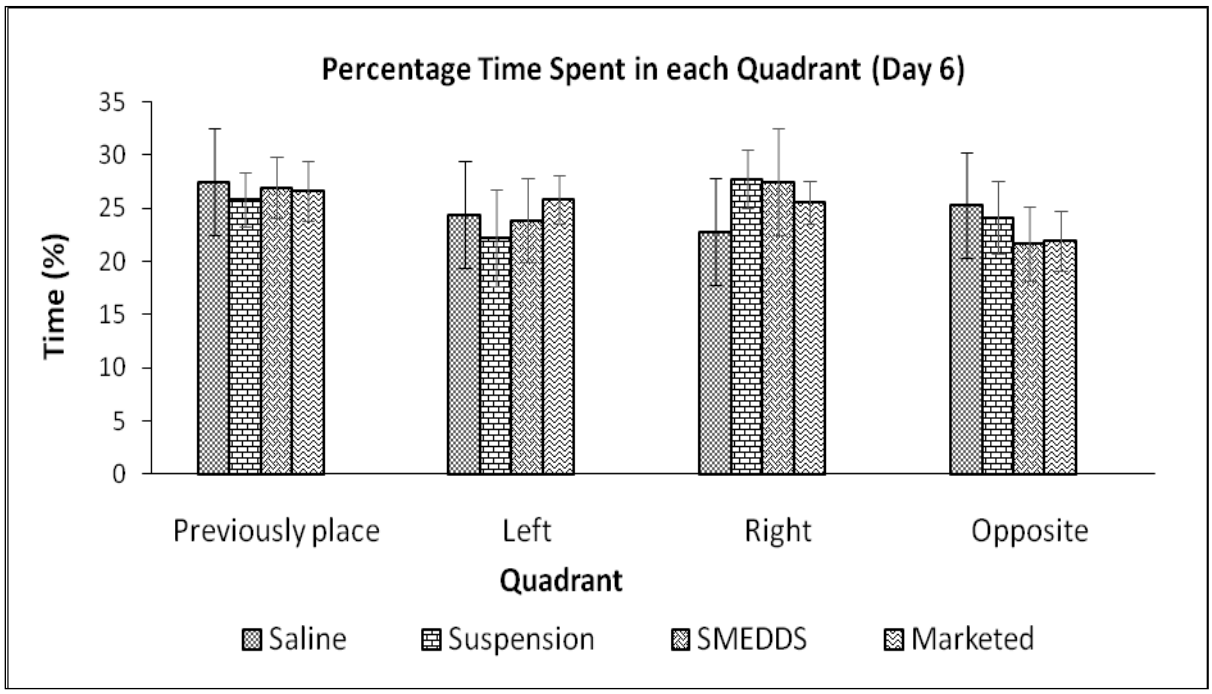

Fig. 10.3 Percentage Time Spent in Each Quadrant on Day 6.

Each point represents Mean ± SEM (n=6)

Table 10.4 Percentage Time Spent in Each Quadrant on Day 7

Time(%)(day:7)				
Quadrant	**Saline**	**Suspension**	**SMEDDS**	**Marketed**
Previously place	27.22± 4.55	35.0 ± 4.59*	43.61 ± 3.23***	39.44 ± 7.04**
Left	23.33± 3.94	22.22 ± 3.60	17.22 ± 5.44	22.78 ± 4.55
Right	25.28 ± 5.10	25.27 ± 2.45	16.67 ± 3.50	18.33 ± 2.58
Opposite	24.17 ± 3.29	17.5 ± 3.11	22.5± 3.12	19.72 ± 3.23

Each point represents Mean ± SEM (n=6)
One-way Anova followed by post hoc Bonferroni test using graph pad prism 6
*p<0.5, **p<0.01, ***p<0.001 compared to saline.

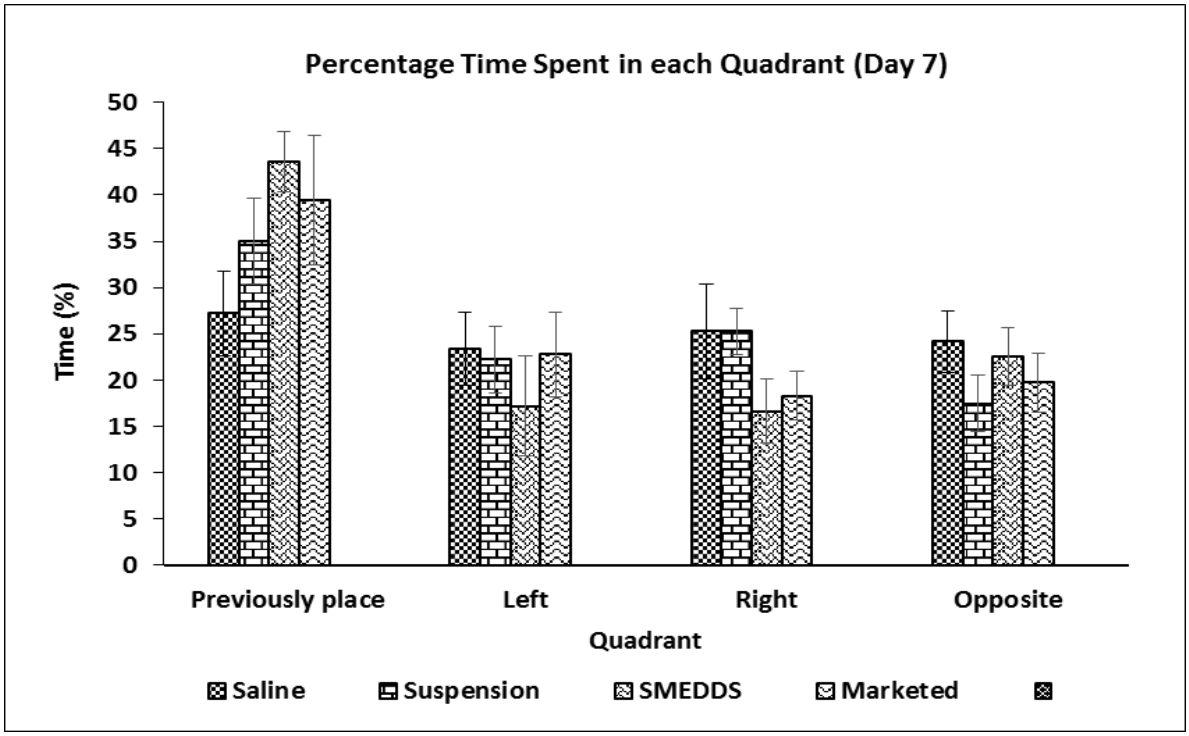

Fig. 10.4 Percentage Time Spent in Each Quadrant on Day 7.

Rats treated with modafinil showed significant difference ($P < 0.05$) in percentage time spent in quadrant where platform was previously placed compared to the saline treated rats. Each point represents Mean ± SEM (n=6)

Table 10.5 Percentage Time Spent in Each Quadrant on Day 8

Time (%) (day:8)				
Quadrant	**Saline**	**Suspension**	**SMEDDS**	**Marketed**
Previously place	28.06± 2.45	41.94 ± 2.45**	51.11 ± 3.60 ***	42.22 ± 3.44**
Left	24.44± 3.75	22.22 ± 3.44	15.00 ± 2.36	17.78 ± 2.72
Right	23.61 ± 4.64	21.11 ± 2.51	16.11 ± 2.72	20.56 ± 2.28
Opposite	25.00 ± 3.80	14.72 ± 2.22	17.77 ± 3.28	19.44 ± 4.80

Each point represents Mean ± SEM (n=6)

One-way ANOVA followed by post hoc Bonferroni test using graph pad prism 6

*p<0.5, **p<0.01, ***p<0.001 compared to saline.

Despite the drug reversal, modafinil rat continued to perform better than saline rat.

Each point represents Mean ± SEM (n=6)

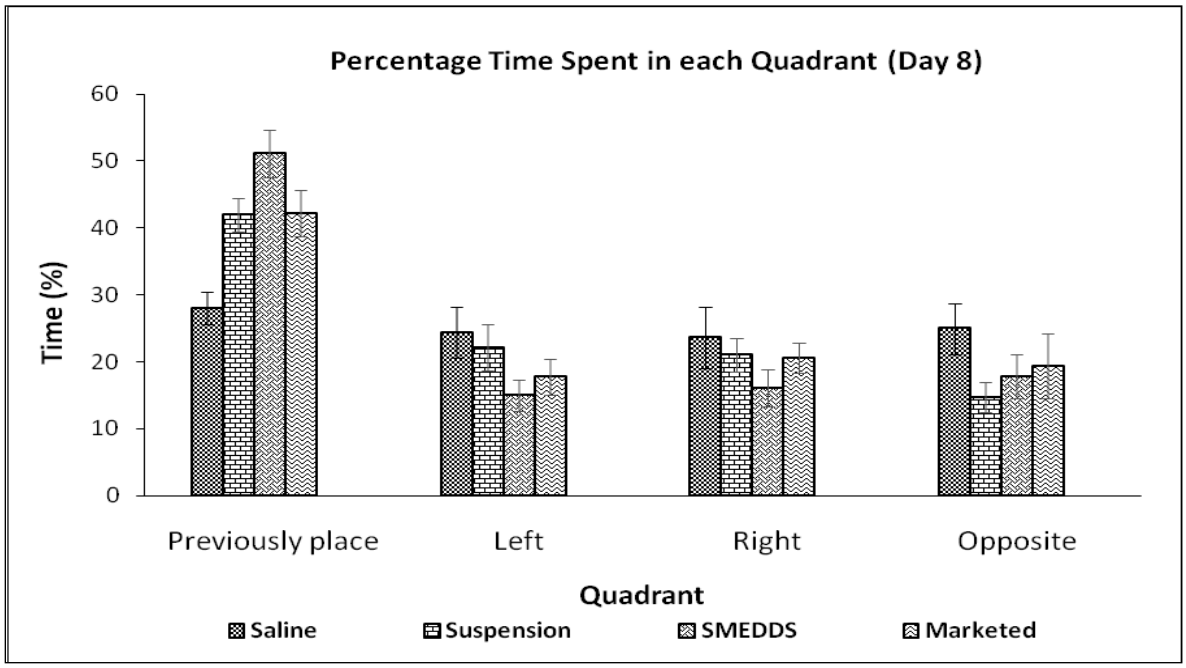

Fig. 10.5 Percentage Time Spent in Each Quadrant on Day 8.

The effects of Modafinil formulations after oral administration on the escape latency achieved in the Morris water maze test are shown in Fig. 10.1 and 10.2. Escape latency period in learning and intact reference memory (test 1) and short-term working memory (test 2) remained unchanged for the first 4 days of testing period in all the groups. Their finding concluded that after day 6 the animal made a correct choice. After that a significant decline in escape latency were observed for both the test in all groups. In case of modafinil suspension and marketed preparation decrease in the escape latency was observed, but it was slow compared with SMEDDS formulation of Modafinil and was non-significant. From 5th day onwards modafinil formulation treated rat learned the location of the platform as well saline-treated rat, and there was no significant difference between them; as shown in Fig. 10.1 and Fig. 10.2 indicated by a gradual decrease in escape latency in all formulations. Minimum escape latency was achieved on day 5th and thereafter no significant decrease in escape latency was observed. Therefore, paired comparisons between saline treated and drug treated formulation were analyzed by the quadrant in which platform was previously place to evaluate learning task. After removal of platform as shown in Fig. 10.3, the time spent in each quadrant, which did not differ in all this groups on 6th day of trial; neither group spent significantly ($P<0.5$) more time in quadrant where platform was previously placed, indicating that not a single group had learned a task. Because rat once located the platform could not find it there. On 7th day rats treated with modafinil showed in Fig 10.4, significant difference ($P<0.05$) in percentage time spent in quadrant where platform was previously placed compared to the saline treated rats which demonstrated that the modafinil rat memorized the task by the day seven of training however saline rat didn't. On 8th day despite the drug reversal, rats treated with modafinil continued to perform much better than saline rat (Fig 10.5). This study demonstrated that animals treated with saline didn't result in any visible improvement in memory capacities and learning when compared with modafinil. Also, rats treated with modafinil remembered this training when tested with saline (no drug on 8th day) and rats treated with saline remained uninformed of the place of the platform when drug was tested on 8th day. This study demonstrated noticeable improvement in learning and memory capacities with modafinil. Improvement was best with the modafinil SMEDDS than with modafinil suspension and conventional marketed.

10.4.2 Learning and Memory Effect of Vinpocetine Formulations by Intranasal

Table 10.6 Learning and Intact Reference Memory

	Escape latency				
Days	**Saline**	**ME**	**MME**	**Solution**	**Suspension**
1	55.83 ± 3.60	54.17 ± 3.66	56.00 ± 3.69	50.00 ± 4.61	56.83 ± 2.23
2	53.83 ± 4.31	50.00 ± 4.34	53.00 ± 5.33	54.33 ± 4.41	52.83 ± 5.27
3	48.00 ± 6.10	49.00 ± 2.10	47.00 ± 5.76	49.33 ± 4.68	45.00 ± 3.58
4	45.00 ± 6.36	40.00 ± 5.14	36.17 ± 6.37	37.83 ± 4.67	44.00 ± 5.18
5	38.33 ± 6.81	31.17 ± 5.88	27.00 ± 4.94	35.00 ± 6.67	32.00 ± 5.33
6	30.67 ± 6.77	24.17 ± 5.81	24.00 ± 6.42	27.67 ± 5.01	29.00 ± 5.73
7	24.67 ± 4.89	20.83 ± 3.71	18.67 ± 5.65	30.33 ± 6.41	24.83 ± 5.26
8	25.00 ± 5.93	18.83 ± 4.88	20.00 ± 5.40	28.00 ± 6.69	25.83 ± 5.27

Each point represents Mean ± SEM (n=6)

One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.

*p<0.5, **p<0.01, ***p<0.001 compared to saline.

No significant difference was found in escape latency of all Vinpocetine formulations as compared to saline treated rat.

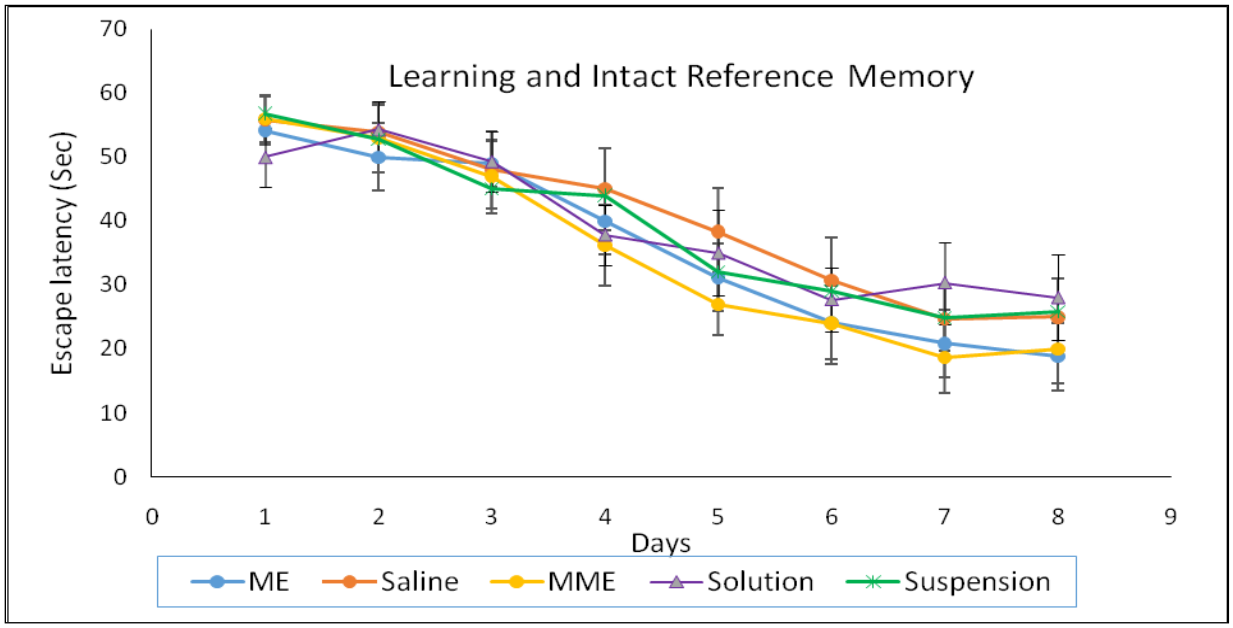

Fig. 10.6 Learning and Intact Reference Memory

Escape latency for each day of training. No significant difference (p<0.5) were found in Escape latency of all Vinpocetine formulations as compared to saline treated rat. Each point represent Mean ± SEM (n=3)

Table 10.7 Short Term Working Memory

	Escape latency				
Days	**Saline**	**ME**	**MME**	**Solution**	**Suspension**
1	52.33 ± 5.01	52.33 ±4.84	54.00 ± 4.82	53.83 ± 3.87	50.83 ± 4.36
2	48.00 ± 4.82	46.00 ± 4.15	51.83 ± 4.71	52.00 ± 4.29	50.00 ± 4.90
3	41.00 ± 4.60	38.67 ± 3.98	40.00 ± 4.29	48.50 ± 3.89	47.83 ± 3.12
4	34.17 ± 4.02	30.83 ± 3.97	33.67 ± 4.50	41.33 ± 4.32	38.17 ± 4.88
5	30.17 ± 4.67	27.17 ± 5.12	31.83 ± 4.96	35.00 ± 4.60	36.17 ± 3.54
6	25.67 ± 4.68	25.17 ± 3.71	22.83 ± 5.67	30.33 ± 5.57	28.00 ± 4.47
7	25.83 ± 5.23	21.33 ± 4.23	18.67 ± 4.27	24.67 ± 5.08	29.17 ± 3.92
8	26.17 ± 4.79	18.67 ± 5.28	18.83 ± 4.58	23.83 ± 4.54	24.17 ± 4.88

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
No significant difference was found in escape latency of all Vinpocetine formulations as compared to saline treated rat.

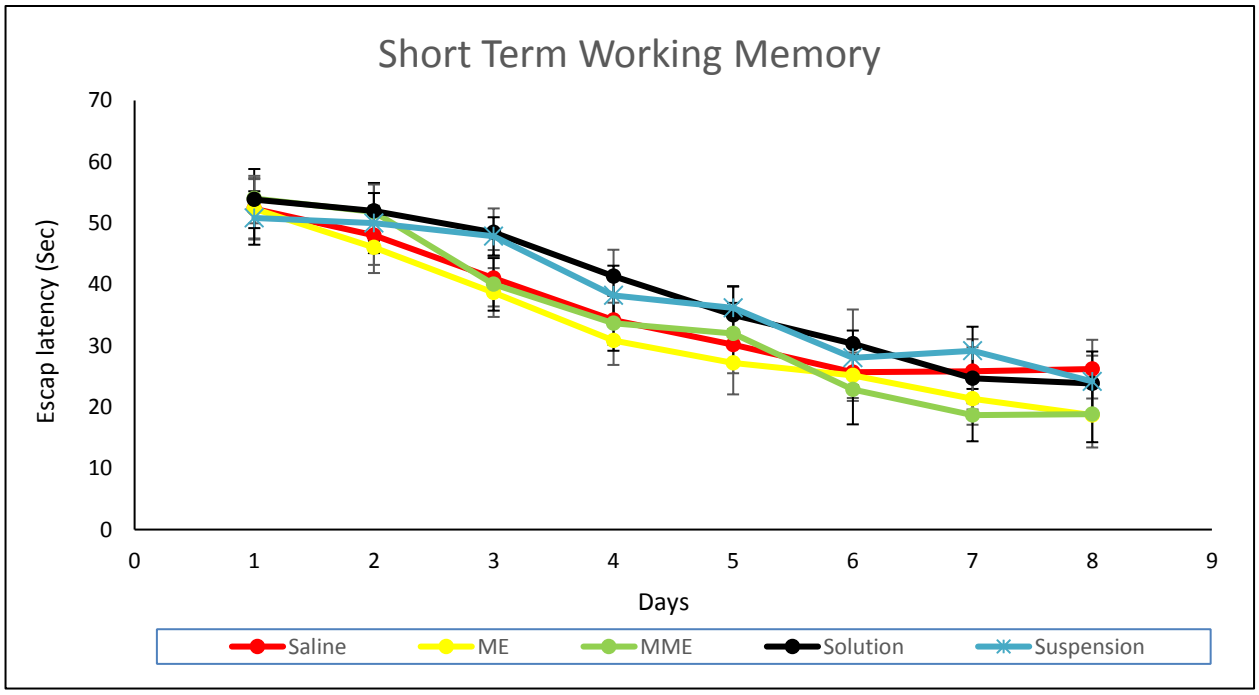

Fig. 10.7 Short Term Working Memory

Table 10.8 Percentage Time Spent in Each Quadrant on Day 6

Time(%)(day:6)					
Quadrant	**Saline**	**ME**	**MME**	**Solution**	**Suspension**
Previously place	25.56± 3.60	37.50±4.31*	34.72±2.45*	27.22± 2.72	28.33 ± 2.98
Left	28.33± 3.33	22.22 ± 3.56	21.67 ± 3.50	24.44 ± 2.28	24.44 ± 5.02
Right	21.67 ± 4.71	21.11 ± 2.91	21.11 ± 2.72	23.33 ± 3.33	23.89 ± 3.60
Opposite	24.44 ± 3.44	19.17 ± 3.61	23.33 ± 4.35	25.00 ± 2.79	23.33 ± 4.08

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
Vinpocetine ME and MME treated rat shows significantly more time spent whereas neither saline rat nor Vinpocetine loaded solution and suspension rat spent more time at the place where platform was formerly placed in the quadrant.

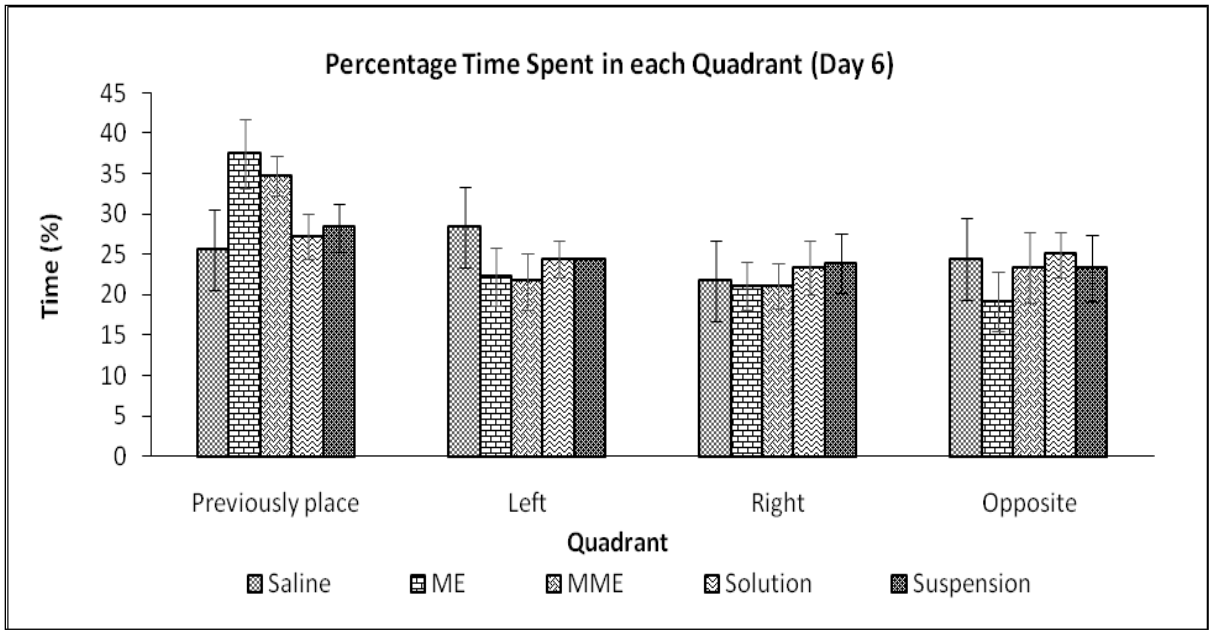

Fig. 10.8 Percentage Time Spent in Each Quadrant on Day 6.

Vinpocetine loaded ME and MME treated rat spending more time in the quadrant where platform was previously place whereas other vinpocetine formulations and saline rat did not.

Table 10.9 Percentage Time Spent In Each Quadrant on Day 7

Time(%)(day:7)					
Quadrant	**Saline**	**ME**	**MME**	**Solution**	**Suspension**
Previously place	22.22± 3.44	32.22±3.27*	32.22±3.27*	25.56± 3.10	24.44 ± 3.44
Left	26.11± 3.10	21.67 ± 3.5	20.56 ± 2.72	24.72 ± 3.56	26.94 ± 3.05
Right	25.00 ± 2.36	21.67 ± 3.33	25.00 ± 2.79	25.83 ± 3.61	24.72 ± 3.23
Opposite	26.67 ± 2.98	24.44 ± 3.10	22.22± 3.44	23.89 ± 3.44	23.89 ±3.60

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
Vinpocetine ME and MME treated rat shows significantly more time spent where platform was previously placed whereas, saline rat and vinpocetine loaded solution and suspension rat did not.

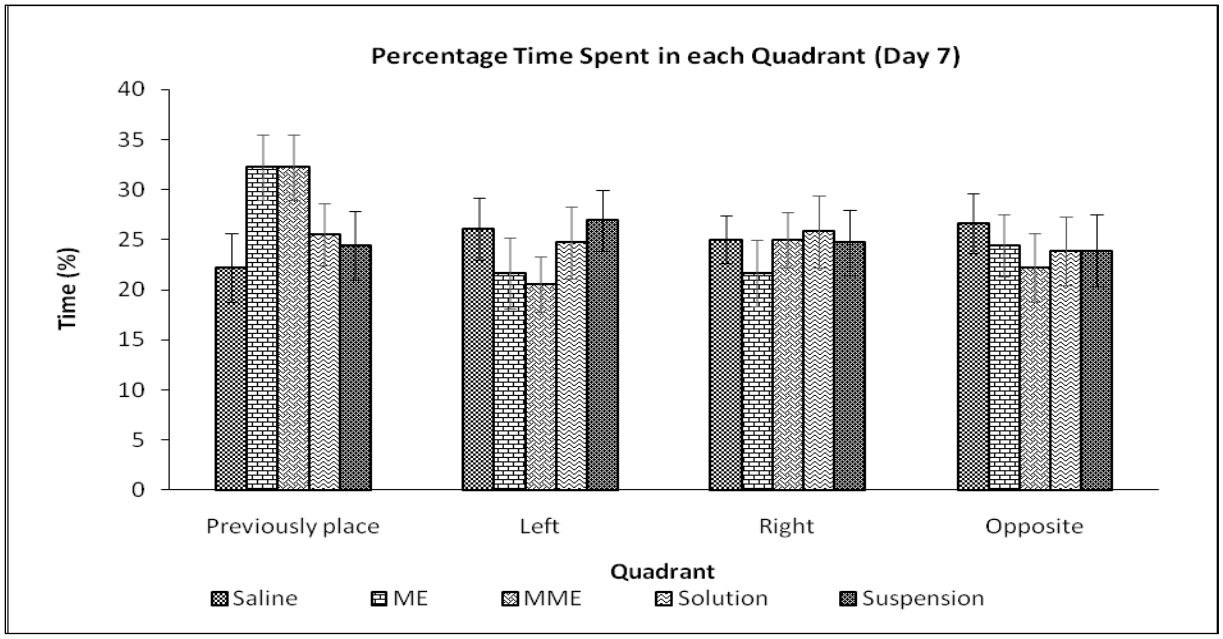

Fig. 10.9 Percentage Time Spent in Each Quadrant on Day 7.

Vinpocetine ME and MME treated rat learned the task, spending significant more time in the quadrant where platform was previously placed whereas Solution, Suspension and Saline rat did not.

Table 10.10 Percentage Time Spent in Each Quadrant on Day 8

Time(%)(day:8)					
Quadrant	**Saline**	**ME**	**MME**	**Solution**	**Suspension**
Previously place	23.61 ± 3.56	56.67 ± 5.68***	55.83±3.12***	28.06±4.88*	35.28±3.57**
Left	25.83 ± 4.56	15.28 ± 4.40	15.56 ± 3.28	22.50 ± 3.91	23.33 ± 6.32
Right	23.89 ± 4.67	13.06 ± 3.23	13.89 ± 3.28	24.17 ± 4.44	22.5 ± 4.05
Opposite	26.67 ± 3.33	15.00 ± 4.08	14.72± 3.23	25.28 ± 3.06	18.89 ± 3.90

Each point represents Mean ± SEM (n=6)
One way ANOVA followed by post hoc bonferroni test using graph pad prism 6.
*p<0.5, **p<0.01, ***p<0.001 compared to saline.
All Vinpocetine treated rat shows significantly more time spent in the quadrant where platform was previously placed whereas saline rat did not.

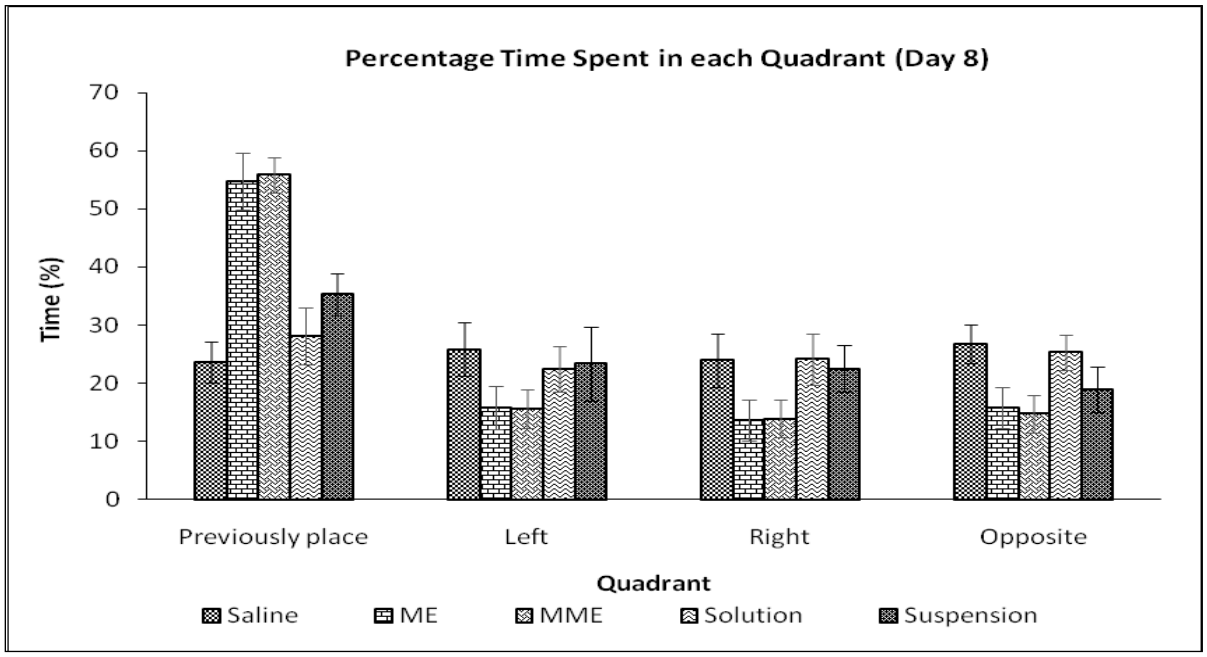

Fig. 10.10 Percentage Time Spent in Each Quadrant on Day 8.

The effects of Vinpocetine formulations after nasal administration of formulation on the escape latency for each of training trial achieved in the Morris water maze test are shown in Fig. 10.6 and Fig.10.7. Escape latency period in learning and where platform was previously placed, intact reference memory (test 1) and short-term working memory (test 2) remained unchanged for the first 4 days of testing period in all the groups. The result was similar to other modafinil oral formulation (SMEDDS) and there was no significant difference between oral Modafinil

formulation and nasal vinpocetine formulation and oral vinpocetine suspension. After that a significant decline in escape latency were observed for both the test in all groups. From 5th day onwards Vinpocetine formulation treated rat learned the location of the platform as well saline-treated rat, and there was no significant difference between them; as shown in both Fig.10.6 and 10.7 indicated by a gradual decrease in escape latency in all formulations and minimum escape latency was achieved on day 6th. Animal learned to find a platform after 4th day, they made a correct choice on day 6 for both test-1, learning and intact memory and test-2, short term memory in both oral and nasal formulation as well for saline. Therefore, paired comparisons between saline treated and drug treated formulation were analyzed to evaluate learning task. After removal of platform, the time spent in each quadrant, Vinpocetine ME and MME treated rat spending more time in the quadrant where platform was previously placed than time spent in the quadrant whereas saline rat did not whereas other vinpocetine formulations and saline rat did not. This was because rat once located the platform could not find it there and therefore, they tried to find it and hence spent a more time in the same quadrant. As shown in fig.10.8, for saline, solution and oral suspension, time spent in each quadrant did not differ in all the groups on 6th day of trial. Neither group spent significantly more time in quadrant where platform was previously placed, indicate that not a single group had learned a task when oral formulation was given while rats in nasal group started to learn the task faster than oral formulation. This show nasal ME and MME formulations were better than the oral formulation as well solution, as they directly reached to brain and gave effect while oral formulation did not reach significantly faster than nasal. As represent in fig.10.9, on 7^{th} day rats treated with Vinpocetine ME and MME showed significant difference ($P<0.05$) in percentage time spent in quadrant where platform was previously placed compared to the solution, suspension and saline treated rats. This study demonstrated that rat treated with Vinpocetine ME and MME learned the task by the seventh day of training, whereas solution, saline and suspension rat did not. This is because suspension by oral route may not reach to brain in sufficient quantity because of first pass metabolism and in case of solution it may reach but was washed out faster and may not give a better effect than microemulsion. On 8th day despite the drug reversal, rats treated with Vinpocetine ME and MME continued to perform much better than saline rat, which illustrate in fig.10.10. However, Vinpocetine ME and MME rat continued to perform significant ($p<0.05$) better than suspension, solution and saline rat. Furthermore,

suspension and solution treated rat learn better than saline with the reversal of drug formulation whereas saline treated rat did not learn.

This result proves that Vinpocetine and Modafinil improved learning and memory and the improvement was best with Vinpocetine loaded ME and MME than suspension and solution, better with Modafinil loaded SMEDDS than suspension and marketed formulation. No visible improvement in memory capacities and learning in saline treated animals was demonstrated in study when compared with drug formulations. In addition, rats treated with both drug remembered this training when tested with saline (no drug on 8th day) and rats who were treated with saline were uninformed of the platform location when tested on 8^{th} day with drug. Single dose was not effective for learning and memory, minimum of one-week treatment gave significant improvement in learning and memory task. Initially escape latency decrease may be because of two probable reasons: (1) the rats learn and remember to swim away from the wall of the maze vessel and therefore by accidental upsurge contact to the platform; (2) learn to relocate the platform. Escape latency stabilized between 6-8 days because the rats learned to take comparatively direct paths to the hidden platform. This study demonstrate that both formulations were used for the improvement of memory by learning task which will be helpful for the management of Dyslexia and/or ADHD.

10.2 References

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