

The effect of chewing Khat leaves on human mood

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ABSTRACT

Objective: Chewing fresh leaves of the Khat plant (*Catha edulis*), represents a widespread habit with a deep-rooted sociocultural tradition in Yemen. Khat is chewed for its central stimulant properties and to dispel feeling of fatigue and its use is believed to be associated with disturbance of mood. We studied the effect of chewing Khat leaves on human mood by using a standard questionnaire method, the Hospital Anxiety and Depression scale.

Methods: A prospective study was conducted in the Faculty of Medicine and Health Sciences, University of Sana'a during the period January to June 2000. It comprised 200 healthy volunteers, interviewed on 2 occasions a week apart. Subjects either chewed Khat at least 3 hours daily for 3 days or abstained from chewing for at least 7 days prior to mood assessment using the Hospital Anxiety and Depression scale. Subjects were studied in random order.

Results: Using the Hospital Anxiety and Depression scale, there was a significant increase ($P < 0.0001$) of median score on the scale indicating mood disturbance during the Khat-arm of the study as compared to the control-arm. The effect was particularly evident shortly after the Khat session. Reactive depression symptoms were predominant.

Conclusion: Khat chewing did result in functional mood disorder. This effect is believed to be caused by the sympathomimetic action of cathinone on the central nervous system. The clinical implication of this study is that Khat-chewing might exacerbate symptoms in patients with pre-existing psychiatric disease.

Keywords: Khat, *Catha edulis*, cathinone, Hospital Anxiety and Depression scale.

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There are many drugs of natural origin that man uses for altering mood. Some have become known and used worldwide, whereas others have remained more or less confined to the areas of their origin.¹ This is the case of the leaves of the Khat plant (*Catha edulis*). The plant *Catha edulis* belongs to the family of *Celastraceae*. Chewing its fresh leaves is a widespread habit with a deep-rooted sociocultural tradition in Yemen.² It is generally consumed in a social setting and chewed for its central stimulant properties and to dispel feelings of fatigue.³ The chemical constituents of the Khat leaves

which are thought to be responsible for the pharmacological actions are mainly the phenylalkylamine type alkaloids cathinone and cathine. The former is structurally related to amphetamine and has similar pharmacological actions.⁴ The more rapid and intense action of cathinone compared with cathine is explained by its higher lipid solubility, facilitating access into the central nervous system.^{1,5} In the central nervous system Khat chewing could manifest itself as moderate degree of euphoria and mild excitement resulting in promotion of social interaction and

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causing loquacity.⁵⁻⁸ While attaining a state of subjective well-being, the chewers feel an increase of alertness and energy together with enhanced depth of perception.^{1,3} These effects were found to be maximum between 1.5 – 3.5 hour after starting of the Khat chewing and they were progressively replaced by mild dysphoria, sedation,⁸ anxiety, reactive depression,^{2,9} insomnia^{2,9-11} and anorexia.^{2,9,12} Also, a number of reports of psychiatric disorders secondary to Khat chewing with different features of psychosis were documented.¹³⁻¹⁷ However, many of the limited studies available have methodological problems in objective assessment of Khat-induced mood changes. Therefore, the present study was aimed at examining the acute effect of Khat chewing on human mood in healthy adult volunteers using a standardized protocol, the Hospital Anxiety and Depression (HAD) scale.

Methods. Subjects. Two hundred healthy adult male subjects aged 19-38 years were involved in this study. They attended Khat chewing sessions in Sana'a, Republic of Yemen, each time at the same time of the day. They were not accustomed to chew Khat on a regular basis. All subjects denied any history of psychiatric or central nervous system disease and they were taking no medications or alcohol. All volunteers were told not to take tea, coffee or softdrink containing caffeine during the study, and to avoid smoking.

Measurements. The study was performed in 2 different sessions; one was the Khat-arm and the 2nd was the control-arm in the same environment but no Khat was taken. The sequence of Khat-arm and control-arm of the study was determined randomly, with one-week washout between the 2 arms. Height and weight measured by using standard methods and body mass index (BMI: kg/m²) was calculated. Each subject was interviewed to assess his mood status

using the HAD scale¹⁸ in both arms of the study. Those with evidence of clinically significant anxiety and depression symptoms at baseline were excluded from the study. The HAD scale defines ≤ 7 score = as non-case (absence anxiety or depression), 8-10 score = as borderline (anxiety or depression symptoms) and

11 score = as definite (anxiety or depression symptoms). This scale was filled by each subject 4 times in each session, one hour before chewing Khat leaves (baseline), 2-3 hours after starting to chew, one hour after spitting out the Khat leaves and 24 hours after starting Khat chewing. During the Khat-arm study each participant chewed a fresh bundle of the same type of Khat for at least 3 hours daily, and then spat out the leaves for each of the 3 study days. The average score of the 3 days was calculated, then the mean and median score was calculated, for analysis purpose. For purpose of analysis, participants were stratified into 3 groups, those with definite anxiety symptoms; those with definite depressive symptoms and those with combined definite anxiety and depression symptoms.

Statistical analysis. Statistical analysis was performed using a micro-computer Statistical Package for Social Sciences (SPSS) (SPSS Inc, Chicago, IL, version 9.0, 1999). Wilcoxon's Matched pairs test was used to assess the null hypotheses that score values on the HAD rating scale during Khat-arm study days will not be difference from those during the control-arm study days. Analysis of variance (ANOVA) was used for trend analysis. Ninety-five percent confidence intervals (CI) were calculated for single sample proportions in order to indicate precision of sample estimate and the variability of the characteristics being studied. A p-value of < 0.05 was taken as statistically significant.

Results. The median values (range) of subjects' age and BMI were 26 (19-38) years and 21 (19-26)

Table 1 - Trend analysis by ANOVA for the HAD-A and HAD-D mean (\pm standard error of mean) values of scores for Khat-arm and control-arm among Yemeni adult volunteers (N=200).

Mood status	Basal values (Zero time)	2-3 hours during Khat chewing	One hour after spitting out Khat chewing	24 hours after starting Khat chewing	ANOVA P-value
Khat-arm					
Anxiety	2.1 \pm 0.12	5.0 \pm 0.24	8.4 \pm 0.30	2.0 \pm 0.13	<0.001
Depression	2.7 \pm 0.13	6.0 \pm 0.25	12.0 \pm 0.31	2.8 \pm 0.14	<0.001
Control-arm					
Anxiety	2.2 \pm 0.13	2.1 \pm 0.12	2.1 \pm 0.12	2.1 \pm 0.10	NS
Depression	2.8 \pm 0.14	2.7 \pm 0.11	2.6 \pm 0.12	2.4 \pm 0.12	NS
NS - non-significant, HAD-A - hospital anxiety and depression-anxiety, HAD-D - hospital anxiety and depression-depression.					

Table 2 - The comparisons of HAD-A and HAD-D median scores (range) between Khat-arm and control-arm among Yemeni adult volunteers (N=200) by using Wilcoxon's Matched pairs test.

Mood status	Basal values (Zero time)		2-3 hours during Khat chewing		One hour after spitting out Khat		24 hours after starting Khat chewing	
	Anxiety score	Depression score	Anxiety score	Depression score	Anxiety score	Depression score	Anxiety score	Depression score
Control-arm								
Median	2	2	3	2	3	3	2	2
(range)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 7.0)
Khat-arm								
Median	2	2	5	6	8	12	2	3
(range)	(0.0 - 7.0)	(0.0 - 7.0)	(0.0 - 19.0)	(0.0 - 19.0)	(1.0 - 21.0)	(1.0 - 20.0)	(0.0 - 8.0)	(0.0 - 9.0)
p-value	0.134	0.184	0.0001	0.0001	0.0001	0.0001	0.088	0.06
HAD-A - hospital anxiety and depression-anxiety, HAD-D - hospital anxiety and depression-depression.								

kg/m². None of the participants in the 2 arms at baseline had anxiety or depression symptoms when tested by the HAD scale (≤ 7 score). There was no significant difference between the mean or median score values for anxiety and depression at baseline in the 2 study arms (**Tables 1 & 2**). By using ANOVA, our results in the Khat-arm showed a significant and progressive increase in mean score values for anxiety and depression at 2-3 hours after starting to chew Khat ($P < 0.0001$ for each) and one hour after spitting out Khat leaves ($P < 0.0001$ for each) compared with mean baseline scores. On the contrary, the control-arm study days showed no significant increase in mean score values of symptoms of anxiety and depression (**Table 1**). Median score values of anxiety and depression after chewing Khat for 2-3 hours were significantly higher ($P < 0.0001$ for each) than those at the corresponding times in the control-arm. The same significant difference persisted one hour after spitting out the Khat ($P < 0.0001$ for each) (**Table 2**). Twenty-four hours after starting of Khat chewing median score values for anxiety and depression were significantly lower ($P < 0.0001$ for each) than the peak value observed at one hour after spitting out Khat leaves but did not differ significantly ($P > 0.05$ for each) from those at the baseline score values (**Table 2**). After 2-3 hours of Khat chewing, borderline anxiety or depression (score 8-10) was observed in 10.5% (95% CI: 6.3 to 15%) and 26.5% (95% CI: 20.1 to 32.6%) of cases while, definite anxiety or depression (score 11) was observed in 8% (95% CI: 4.6 to 13%) and 9.5% (95% CI: 6 to 14.4%) of cases. Combined definite anxiety and depression was present in 9% (95% CI: 5.4 to 13.8%) of subjects.

One hour after spitting out the Khat leaves borderline anxiety and depression (score 8-10) was observed in 26% (95% CI: 20 to 32%) and 21.5% (95% CI: 16 to 27.2%) of subjects while, definite anxiety and depression (score 11) was observed in 32.5% (95% CI: 26 to 39%) and 50% (95% CI: 43 to 57%) of subjects. Combined definite anxiety and depression was found in 59% (95% CI: 52.2 to 65.8%) of subjects. At 24 hours after starting Khat chewing, borderline anxiety and depression (score 8-10) was observed in 0.5% and 1.5% of subjects.

Discussion. The principal objective of this study was to explore any human mood disturbance during and after Khat sessions, as measured by HAD scale, in Yemeni adult healthy volunteers. The HAD rating scale provides a reliable instrument for screening of emotional disturbances in non-psychiatric subjects. It has the advantage of being not contaminated with psychosomatic symptoms and being validated for measuring the severity of anxiety and depression.¹⁸ The findings in our study proved that there were considerable mood changes towards anxiety and depression during Khat chewing sessions as compared to both baseline status and the control arm of the study. In spite of increases in the scores, the majority of the subjects did not show definite anxiety or depression on the HAD scale. This might be due to euphoric effect produced by cathinone which stimulates the release of neurotransmitters from presynaptic storage sites.^{19,20} Moreover, the timing of these changes was consistent with the changes in plasma cathinone levels after Khat chewing as described by Brenneisen et al¹⁹ and

Halket et al.²¹ Reactive depression, anxiety and irritability were noted to be frequent adverse effects of Khat consumption.²² These findings, particularly reactive depression, have been reported to be associated with chewing Khat.^{8-10,15} Similarly, we report here the occurrence of borderline and definite anxiety and depression among a substantial number of subjects during Khat chewing session. Aggressive behavior and toxic psychosis secondary to Khat chewing is said to be a rare phenomena.^{6,9} It seems to occur after consumption of exceptionally potent material taken in excess or in a predisposed person.^{9,23} In a case report in the United Kingdom, Khat consumption induced paranoid psychosis with added complication of suicide attempt.²⁴ The effect of Khat on mood in our study subjects reached a peak one hour after spitting out the Khat leaves. The most likely mechanism of anxiety is sympathetic over activity as a result of the sympathomimetic action of Cathinone, while reactive depression might result from the catecholamine depletion in the central nervous system. This effect on anxiety and depression seems to be temporary, as it had disappeared by the next day. The subjects studied were not regular Khat chewers and it would be of interest to know whether tolerance to the mood changing effect of Khat occurs in chronic users.

In conclusion, Khat chewing can induce a substantial degree of mood disturbance, particularly depression in healthy subjects. Therefore, it may exacerbate symptoms in patients with pre-existing anxiety and depression. Such patients should be advised to stop taking Khat. In view of the risk of inducing psychosis in predisposed persons on rare occasions, we recommend that psychiatric patients should abstain from the habit of Khat chewing.

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