EVALUATION OF THE EFFECT OF KHAT (*Catha edulis*) Forsk ON SPATIAL LEARNING AND MEMORY IN CBA MICE USING THE MORRIS WATER MAZE TASK.

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SUMMARY

Khat (*Catha edulis* Forsk) is a psychoactive plant commonly used in East Africa, horn of Africa and the Arabian peninsula. Its effects are mainly modulated through the dopaminergic system similar to amphetamines. Psychoactive substances/drugs of abuse effect their changes centrally by acting on the brain, altering the neurotransmitter system and structurally affecting the limbic Papez system. These substances can affect learning and memory by interfering with the medial temporal lobe structures and thus affecting spatial learning and memory. This study evaluated the effect of khat on CBA mice using a Morris water maze task which is a test of spatial learning and memory. Twenty CBA mice were divided into 5 groups and administered, intraperitoneally, 0.5 mls normal saline, 40, 120, and 360 mg/kg body weight of khat extract, respectively. The doses were given once daily for 17 days during which the animals were submitted to acquisition, reversal learning and reference tests in the Morris water maze. The study also investigated the effect on learning and memory of escalating, repeated high (run) doses of khat extract given to CBA mice. Twenty nine CBA mice were divided into groups of 5-7 animals. The animals were first subjected to an escalating dose regime and then followed by repeated high (run) doses, or an escalating dose regime followed by single daily dose, or an escalating dose regime followed by saline or saline followed by escalating dose regime of khat extract. The mice were tested in a Morris water maze for spatial learning and memory. The escape latency, swim path length, swim speed, quadrant time and quadrant swim distances were measured by the use of stop watch and video recording tracings.

The data were analyzed using SPSS statistical package, in which multivariate analysis of variance (MANOVA) was carried out on the independent variables (days, doses,
and groups) against the dependent variables (escape latency, swim distance, swim speed). Bonferroni post hoc tests were carried out on dependent variables, and $P < 0.05$ was considered significant.

High doses of khat extract (360 mg/ kg body weight) significantly increased ($P < 0.05$) the line crossings while low doses (10, 30, 40 and 120 mg/kg) and very high doses (540 mg/kg) body weight of khat extract had no effect on line crossings in Swiss and CBA mice. High doses (120, 270, 360 mg/kg) body weight of khat extract significantly ($P < 0.05$) inhibited the centre square and rearing frequencies in the two species of mice, whereas, low doses (10, 30, 40 mg/ kg) body weight of extract significantly increased ($P < 0.05$) the two measures. Repeated khat treated CBA mice had significantly ($P < 0.05$) higher line crossings than Swiss mice treated with the same dose. Similarly, the centre square and rearing frequencies were significantly higher ($p < 0.05$) in CBA mice than the Swiss mice and the control. The study demonstrates that repeated khat causes behavioural sensitization in mice and affects locomotor behaviors similarly regardless of the dose regime.

Mice treated with higher (360 mg/kg body weight) khat extract had their learning and memory significantly ($P < 0.05$) impaired. The extract, further significantly ($P < 0.05$) impaired learning and memory of CBA mice at higher (360 mg/ kg body weight) during reversal sessions. The study shows that higher dose (360 mg/kg body weight), behavioural switching in CBA mice was interfered with as evidenced by the mice spending more time and swimming longer distances in the former platform quadrant as opposed to the current target platform quadrant.
Mice treated with escalating then repeated runs (Binge) regimen of khat extract significantly ($P < 0.05$) improved their learning but their retention were also significantly ($p < 0.05$) impaired. Khat extract administered as escalating followed by single daily dose, significantly ($P < 0.05$) improved their learning as well as memory, whereas, mice injected with saline then repeated high doses of khat extract had their learning and memory adversely affected. In addition, CBA mice treated with escalating dose followed by saline had their learning and memory impaired. The study shows that khat extract at a high dose adversely affected learning and memory though, the mechanism of this is not clear, but could involve the dopaminergic neurotransmitter system.