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THE ACUTE EFFECTS OF HYDRO-ALCOHOLIC KHAT (*CATHA EDULIS FORSK*) EXTRACT ON LOCOMOTORS AND ANXIETY BEHAVIOURS IN MICE

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ABSTRACT This in *vivo* random experimental animal study was conducted to evaluate the acute dose- and time- responses of crude *Catha edulis* extract on locomotors activity and anxiety-like behaviour in mice. A total number of 24 mice were used for this study. Serum was collected after the onset of oral administration of 100, 200 and 400mg/kg doses. The locomotors and anxiety- like behaviours were tested in the mice by subjected them to light /dark box activity test for an hour after oral administration. Data were acquired by the surveillance video tracking data acquisition system. results shown an increase in motor activity, and induce anxiety-like behaviours following the initial 15 to 20 minutes of anxieolytic-like effects with respect to dosage (4 groups, n=6 for each group). The increased locomotors activity is more likely induced by *Catha edulis's* ability to enhance dopaminergic transmission from dopaminergic neurons like substantial nigra compacta to striata of the basal ganglia and retarding dopamine reuptake effect of Cathinone. The initial anxieolytic effect of *Catha edulis* more likely associated with more rapid onset of action of Cathinone, which agrees with its higher lipophilic character that facilitating entry into the CNS and a shorter duration of action, which agrees with the rapid metabolism of Cathinone.

KEYWORDS : *Catha edulis,* locomotors activity, anxiety like behavior

INTRODUCTION

Khat chewing has a history of at least seven centuries in Ethiopia as a mild-stimulant plant. A survey of 3200 respondents across Ethiopia had shown that, the use of khat has become popular among all segments of the population and in all parts of Ethiopia (Selassie and Gebre, 1996). Recently khat chewing estimates of the prevalence of the country (Alem *et al*., 1999) approach 50%, with 17% self-described as daily users, predominantly men (a reported 5:1 male to female ratio). Ethiopia is the world's largest producer of khat, which is the country's fastest growing export. About a third of the production is exported to Djibouti and Somalia, but the bulk of it is marketed and consumed within the country, mostly in the Somali administrative region (Green, 1999). The effects of khat chewing were reported in the literature as early as 1237 by the Arabian physician Naguib Ad din (Lebras and Fretillere, 1965), who proposed the use of khat for the treatment of depressive states. By the same year, other writers also reported that it was effective in blunting the sensation of hunger and fatigue (Krikorian, 1984; Lebras and Fretillere, 1965).

People chew since khat contains psychoactive components namely, Cathinone and Cathine which are able to stimulate central nervous system, increases locomotors activity and results in sympathomimetic effect which are analogous to the effects of amphetamine (Kalix, 1990). Because of their psycho-stimulant properties, fresh, young shoot and tender leaves of khat are commonly chewed in eastern Africa and Arabian Peninsula countries for hundreds of years to attain a state of euphoria as well as to alleviate fatigue, enhance work capacity, stay alert, reduce hunger, and to enhanced self-esteem (Ageely, 2009).

Khat leaves contain Cathinone (Benzoylethanamine) and Cathine (Nor pseudoephedrine) which are believed to be responsible for most of the pharmacological actions of khat due to their similarity in structure and activity to amphetamines (Wagner *et al*., 1982). These two alkaloids act by increasing levels of dopamine (DA), serotonin and noradrenalin (Kalix and Braenden, 1985). For this reason khat is also called a "natural amphetamine." In addition to khat, large amounts of non-alcoholic drinks are also consumed during chewing. There is pharmacological synergism with drinks containing methylxanthines (e.g. tea and cola), which therefore enhances the effects of khat.

Cathinone, the active ingredient of khat, has been characterized as an amphetamine-like sympathomimetic amine (Kalix, 1996) with a half-life of approximately 3hrs in humans (Widler *et al*., 1994; Toennes *et al*., 2003). It is believed to contribute for the major pharmacological effects such as euphoria, alertness and anorexia. According to Toennes and Kauert (2002), Cathinone, which has shorter half-life than Cathine, can only be detected in blood about 10 hours after ingestion. It is eliminated almost exclusively in the form of norephedrine and only about 2% of it remains unchanged. The biotransformation of Cathinone to norephedrine consequently increases the concentration of norephedrine to be excreted. Unlike Cathinone, Cathine has longer half- life and it is eliminated very slowly (Tariq *et al*., 2002). Cathinone reaches a maximum plasma level 1–2hrs after oral administration; the effect of Cathinone on the user occurs more rapidly than the effect of amphetamine, roughly 15 min as compared to 30 min (Cho and Kumagai, 1994).

In experimental animals, khat extract causes gastritis and duodenitis (Kalix, 1992). Apart from these, chronic khat use causes neurodegenerative disease resulting in CNS problems (Carvalho, 2003). The symptoms for central nervous system problems are

anorexia, insomnia (delayed bedtime), late wake up the next morning and low performance the next day, which might be due to the central and peripheral actions of Cathinone and Cathine in the khat. This is likely to be associated with reduced functioning of dopamine D2 (dopamine D2 receptors) receptors in the striatum and dysfunctions in Prefrontal Cortex (PFC) and Orbitofrontal Cortex (OFC) – areas that have been shown to play major roles in the control of goal-directed action. DA plays a key role in inhibitory action control (Colzato *et al*., 2009, 2010). As long as *Catha edulis* has central nerve system stimulating and pleasurable effect on the basis of the previous study, we postulate that it may induce anxieolytic effect. Thus, the objective of this works is to assess a dose response of *Catha edulis* extract (as psycho stimulant) on locomotors and anxiety behaviors in mice.

MATERIALS AND METHODS

Fresh Khat Collection

Six bundles of fresh khat of "Aweday" type were purchased at a local market from one retailer in Bole ,Addis Ababa, who received daily supply from Aweday, its natural habitat, 525 km South of Addis Ababa, Ethiopia. Then these fresh materials of Khat were wrapped in a plastic bundle as chewers do and taken to Ethiopian food and nutrition research institute, for extraction. The fresh materials were washed to remove dust and debris with distilled water.

Extraction

Shoot leaves were collected, and chopped/ crushed with pestle and mortar on a glass plate and weighted (500 grams) by electronic digital balance and placed in Erlenmeyer flasks (≤200g per flask) wrapped with aluminum foil to avoid light induced decomposition. And then ethanol (70%) was added to cover the minced leaves in ratio of 4mL: 1g. Then, put in to rotary /orbital shaker (DS-500) for 24 hrs at the speed of 120rpm at ambient temperature under dark condition. Then filtered the filtrates with Whatman filter paper # 1 and collected and kept in another flask. Rotary evaporator (RE300) is used to remove all traces of ethanol which was used for extraction at a digital water path (RE300DB) at a speed of 3 rotations per second, 40^0c temperature and 70kpa vacuum pump (RE3022C) pressure. Finally, the fraction was left overnight in a deep freezer and then lyophilized using freeze dryer (Christ 100400 Bio block Scientific, France) and approximately 40 gram of crude khat extract was yield.

Experimental animals preparation and its habituation

For this experiment, all experimental animals (24 male) were obtained from Ethiopian food and nutrition research institute, department of Laboratory animal breeding. The animals were housed in mice cages in physiology lab, Department of Physiology, Black Lion Specialized Hospital, Addis Ababa University.

Description of experimental apparatus and its habituation Procedure

The light/dark box (45 x 27 x 27 cm): It is made of plywood and consisted of two chambers connected by an opening (7.5 x 7.5 cm) located at floor level in the center of the dividing wall. The floor is divided into 9 x 9 cm squares and is covered with Plexiglas. The smaller chamber (18 x 27 cm) was painted black and the larger chamber (27 x 27 cm) was painted white. This apparatus was placed on the other side of the wall where the Surveillance Video Tracking System (Animal activity monitoring system) is located (Costall *et al*., 1989)

Surveillance video tracking system: It is an animal activity monitoring system. It is a video camcorder located approximately 120cm above the center of the maze and record mouse behavior and locomotors activities on computers for later analysis.

METHODS

Study Design: Laboratory based experiment involving quantitative and descriptive analysis of data.

Study Area: Laboratory of Department of Physiology, Faculty of Medicine, Addis Ababa University; Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia.

Study protocol: A total number of 24 male mice weighted (25-32g) were used. They were divided into 4 groups of 6 mice in each group. The cages were cleaned, bedding and changed every other day. The mice were kept on a twelve-hour light/dark cycle and fed on standard rodent pellets and water *ad libitum*. The study was conducted in accordance with the internationally accepted principles for laboratory animal use and care (NIH publication # 85 – 23 revised 1985).Each mouse was habituated to the experimental set up by transferring it to the observation chamber for 30 minutes daily for five days before the start of the experiments. All experimental procedures on mice were conducted during the light cycle. In the subsequent days, these twenty four mice were taken from the cage and weighed using electronic digital balance in order to group and determine the dose which is administered. The mice were divided in to four categories; one control and three treatment groups (100,200 and 400mg/kg). Each of the control group mouse administered normal saline of 0.5ml/kg orally via oral gavages. Using a predetermined schedule based on doses of fresh khat extract solution (1g: 5ml) with the respective dose (100,200 and 400mg/kg.). Each mouse was then placed in the center of the white chamber facing the opening were allowed to explore the apparatus and observed at five minutes interval for fifty five minutes as described by (Bures *et al*., 2009). After 30 minutes, each mouse was removed from the box by the base of their tails and returned their home cage. The maze was then cleaned with the solution of 70% ethyl alcohol and permitted to dry between tests. An observer sitting quietly about 1m from the apparatus recorded the behaviour of mice in the box. A video camcorder located approximately 120cm above the center of the maze recorded mouse behaviour and locomotors activities which was displayed on computers. Behaviours were later scored by video play back using Hindsight for MS-Dos Version 1.5 computer soft ware for later analysis. Each mouse was used only once to avoid the possibility of developing tolerance, drug toxicity or both. Prior to experiment all mice were clinically observed and screened for any abnormal behaviour, physical abnormalities at least once daily.

Behavioural parameters

In light dark activity box test apparatus, transitions and rearing frequencies, locomotion, grooming, dark box and light box durations behavioural parameters were measured. These include transition frequency; rearing frequency, grooming (time spent in active sitting) and time spent in movement were measured as indices of motor activity for 60 min (Kimani *et al*., 2008). Values of these parameters were calculated in every 5 min over an hour.

Operational definitions & its way of calculation

Transition: - was scored by number of times the animal passes in or out of the light and dark chambers. Rearing by the number of times the mouse lifted itself on its hind limbs with both forelimbs off the ground or leans against a wall of the box with its front paws, and grooming when a mouse placed its tongue on its paws or other body parts/grooming the body while stationary.

Dark box duration: was measured by the length of time the animal spent in the dark sides of the box, while the light box duration the length of time the animal spent in the light sides of the box. The five minute observation period was divided into twenty seconds intervals and each behaviour was scored as follows: 0 when no movement occurred, 1 when movement occurred for 5 seconds, 2 when movement occurred for 10 seconds, 3 when it occurred for 15 seconds, and 4 when it occurred for 20 seconds. Overall score of the five minutes observation period represented the summation means of every 20 seconds activity. They were put in light dark box to record their locomotors behaviours before khat administration. They were given khat through the intragastic /oral gavages. Their behaviours were recorded using surveillance video tracking system on computers for later analysis. Frequencies of transition, grooming,

rearing, dark box durations and light box durations were specific behaviour parameters used for calculations. Values of these parameters were calculated in every 5 min for one hour. After the experiments, video tapes were replayed and the measurements of locomotors activity as well as anxiety were manually tallied and their means calculated and then these behaviour parameters are compared and determined the acute effects of the plant extract on these behaviours.

Principles

When given a choice between dark and light open areas, rodents naturally tend to explore the dark environment. Avoidance of light spaces is believed to reflect their aversive or "anxiety-provoking" properties. When treated with anxiolytic drugs, rodents spend more time in these areas, an effect purportedly due to a decrease in anxiety. Thus, the light-dark exploration task has been used to assess the anxiolytic or anxiogenic properties of drugs, as well as anxiety-related phenotypes of genetically manipulated animals. The data are subsequently reduced to the following parameters in each area: Transitions frequency, rearing frequency, grooming, time spent in dark box, time spent in light box, and time spent in active movements based on the innate aversion of rodents to brightly illuminated areas and the spontaneous expletory behavior of rodents in response to mild stressors, that is novel environment and light (Crawley and goodwin, 1980). Transitions have been reported to be an index of activity-exploration because of habituation over time, and the time spent in each compartment to be a reflection of aversion. Activities like frequency of rearing, time spent in active sitting (time spent actively grooming and tending to move) and time spent in movement are reduced to locomotors activity. The extent to which an anxiolytic compound can facilitate exploratory activity depends on the baseline level in the control group.

Statistical analysis

All data for transition, rearing frequencies, light and dark box durations, movement and grooming duration were expressed as mean ± SE.M. The differences in the mean values of these parameters among groups were analyzed using multivariate ANOVA followed by Tukey's multiple comparison tests. The level of statistical significance was set (at most $p < 0.05$).

RESULTS

The acute dose responses of *Catha edulis* extract on locomotor and anxiety like -behaviours

The acute dose response of *Catha edulis* extract had shown significantly enhanced locomotors activity and elicited anxiogenic behaviour progressively following the initial 15 to 20 minutes anxiolytic like effect in mice. This result depending on the value measured, analyzed and compared from the parameters that are considered as indicators for the analysis of behavioral study.

Dose response of *Catha edulis* extract on transition frequencies

As shown in table 1, the mean transition frequencies of Rx400 ($P< 0.001$), and Rx200 ($P< 0.05$) mice had significantly higher than the baseline (CG); while Rx100 mice had better transition frequencies than the baseline, though it had shown insignificant change.

Table 1: Dose related effects of *Catha edulis* extract on the transition frequencies per each 5 minutes over one hour duration light/dark box activity test in mice.

Groups	Dose administrated	Transition frequency (f) (Mean ± SE.M)	Min.	Max.	Level of significance
CG	0.5ml normal saline	3.47 ± 2.41	1.2	7.2	
Rx100	100mg/kg *C. edulis*	4.2 ± 1.83	1.8	7.5	P>0.05
Rx200	200mg/kg *C. edulis*	7.42 ± 1.39 *	5.2	9.3	P<0.05
Rx400	400mg/kg *C. edulis*	9.45 ± 2.23 **	6	13.4	P<0.001

Data were expressed as mean ± SE.M; ** highly significant,* significant; CG=control group, Rx100, Rx200, and Rx400 are 100,200 and 400mg/kg oral *Catha edulis* extract administrated mice; while Min & Max are minimum and maximum transition frequency values respectively.

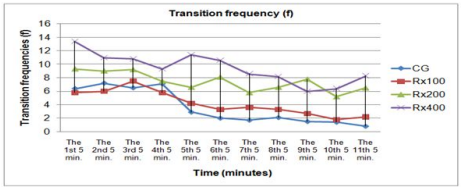

Figure1. Acute dose response of *Catha edulis* extract on transition frequencies per 5 minutes over one hour duration light/dark box activity test.

Dose response of *Catha edulis* extract on rearing frequencies

Table 2 shows the mean rearing frequencies of Rx100, Rx200 and Rx400 mice had shown significantly ($P < 0.001$) lower as compared to baseline both in the dark and light boxes.

Table2: Acute dose response of *Catha edulis* extract on rearing frequencies per each 5 minutes over one hour duration light/dark box activity test in mice.

Groups	Dose administrated	Rearing frequency (f) mean ± SE.M		Level of significance
		LB	DB	
CG	0.5ml normal saline	6.63 ± 4.06	3.58± 2.69	
Rx100	100mg/kg *C. edulis*	1.45 ± 0.87 *	0.58± 0.82 *	P<0.001
Rx200	200mg/kg *C. edulis*	0.42 ± 0.43 *	0.32 ± 0.54 *	P<0.001
Rx400	400mg/kg *C. edulis*	0.28 ± 043 *	0.06 ± 0.15 *	P<0.001

Data were expressed as mean ± SE.M; * significant, DB=dark box, LB= light box; CG=control group, Rx100, Rx200, and Rx400 are 100,200 and 400mg/kg oral *Catha edulis* administrated mice respectively.

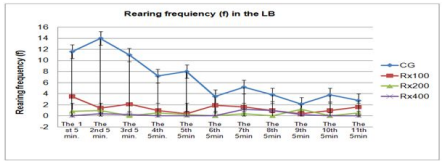

Figure2. The acute dose response of Catha edulis extracts on rearing frequencies per each 5 minutes over one hour light/dark box activity tests.

The acute dose response of *Catha edulis* extract on time spent in the dark box

As shown in table 3, the mean time spent of Rx400 and Rx200 mice in the dark box had shown significantly ($P < 0.001$) higher as compared to the baseline (CG) and Rx100.

Table 3: The acute dose response of *Catha edulis* extract on duration (time spent) in each compartment per each 5 minutes in mice over one hour duration activity test.

Groups	Dose administrated	Duration (Seconds)						Level of Significance
		LB			DB			
		Mean ± SE.M	Min.	Max.	Mean ± SE.M	Min.	Max.	
CG	0.5ml normal saline	90.02 ±44.63	37.8	147	210.14± 44.41	153	262.2	
Rx100	100mg/kg *C. edulis*	89.98 ± 24.28	50.2	135	200.02 ± 26.52	149.8	249.8	
Rx200	200mg/kg *C. edulis*	59.06± 28.24	33.4	104.6	240.92 ± 28.24 *	189	266.6	P< 0.001
Rx400	400mg/kg *C. edulis*	51.52 ± 41.51	18.6	133.4	249.04 ± 40.05 *	174.2	281.4	P< 0.001

Data were expressed as mean ± SE.M; * significant, DB=dark box, LB= light box; CG=control group, Rx100, Rx200, and Rx400 are 100,200 and 400mg/kg oral *Catha edulis* administrated mice respectively.

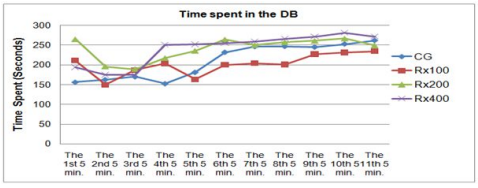

Figure3. An acute dose responses of *Catha edulis* extract on time spent in the dark box (DB).

The acute dose response of *Catha edulis* extract on movement duration

As shown in table 4, the mean movement duration of Rx400 (P< 0.001), and Rx200 (P< 0.05) mice had spent higher movement duration than baseline (CG); while Rx100 mice had better movement duration than CG mice, but it had shown no significant change (n = 6 mice in each group). Rx400 (P< 0.001), and Rx200 (P< 0.05) mice had spent 74.18% (184.76/249.04) and 62.16% (149.76/240.92) in movement of their total time duration in dark box respectively; while Rx100 mice and control groups had spent 44.65% (89.2/200.02) and 26.58% (55.87/210.14) of their total time spent in dark box respectively. Similarly, Rx400, 200, and 100 mice had spent 96% (49.47/51.52), 89.9% (53.15/59.06), 93% (84.24/89.98) of their total time in movement in the light box respectively and control groups had spent 77.5 (69.78/90.02) of their total time spent in this compartment.

Table4: Acute dose response of *Catha edulis* extract on movement duration in mice.

Groups	Dose administrated	Movement duration (Seconds) mean ± SE.M		Level of Significance
		LB	DB	
CG	0.5ml normal saline	69.78 ±36.81	55.87 .81	
Rx100	100mg/kg *C. edulis*	84.24 ± 22.51	89.32 ± 10.60	P> 0.05
Rx200	200mg/kg *C. edulis*	53.15 ± 25.42	149.76 ± 17.22 *	P< 0.05
Rx400	400mg/kg *C. edulis*	49.47 ± 39.01	184.76 ± 32.32 **	P< 0.001

Data were expressed as mean ± SE.M; ** highly significant, * significant, LB= Light box, DB= Dark box; CG=control group, Rx100, Rx200, and Rx400 are 100,200 and 400mg/kg oral *Catha edulis* administrated mice respectively.

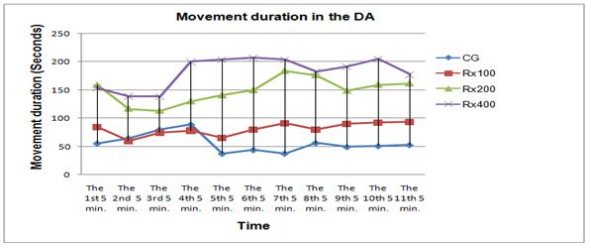

Figure 4: The acute dose response of *Catha edulis* extract on movement duration of mice in the DA (dark area).

The acute dose response of *Catha edulis* extract on grooming duration

Table 5 showed the mean grooming duration of Rx400, 200, and 100 mice had shown significantly (p<0.05) lower duration in both compartments as compared to the baseline.

Table5: Acute dose response of *Catha edulis* extract on grooming duration in mice.

		Grooming duration (Seconds) (mean ± SE.M)		Level of significance
		LB	DB	
CG	0.5ml normal saline	10.77± 19.99	111 ± 75.63	
Rx100	100mg/kg *C. edulis*	1.1 ± 2.14 *	1.45 ± 2.56 *	P<0.05
Rx200	200mg/kg *C. edulis*	0 ± 0 *	0.9 ± 2.42 *	P<0.05
Rx400	400mg/kg *C. edulis*	0 ± 0 *	1.02 ± 2.58*	P<0.05

* Highly significant; data were expressed as mean ± SE.M; LB= Light box, DB= Dark box; CG=control group, Rx100, Rx200, and Rx400 are 100,200 and 400mg/kg oral *Catha edulis* administrated mice respectively.

DISCUSSIONS

The light/dark test is based on the innate aversion of rodents to brightly illuminated areas and on the spontaneous exploratory behavior of rodents in response to mild stressors, that is, novel environment and light (Crawley and Goodwin, 1980). This test is useful to predict anxiolytic-like or anxiogenic-like activity in mice. Transitions have been reported to be an index of activity-exploration because of habituation over time, and the time spent in each compartment to be a reflection of aversion. In the test, an increase in transitions without an increase in spontaneous locomotion is considered to reflect anxiolytic activity (Michel and Martine, 2002). On the other hand, an increase in rearing frequencies is reflective of increased locomotion, exploration and/or a lower level of anxiety (Brown *et al*., 1999; Podhorna and Brown, 2002). Anxiolytics have been found to increase locomotion and time spent in the light zone, whereas anxiogenics decrease them (Imaizumi *et al*., 1994), and mice placed in the brightly lit white area shown a reduced latency in moving into the black section, an increase in time spent in the black section, with markedly increased rearing and line crossings in this area, whereas all such measures are markedly decreased in the white section (Shimada *et al*., 1995).

Studies carried out using laboratory animals, have reported increased locomotors activity in rats fed with *Catha edulis* (Maitai, 1977). According to Kalix (1990), people chew khat as it contains psychoactive components namely, Cathinone and Cathine which are able to stimulate CNS, increase locomotors activity and result in sympathomimetic effect which are analogous to the effects of amphetamine. Similarly, other studies have presented evidence showing that (-) Cathinone is capable of producing conditioned place preference in rats at a dose (1.6 mg/kg) that produces increased locomotors activity (Calcagnetti and Schechter, 1992). Elsewhere, repeated oral administration of a standardized *Catha edulis* extract (at a dose of 1 mg Cathinone per kg body weight) or (-) Cathinone (1.5 mg/kg) to rats appeared to induce a strong locomotors sensitization (Banjaw *et al.,* 2005). Khat at 200 and 300 mg/kg dose as well as amphetamine (50 mg/kg) produced a consistent improvement in motor performance. The effects observed were comparable and better than amphetamine (Berhanu and Ephrem *et al.*, 2010).

From this study, the results had shown that *Catha edulis* extract significantly enhanced locomotion and induced anxiogenic behavior progressively following the initial 15 to 20 minutes anxiolytic like effect in mice. This result depending on the value measured, analyzed and compared from the parameters we looked above. On the basis of this, the mean transition frequency of Rx400, and Rx200 mice had shown significantly higher transition frequencies (P < 0.001) and (P < 0.05) respectively than control group mice; While Rx100 mice had shown better transition frequencies than control group; this however had no significant effect. This had shown that the locomotors effect of *Catha edulis* improved as dose increased. Furthermore, the mean movement duration of Rx400 and 200 mice had significantly had taken higher movement duration (P < 0.001). This behavior particularly evident in horizontal and vertical spontaneous movements in the dark compartment than control ones, to which they spent their time more in active sitting (grooming activity) and less inactive sitting. With regard to the time spent in the two compartments, they also spent much greater time in the dark area than light area. On the contrary, the mean rearing frequencies of Rx100, 200 and 400 mice had shown lower rearing frequency (P < 0.001) as compared to control group both in the dark and light boxes. This is mainly occurred in the light box. On the basis of these parameters, though *Catha edulis* extract enhanced locomotors, exploration activity and elicited anxiogenic like effect progressively following the initial 15 to 20 minutes anxieolytic like effect. This is strengthened by the presence of higher time spent (duration) in the dark box compartment (200.02 ± 26.52, 240.92 ± 28.24,249.04 ± 40.05) than light box compartment 89.98± 24.28,59.06 ±28.24,51.52 ±41.51) of Rx100, 200, and 400 mice. However, time spent (duration) of saline-administered mice in the dark box also had shown higher time spent after 30minutes as Rx200 and Rx400 mice; but; they spent their time differently. While Rx200 and Rx400 mice spent more time in

spontaneous horizontal and vertical movements; saline-administered mice were spent their time more in active sitting (grooming activity) and less inactive sitting.

CONCLUSIONS

From the results of acute locomotors and anxiety behavioral of this study, We conclude that, acute oral administration of *Catha edulis* extract enhance locomotors activity as well as progressive anxiogenic behaviors following the initial few minutes (15 to 20 min.) of anxieolytic like effect after the onset of oral administration. This agrees with many previous researches done on locomotors as well as anxiety behavioral studies. The increased locomotors activity is more likely to be attained by *Catha edulis's* ability to enhance dopaminergic transmission from dopaminergic neurons like substantia nigra compacta to striata of the basal ganglia. Then, these GABAnergic neurons of the striata inhibit the external segments of the globus palidus, which are the output projections to thalamus suppressed tonically in normal condition. Thus, this inhibition of the inhibition releases the tonically suppressed thalamo-cortical activity and facilitates movement. In case of anxiety behavioral study done before in humans had shown, fresh Khat chewing elicited anxieolytic effects due to is euphoric effect of Cathinone which is partially contradicted with this study done in mice. This partial difference is probably due to the level of Cathinone to Cathine ratio in fresh khat shoots leaves are different from crude khat extract. Hence, isolation of the principal active component, Cathinone which is mainly found in the young leaves and shoots was released immediately within few minutes via chewing in the oral cavity while the khat extract prepared for this animal experiment via reagents and machines was released in few days of extraction processes. Thus, this may agree with the fact that when khat leave were dried, the more potent chemical, Cathinone, decomposes within 48 hours leaving behind the milder chemical, Cathine. Therefore, the initial few minutes of anxieolytic like effect may associate with higher level of Cathinone before it is rapidly metabolized in to its components. The later progressively elicited anxiogenic behavior more likely associate with release of the stress hormone releasing hormone (adrenocorticotrophin, ACTH),an increase adrnocortical function or sympathetic over activity as a result of the sympathomimetic action of Cathinone. To conclude, even though there was no similar experimental studies done before on the acute dose- and time- response of *Catha edulis* extract on locomotors and anxiety-like behaviors, the available findings done under various settings agreed well with this study.

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