

The Effect of Khat on the Levels of Cortisol and Lipid Profile in Healthy Khat Chewers

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ABSTRACT

Effect of khat chewing on the levels of cortisol, total- cholesterol, triglyceride and lipoproteins cholesterol (HDLc and LDLc), in healthy khat chewers were studied in fifty healthy Yemeni male adults. After 12 hours fasting (in controls) or after 12 hours from the last session for khat chewing , serum concentration of these parameters were determined. The results showed that the mean levels of serum cortisol as well as the serum concentration of HDL-cholesterol were decreased as compared to non khat chewer individuals (control group) ($p < 0.05$), while the serum triglyceride mean level was consistently higher after chewing khat and differences were statistically significant (p -value < 0.05) as compared to the control group. On the other hands the mean concentration of total cholesterol and LDL-c in serum of khat consumers showed a non-significant change, as compared to the control group (non khat chewers).

INTRODUCTION

Khat is chewed for its stimulating effects in Yemen and in many East African and some Arab peninsula^[1]. khat is a common name for *Catha Edulis* Forsk. Fresh leaves and stem tips of khat are used. Khat contains psychoactive ingredients known as cathinone, a highly potent central nervous system stimulant and cathine, a milder form of cathinone.

Cathine and cathinone are considered to be constituents that are mainly responsible for the stimulating properties of khat leave^[2-4].

Another compound was isolated from khat, called tannin, a complex polyphenolic compound. Upon acid hydrolysis it is analyzed into many substances responsible for many

health problems^[5].

These findings were, also, supported by Qirbi and Farag (1991)^[6] who reported that their in vitro study showed a highly significant concentration of tannic acid and magnesium in khat which varies according to the area (market) in which khat is grown all over the Yemen.

Several million people are frequently users of khat. In Yemen it has been described as a cultural and crop rather than an agricultural crop and its social importance is reflected by the existence of specially designed room for khat chewing in most Yemeni house^[7]. The khat session plays an important role at wedding and other family events (also it is used by crafts men, laborers especially by farmers to reduce physical fatigue).

The juice of the chewed leaves is swallowed while the leaf fibers are stored between the cheeks and gums. Part of the juice is absorbed through the membranes and at the end of the session, the leaf residues are rejected^[7].

In Khat users, **Hughes (1973)**^[8] attributed the common constipation symptoms to the astringent properties of khat tannins, but the habitual users try to attenuate that undesirable effect by their feeding habits, notable by having a meal with high fat content in order to facilitate intestinal transit prior to khat chewing^[6]. However, that inhibitory effect of khat on the gastrointestinal tract in general and its absorptive power in particular could not be fully explained.

Kennedy et al. (1983)^[3], have reported that khat has two modes of gastrointestinal effects; the first is direct physical effect of the ingested material, tannins being the important ingredient, and the second is the effect of other khat alkaloid on the secretory and absorptive activities of the gastrointestinal tract. In addition, **Al-Safadi and Al-Qirbi (1989)**^[9] studied the effect of khat on stomach rabbit cells and they concluded that there was a decrease of the secretory cells of rabbits stomach. They, also, found an increased degenerative absorptive cell in khat-fed rabbits. Also, studied gastrointestinal disturbances associated with khat chewing and proved enhanced gastric acid secretion in humans due to stimulation effect on CNS indirectly and that effect could be produced in the same individual after stopping khat chewing for 4 weeks.

The toxicological effects of

catha.edulis leaves, both short- and long-term, have been reported^[10,11] in an animal mode.

Administration of khat produced some effects on the metabolism in some organs of the body some changes occurred in the metabolism of erythrocytes^[12], brain tissues and liver of rabbits^[13].

Al-Akwa (2000)^[14] reported that khat chewing lowered fasting glucose level in fed rats since the decrease in absorption might affect the post-prandial level rather than the fasting level. So, other mechanism lowering serum glucose may share in this phenomenon.

The lowering effect of Khat on serum glucose level could be attributed to the presence of other ingredients in Khat other than cathine and cathinone.

Recently, khat chewing was reported to impair liver function^[15] and decreases triglycerides that can be^[16] explained by its sympathomimetic action which increase lipolysis^[17]. On the other hand, cortisol hormone, also, promotes lipolysis, rendering it possible that increased levels of FFAs in the circulation^[18]. In rabbits, khat induced an increase in adrenal phosphorylase activity, serum free fatty acids and urinary 17-hydroxycorticosteroids^[19].

Administration of khat to rat reported to decrease the activities of free radical metabolizing enzyme systems (Al-Qirim et al, 2002)^[20].

Aim of the study

The present study aimed to throw light on cortisol and lipid profile, (total cholesterol, triglycerides and lipoprotein) in the sera of khat

chewers compared to control group, (non khat chewers).

MATERIAL AND METHOD

Two groups of healthy Yemeni adults (total 60 males, age 22- 45 years old) were selected. The first group composed of 30 non- khat chewers (control). The second group composed of 30 khat chewers. Both groups were healthy at the time of the study as determined by their routine tests. Five ml of blood samples was taken from each individual. Serum was separated from this fresh blood samples and frozen at -20°C until analysis.

The level of cortisol was determined by radioimmunoassay (RIA) using Coat -A- count kit supplied by Dpc; Cat. No. TKCO1.

While total cholesterol level was determined by the enzymatic method. HDL cholesterol was determined by this method in which other lipoproteins (LDL, VLDL and chylomicrons fractions) were precipitated by phosphotungstic acid in the presence of magnesium ions. After centrifugation, the supernatant of HDL-Cholesterol fraction was determined. LDL-cholesterol and triglyceride were determined enzymatically^[21]. The data were

coded and analyzed using SPSS 10.0 for windows. T test was used for comparison of parameters. Mean \pm SD were compared by one way of analysis of variance or unpaired "t" test. Whenever a test is found significant, the degree of significance (P value) was mentioned.

RESULTS

In the present study, the effect of long-term khat chewing on serum cortisol, total-cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol in healthy khat chewers were examined and compared with values in normal subjects.

The results of the current study show that a significantly decrease in mean serum cortisol levels and HDL-cholesterol in healthy khat chewers as compared to non-khat chewers, (Table-1, Figure-1 and Figure 2).

On the other hand, there was a significant higher mean serum triglyceride levels in healthy khat chewers as compared to control group (non-khat chewers), (Table-1 and Figure-3).

While non significant changes in the mean serum LDL-cholesterol and total cholesterol were found in khat chewers as compared to control group, (Table-1).

Table (1): Serum cortisol and lipid profile, (serum TC, TG, HDL-C, LDL-C in khat chewers and control groups (Mean + S.D.)

Parameters	Khat chewers	Control groups	Significance
Cortisol ng/ml	0.424	0.621	S
HDLc, mg/dl	24.72±4.48	33.34±1.83	S
Triglycerides, mg/dl	84.54±10.3	70.67±5.72	S
LDLc, mg/dl	73.6±28.3	76.4±29.1	N.S.
Total cholesterol, mg/dl	110.3+ 29.4	119.2 +31.7	N.S

S: Significant at $P < 0.05$ N.S.: Non Significant

TC: Total cholesterol TG: Triglycerides

HDL-C : High Density Lipoprotein-cholesterol

LDL- C : Low Density Lipoprotein - cholesterol

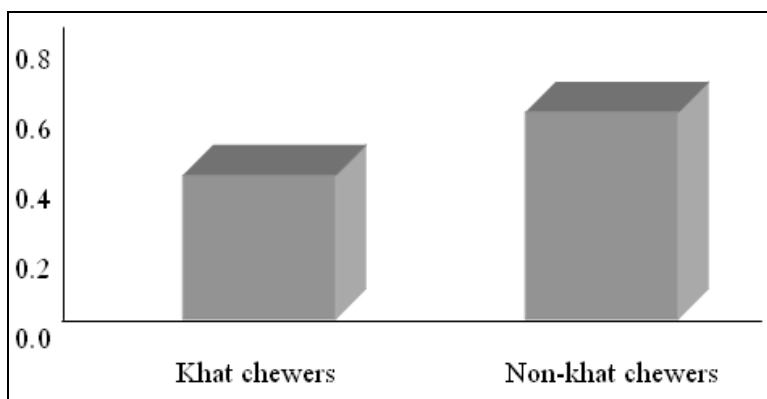


Figure (1) Mean of serum cortisol in khat chewers and control

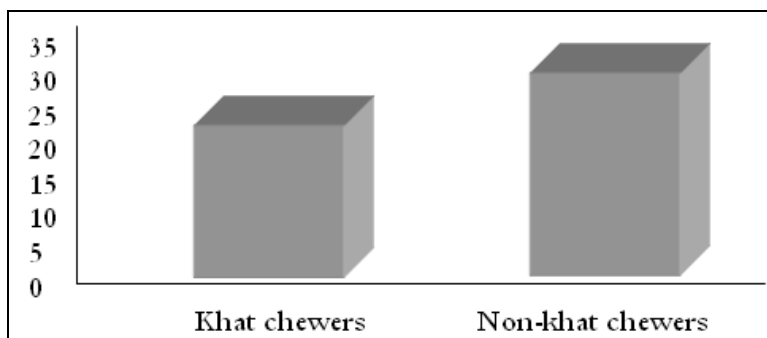


Figure (2) Mean of serum HDL-cholesterol in khat chewers and control

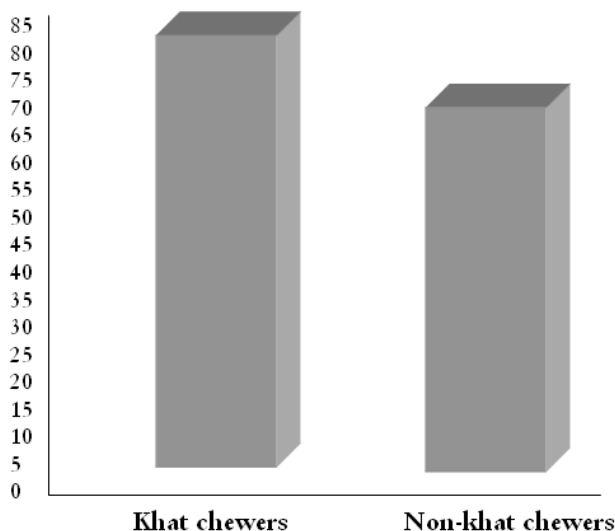


Figure (3) Mean of serum triglyceride level in khat chewers and control.

DISCUSSION

The possible effects of sustained oxidative stress induced by khat consumption may lead to oxidative damage of cellular macromolecules such as DNA, lipids and proteins contributing to the development of several pathologies, notably cancer, hepatotoxicity, nephrotoxicity, cardiovascular toxicity, and neurodegenerative disease^[22]. Al-Qirim et al, (2002)^[20], observed that intragastric administration of khat or its alkaloid under stressful situation can bring about a derangement in free radical metabolism.

Also, toxic effect of pesticides used in khat cultivation may lead to oxidative damage of cellular macromolecules^[23].

In the present study, a trial was made to assess whether the serum

levels of cortisol, HDL- cholesterol, TG, LDL- cholesterol and total cholesterol are affected by khat chewing among population.

A significantly decrease in the level of the mean cortisol in healthy Yemeni khat chewers as compared to the corresponding mean of non-khat chewers. (Table-1 and Figure 1). This lowering effect of khat on cortisol was in agreement with previous study by Mwenda et al. (2006)^[24] who used the olive baboon and observed that khat administration causes a significant decrease in the level of cortisol.

In a study by **Ahmed and El-Qirbi (1993)**^[25], they reported adrenocorticotrophic hormone (ACTH), to be increased in rabbits given *Catha edulis* extract and attributed it to the stimulation of β -adrenergic receptors (**Tariq et al., 1989**)^[26]. Cortisol increases

availability of all fuel substrates by mobilization of glucose^[27], free fatty acids^[28], and amino acids from endogenous stores^[29]

Also, (Table-1), show that the mean HDL-Cholesterol levels of khat chewers were significantly lowered than the corresponding mean of non-khat chewers (control group). The result was supported by the observation of Al-Motarreb et al, (2002)^[30], who reported that the difference between khat chewers and non chewers admitted with acute myocardial infarction was that serum triglyceride and total cholesterol concentrations were above normal and serum HDL was lower than normal.

HDL is commonly referred to as "good" cholesterol because it helps remove excess cholesterol from atherosclerotic deposits and retard the growth of new plaque. Low HDL levels have been shown to be an additional risk factor for increased mortality from coronary artery disease and strokes in the elderly^[31].

A significantly increase in the levels of triglyceride in healthy Yemeni khat chewers as compared to non-khat chewers (control group) was shown in the present study (Table-1 and Figure-3). These results were in contrast with the results of Ramadan et al. (1979)^[32], they observed that triglyceride and lipoproteins decreased as compared to their normal equivalents

In the present study we found that, the means of serum LDL level and total cholesterol levels were not significantly changes in khat chewers when compared with non-khat chewers. This finding was in agreement with previous study by

Ramadan et al. (1979)^[32], they observed that, cholesterol and other lipoproteins(LDL) showed no significant changes. LDL, popularly known as "bad cholesterol," is the primary transporter of cholesterol in the blood.

In atherosclerosis, LDL is taken up in lesions in endothelial cells lining the inner walls of blood vessels, forming deposits in the arterial walls. The deposited LDL undergoes modification, as free radicals oxidize LDL to form foam cells that create a thick, hard plaque. Cholesterol is a fatty (lipid) component found in virtually all cell membranes. In addition to supporting cellular integrity, cholesterol is also required for the biosynthesis of aldosterone, cortisol, and sex hormones.

Far from endangering health, cholesterol is essential to life. In fact, Italian researchers have shown that when serum cholesterol levels are too low (less than 160 mg/dl), mortality in older adults actually increases^[33,34].

The actual mechanisms by which these changes in the levels of cortisol, and lipid profile are taking place are not well understood. However, it is postulated that khat ingredients and toxic effect of pesticides used in khat cultivation may reflect on the level of serum metabolites, which were observed in the significant changes in cortisol and certain lipid profile.

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