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ANTIAMNESIC EFFECT OF *PRUNUS CERASUS FRUIT EXTRACT (CHERRY)* OF NICOTINE – INDUCED MEMORY AND COGNITIVE IMPAIRMENT IN WISTAR RATS

***Olorunfemi O. J. and Okpe Ebifetei**

Department of Human Physiology, Faculty of Basic Medical Sciences, University of Port Harcourt, Choba, Rivers State, Nigeria.

***Corresponding Author: Dr. Olorunfemi O. J.**
Department of Human Physiology, Faculty of Basic Medical Sciences, University of Port Harcourt, Choba, Rivers State, Nigeria.

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ABSTRACT
Antiamnesic effect of ***P**runus **C**erasus* fruit extract of nicotine-induced memory and cognitive impairment in wistar rat was studied. 40 wistar rats of similar weight were randomly divided into 8 group as follows; Group 1 control group (normal saline), Group 2 (treated with nicotine 0.6 mg/kg) intraperitoneal administration and Group 3 to 5 was treated with *P.Cerasus* fruits extracts at a dosage of 200mg/kg, 400mg/kg and 600 mg/kg by gavage method and Group 6 to 8 were administered with *P.Cerasus* + nicotine. The study was investigated within a period of 6 weeks. Results from the study was analyzed with a statistical package using ANOVA (SPSS) and presented in tables and charts with a level of significance at P ≤0.05. Different behavioural tasks, navigational maze task, Barnes maze task, passive avoidance task, Morris water maze task, rotarod task, hand grip task and elevated plus maze task were used to assess the effect of ***P**runus **C**erasus* fruit on memory and cognition and other parameters like anxiety and cognitomotor activities of the rats. The results from the study demonstrated a significant difference ($p<0.05$) in all tasks for spatial learning and memory at 40mg/kg of ***P**runus **C**erasus*. There was also a significant difference in retention latency in learning and memory at 96 hours' and 24 hours' time interval between the negative control and the *P.Cerasus* group and the positive control and the *P.Cerasus* group + positive control. A significant difference was observed in the muscle coordination between the *P.Cerasus* and the negative control in the rotarod and the hand grip task and no significant difference was observed in elevated plus maze task. In conclusion, At a dosage of 400mg/kg *P.Cerasus* enhanced memory and cognition and at a dosage of 600mg/kg *P.Cerasus* ameliorated amnesic effect and also improved cognitomotor functions.

KEYWORDS: *Prunus Cerasus*, Antiamnesia. Cognition function, cognitive impairment.

INTRODUCTION
Plant base food formed the integral component of the human diet and their consumption has been linked to maintenance of health and prevention of diverse kind of diseases. A growing body of evidence has shown that phytochemicals, non-nutritive bioactive compounds, contribute to the antioxidant and anti-flammatory activity of individual fruits and vegetables and are consequently credited with the observed health benefits. The phytochemicals constitue bioactive chemicals that are capable of restoring the endogenous antioxidant state of the body which may be disrupted due oxidative stress that is liable to off set the bodys homeostasis.(Miguel, 2011). The consumption of ***P**runus **C**erasus* has been associated with a reduction in risk for cardiovascular diseases and some cancers and more recently there has been attention directed to their potential to protect against neurodegenerative diseases and improve cognitive performance in older adults (Kent, 2015). From literature, supplement of ***P**runus **C**erasus* improves cognitive impairment due to anti-inflammatory mechanism or by altering directly the signalling involved in neuronal communication, Ca buffering ability and stress signalling pathways among others (K. M. Keane, 2016). Consumption of *Prunus Cerasus* was seen to have positive effect on muslce coordination. (Kyle Levers, 2015) Therefore the aim of this study was to assess the impact of *Prunus Cerasus* consumption on cognitive and cognitomotor functions

MATERIALS AND METHODS
Animal Preparation
All animals were obtained from the animal house, faculty of Basic Medical Science, University of Port Harcourt, Nigeria. Wistar rats weighing 120-200kg were housed in wooden cages for at least two weeks in the animal room and allowed to acclimatize for 2 weeks.

Acquisition Of Fruits

Ripe fruit of *P.Cerasus* was purchased from Sangana street Mile-One Market, Rumuowoji, Port Harcourt, Rivers State, and sent for authentication in the Department of Plant Science and Biotechnology, University of Port Harcourt. methanol extraction was carried out using Solvent method of extraction and the resulting extract was stored in a refrigerator throughout the duration of the study.

Experimental Design And Treatment

40 wistar rats, weighing 120-200kg were randomized into 8 groups, 5 per group. Group (1) negative control fed with normal saline, Group (2) Positive control 0.6*mg/kg of nicotine*, Group 3 *P.Cerasus* 200*mg/kg*, GROUP 4 *P.Cerasus* 400*mg/kg*, GROUP 5 *P.Cerasus* 600*mg/kg*, GROUP 6 *P.Cerasus* 200*mg/kg* + nicotine 0.6*mg/kg*, GROUP 7 *P.Cerasus* 400*mg/kg* + nicotine 0.6*mg/kg*, GPROUP 8 *P.Cerasus* 600*mg/kg* + nicotine 0.6*mg/kg*. Groups 3-8 were treat with for 2 weeks before the administration of nicotine. This is to establish plasma level of *P.Cerasus.*

Statistics

The statistical analysis of the results obtained from the study was done using the ANOVA (Analysis 0f variance) method. Statistical Package for Social Science (SPSS) and Microsoft excel. The results obtained were represented as Mean Standard Error of Mean (S.E.M) with a significant difference of $P \leq 0.05$.

RESULT

Table 1: Showing result for Navigational maze test across the test groups and control.

Groups	Task completion time (Sec± SEM)
Group 1 Negative Control	71.33 ± 3.40
Group 2 (Positive Contol: Nicotine)	140.11 ± 6.63$^{\alpha}$
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	53.33 ± 15.40
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	48.33 ± 15.40
Group 5 (600mg/kg B.W. of *Prunus Cerasus*)	38.00 ± 14.53
Group 6 (200mg/kg B.W. of *Prunus Cerasus* + Nicotine)	53.73 ± 14.53$^{\beta}$
Group 7 (400mg/kg B.W. of *Prunus Cerasus* + Nicotine)	48.92 ± 20.38$^{\beta}$
Group 8 (600mg/kg B.W. of *Prunus Cerasus* + Nicotine)	53.92 ± 9.84$^{\beta}$

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

Navigational maze is used to measure spatial learning and memory. From the table above, there is a significant difference between the positive control and the negative control and there is also a significant difference between the positive control and prunus + nicotine group with the positive control group.

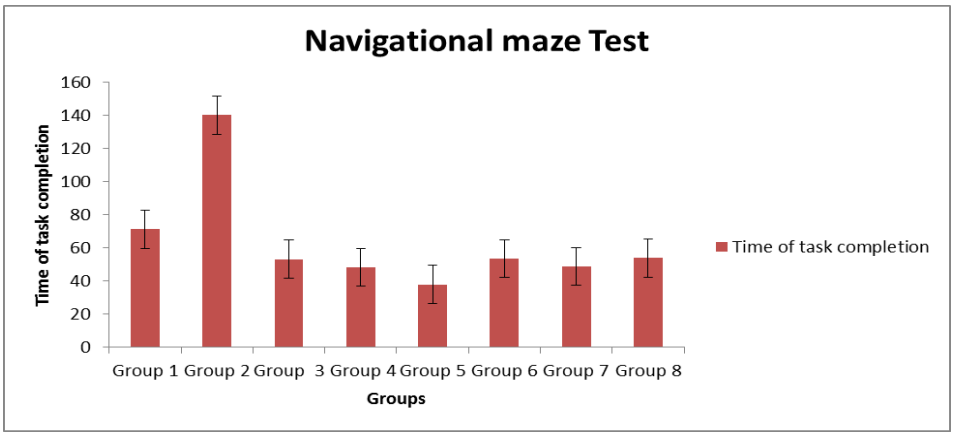

Fig. 1: Bars Representation of result for Navigational maze test across the test groups and control.

Table 2: Pattern of result from the Barnes maze test after exposure of animals to the various test substances

Groups	Barnes maze test	
	No of wrong holes (count± SEM)	Task completion time (Sec ± SEM)
Group 1 Negative Control	3.06 ± 0.22	16.78 ± 1.95
Group 2 (Positive Contol: Nicotine)	3.56 ± 0.16	28.84 ± 3.23 $^{\alpha}$
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	1.13 ± 0.08	3.99± 1.75 $^{\alpha}$
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	1.08± 0.42	5.98± 1.55 $^{\alpha}$
Group 5 (600mg/kg B.W. of *Prunus Cerasus*)	1.33 ± 0.30	5.48± 1.55 $^{\alpha}$
Group 6 (200mg/kg B.W. of *Prunus Cerasus* + Nicotine)	2.27 ± 0.16	13.27± 3.94 $^{\beta}$
Group 7 (400mg/kg B.W. of *Prunus Cerasus* + Nicotine)	3.42 ± 2.92	16.95 ± 3.22 $^{\beta}$
Group 8 (600mg/kg B.W. of *Prunus Cerasus* + Nicotine)	3.92 ± 0.87	16.56 ± 6.24 $^{\beta}$

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

Barnes maze: it is used to measure spatial learning and memory. The table above shows a significant difference between the negative control and positive control group. And also there is a significant difference between the *Prunus* group with the negative control. There is also a significant difference between the *Prunus* + positive control and the positive control.

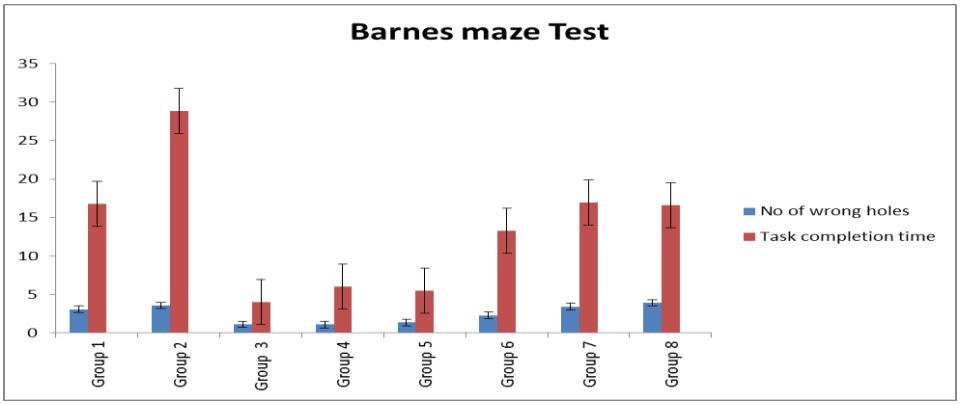

Fig. 2: Bars Representation of the Pattern of result from the Barnes maze test after exposure of animals to the various test substances.

Table 3: Assessment of Spatial Learning and Memory using the Morris water maze.

Groups	Morris Water Maze Test	
	Initial Test (Sec± SEM)	24-Hours Later (Sec± SEM)
Group 1 (Control)	11.20 ±1.22	12.75± 3.56
Group 2 (Nicotine only)	18.63± 9.68	28.25± 5.59 $^{\alpha}$
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	9.05 ± 1.79	10.55± 3.24
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	14.25±4.47	9.69 ± 2.41
Group 5 (600mg/kg B.W. of *Prunus Cerasus*)	7.56± 1.72	8.38 ± 0.56
Group 6 (200mg/kg B.W. of *Prunus Cerasus* + Nicotine)	8.95± 2.48	8.90± 2.50 $^{\beta}$
Group 7 (400mg/kg B.W. of *Prunus Cerasus* + Nicotine)	6.13± 0.44	6.13 ± 0.44 $^{\beta}$
Group 8 (600mg/kg B.W. of *Prunus Cerasus* + Nicotine)	7.56 ± 2.91	7.56 ± 2.91 $^{\beta}$

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

Morris Water Maze (MWM): there was no significant difference at the initial reading but in the final reading, which is after 24 hours, there was a significant difference between the positive control and the negative control. There is also a significant difference between positive control to that of the *Prunus* + positive control group.

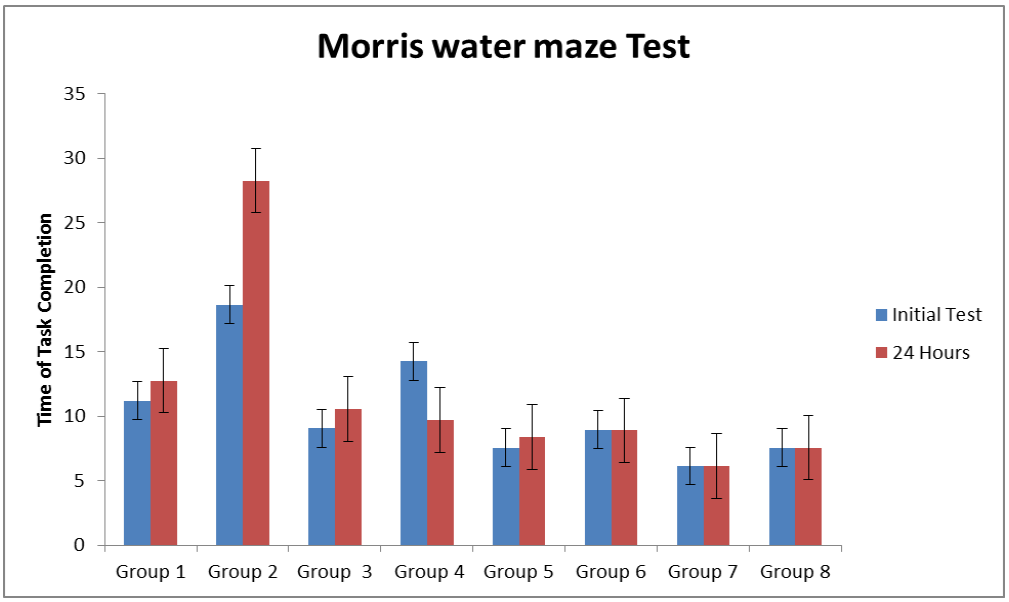

Fig 3: Bars Representation of result of the Assessment of Spatial Learning and Memory using the Morris water maze.

Table 4: Showing result from Hand-grip Performance Task.

Groups	Gripping Latency		
	Zero Minute (Sec± SEM)	**Thirty Minutes** (Sec± SEM)	**One Hour** (Sec± SEM)
Group 1 Control saline	19.60± 5.70	9.93 ± 4.44	12.80± 5.57
Group 2 Nicotine only	13.83 ± 1.25	5.53± 2.26	15.83± 3.86
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	8.60 ± .927 $^{\alpha}$	5.02± 2.25	21.20± 4.97
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	7.25± 1.03 $^{\alpha}$	3.42± 1.71	24.50 ± 9.74
Group 5 (600mg/kg B.W. of *Prunus Cerasus*)	7.00± 1.08 $^{\alpha}$	9.27 ± 4.64	26.00 ± 7.034
Group 6 (200mg/kg B.W. of *Prunus Cerasus* + Nicotine)	8.60± 1.91	7.267± 3.25	16.40± 8.26
Group 7 (400mg/kg B.W. of *Prunus Cerasus* + Nicotine)	7.75± 2.59	5.19± 2.59	14.00 ± 6.49
Group 8 (600mg/kg B.W. of *Prunus Cerasus* + Nicotine)	12.25 ±3.25	5.89± 2.94	12.25± 5.79

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

The table above shows a significant difference between the *Prunus* group and the control in the first aero minutes and no difference in the subsequent minutes and also there is no significant difference between the *Prunus* group and positive control group and positive and the *Prunus* + positive control group.

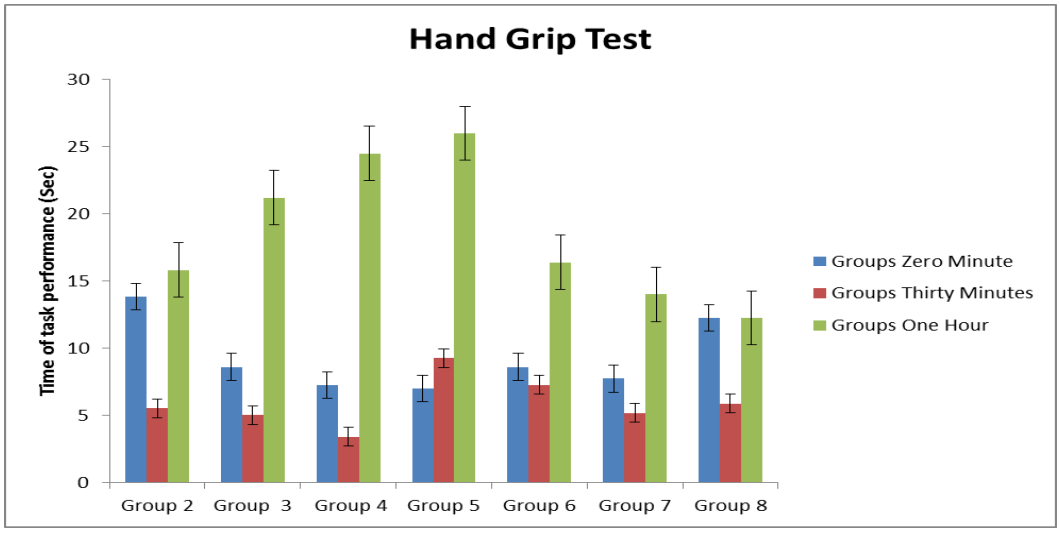

Fig. 4: Bars Representation of result from Hand-grip Performance Task.

Table 5: Assessment of Memory Retention Latency using the passive avoidance test.

Groups	No of shock Received (Count±SEM)	Avoidance Latency [Percentage (%) Avoidance per Time]				
		Half Hour (Sec±SEM)	One hour (Sec± SEM)	Two hour (Sec± SEM)	Twenty-four hour (Sec± SEM)	Ninety-six hour (Sec± SEM)
Group 1 (Control)	1.40 ± 0.25	100	100	100	100	40
Group 2 Nicotine only	2.00± 0.37 $^{\alpha}$	100	100	100	0	0
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	1.00 ± 0.00	100	100	100	100	100 $^{\alpha}$
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	1.00 ± 0.00	100	100	100	100	100 $^{\alpha}$
Group 5 (600mg/kg B.W. of *Prunus Cerasus*)	1.25 ± 0.25	100	100	100	100	100 $^{\alpha}$
Group 6 (200mg/kg B.W. of *Prunus Cerasus* + Nicotine)	1.00 ± 0.00 $^{\beta}$	100	100	100	100 $^{\beta}$	100 $^{\beta}$
Group 7 (400mg/kg B.W. of *Prunus Cerasus* + Nicotine)	1.00± 0.00 $^{\beta}$	100	100	100	100 $^{\beta}$	100 $^{\beta}$
Group 8 (600mg/kg B.W. of *Prunus Cerasus* + Nicotine)	1.00 ± 0.00 $^{\beta}$	100	100	100	100 $^{\beta}$	100 $^{\beta}$

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control

Passive avoidance test: it is a measure of learning and memory. The table above shows a significant difference between the positive control and the negative control in the number of shock received and also a significant difference between the positive control and the *P.Cerasus* + positive control group. After 24 hour there was significant difference between the *P.Cerasus* + positive control group with positive control group. From the table a significant difference is seen also after 96 hours between the *P.Cerasus* group with the negative control group and also a significant difference between the *P.Cerasus* + nicotine group and positive control group.

Table 6: Showing Result from the Rotarod Test after exposure of Test animals to various Test substances.

GROUPS	Rotarod Performance Test
Group 1 Control	26.33±3.73
Group 2 Nicotine	18.28±3.78
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	26.47±7.56
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	12.58 ±1.43 $^{\alpha}$
Group 5 (600mg/kg B.W. of *Prunus Cerasus)*	11.87±1.57 $^{\alpha}$

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

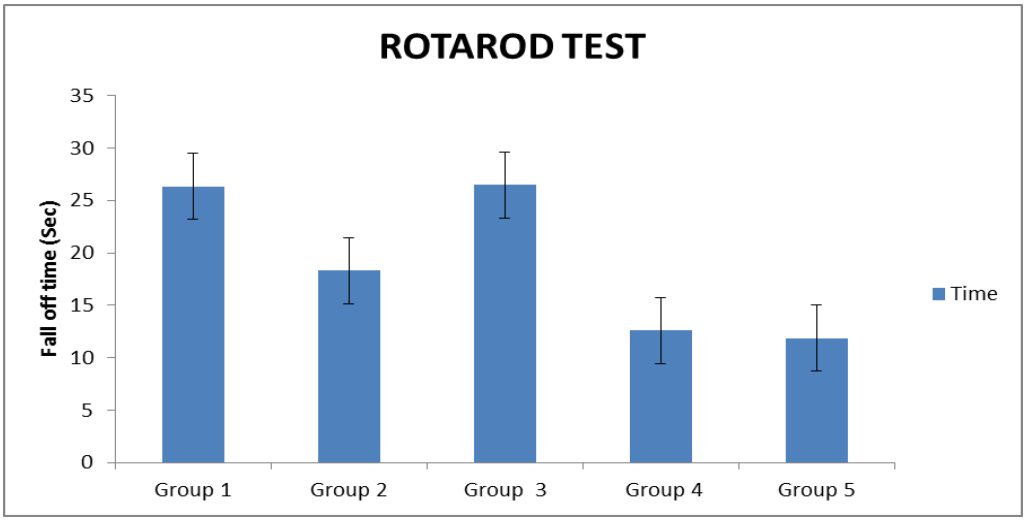

Fig 6: Bars Representation of Result from the Rotarod Test after exposure of Test animals to various Test substances.

Table 7: Showing Result from the elevated Plus Maze Test After exposure of test animals to test substances.

GROUPS	Elevated Plus Maze Test			
	Open arm entry Count±sem	Time in open arm (sec±sem)	Close arm entry Count±sem	Time in close arm (sec±sem)
Group 1 Control	1.13±.0.13	16.73± 3.71	3.40±.0.67	163.13±4.19
Group 2 Nicotine	1.39±.0.26	16.89±2.02	3.00±.0.37	160.33±1.65
Group 3 (200mg/kg B.W. of *Prunus Cerasus*)	1.33± 0..28	20.80±8.92	2.93 ± 0..25	154.93±8.88
Group 4 (400mg/kg B.W. of *Prunus Cerasus*)	1.00± .23570	16.27±7.19	2.67± 0.46	161.46±7.38
Group 5 (600mg/kg B.W. of *Prunus Cerasus)*	0.80 ± 0.13	16.67± 5.44	1.73± 0 .25	160.60 ±6.38

Values are presented in mean ± SEM; $^{\alpha}$ statistically significant compared to the Negative control; $^{\beta}$ statistically significant compared to the Positive control.

Elevated plus Maze: from the table above there is no significant difference between the positive control and the negative control and also there is no signify difference between the positive control group and *P.Cerasus* + positive control group, Rotarod: the table shows a significant difference between the positive and the control group.

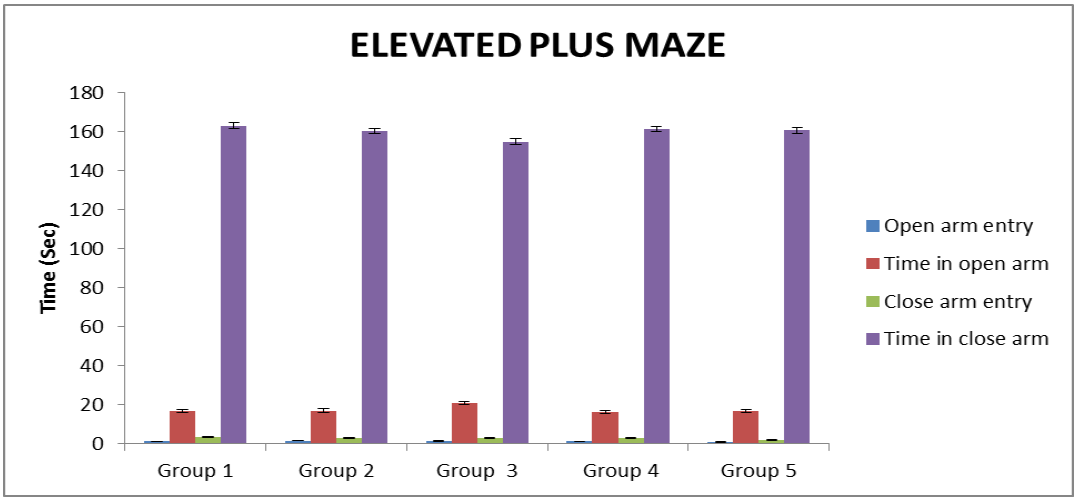

Fig. 7: Bars Representation of Result from the elevated Plus Maze Test After exposure of test animals to test substances

DISCUSSION OF RESULTS

The study demonstrated that daily consumption of *P.Cerasus* improves cognitive functions in a dose dependent manner. From the study, it was observed that in most tasks of memory and cognition, 400mg/kg was more reactive than 200mg/kg and 600mg/kg, within the time interval of 3 minutes and 600mg/kg is less reactive than 400mg/kg, after a 15 minutes acquisition period has been established as compared to the negative control and the nicotine group. In Navigational maze task and Morris water maze tasks 400mg/kg was seen to be more reactive to *P.Cerasus* co-administered with nicotine as compared to Nicotine group. The improve in cognition concur with the work of (Nopporn et al, 2016). that *P.Cerasus* have some beneficial effect on memory and cognition as the dosage increases. The cognitive enhancing properties is attributed to the bioactive phytochemicals that scavenge the body to get rid of free radicals or it could be due to the neurogenetic functions of the phytochemicals as was demonstrated in the work of (Darshan S. Kelley, 2018). It was a;lso demonstrated in Barnes maze task that 200mg/kg *P.Cerasus* was more reactive as compared to the negative control, furthermore 200mg/kg of *P.Cerasus* co-administered with Nicotine was also more reactive as compared to the Nicotine group. the enhancement is attributed to the phytochemicals that function via their antioxidant actions that assist to scavenge free radicals in the brain while their neuro-protective effects include protection of vulnerable neurons against inflammation, enhancement of existing neuronal function, increased blood flow to the brain and neurogenesis initiation in areas of the brain that are associated with cognition. (Noppom *et, al*, 2016;Barbara, et al, 2016.) Similarly, the study also revealed that there was a significant difference in cognitomotor activities in hand grip and Rotarod tasks. It was observed that *P.Cerasus* have a significant difference in cognitomotor activities. Evidence from published reports is reasonably strong to indicate that consumption of *P.Cerasus* decreased markers for oxidative stress, inflammation, exercise-induced muscle soreness and loss of strength, As was observed from previous study (Darshan S. Kelley, 2018;Takeshi, et al, 2012) the fruit is beneficial in motor learning and restore muscular strength. No significant difference was observed in elevated plus maze task, this may suggest that *P.Cerasus* as no effect on anxiety.

CONCLUSION

The study demonstrated that *P.Cerasus* at a dosage of 400mg/kg and 200mg/kg in Morris water maze, Navigational maze task and Barnes maze tasks respectively enhanced memory and cognition. And at a dosage of *600mg/kg P.Cerasus* reinforced memory and cognitive impairment. Furthermore, from hand grip task and Rotarod tasks the study demonstrated *P.Cerasus* as significant effect on cognitomotor functions. The result from the study suggested that *P.Cerasus could* serve as natural supplement in enhancing memory activities and alleviating amnesia.

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