Effect of Qat on the level of blood glucose and lipids among Yemeni patients with type 2 diabetes

Zayed A. Atef, Mohamed A. Bamashmos, Gameel Alghazali

Department of Internal Medicine, Faculty of Medicine, Sana'a University, Sana'a, Yemen

Correspondence to Ahmed A. Zayed, MD, Department of Internal Medicine, Faculty of Medicine, Sana'a University, Sana'a, PO Box - 11566, Yemen. Tel: 00967 733233192; e-mail: drzayedatef@gmail.com

Received 24 March 2017
Accepted 3 July 2017

Egyptian Journal of Obesity, Diabetes and Endocrinology 2017, 3:100–105

Background
The habit of chewing Qat is one of Yemen's social and cultural characteristics. Most Yemeni adults chew Qat regularly. The general belief among the Yemeni diabetics is that Qat chewing helps to lower their blood glucose.
Objective
In this study, we investigated the effect of Qat chewing on the level of blood glucose on patients with type 2 diabetes.
Patients and methods
The study included 260 patients with type 2 diabetes who were divided into two groups:
Group 1 included 130 patients who were non-Qat chewers.
Group 2 included 130 patients who were Qat chewers
All patients underwent clinical examination; fasting, postprandial, and random blood glucose examination before and after Qat chewing; and glycated hemoglobin and lipid profile.
Results
The results of the study demonstrated that there was a significant increase in heart rate and arterial blood pressure after Qat chewing, whereas there were no significant changes in the level of blood glucose before and after Qat chewing. Moreover, we found that there were no effects in the levels of total cholesterol and triglyceride, whereas there was a nonsignificant decrease and a nonsignificant increase in the levels of low-density lipoprotein-cholesterol and high-density lipoprotein-cholesterol, respectively, among the Qat chewers.
Conclusion
We found that there was a significant effect of Qat on heart rate and hypertension. There was no significant effect of Qat on the blood glucose or lipids levels. The only effect, which leads to wrong belief, is that Qat chewing produces feeling of euphoria, stimulation, heightened awareness, increased confidence, alertness, and energy, resulting in temporary alleviation of fatigue which the diabetic patients experience. All these effects are because of the cathinone and moderate sympathetic effects.

Keywords:
Qat chewing, type 2 diabetes mellitus

Egypt J Obes Diabetes Endocrinol 3:100–105

2356-8062

Introduction

The phenomenon of chewing Qat is one of Yemen's social and cultural characteristics. Most Yemeni adults chew Qat regularly, as it is not forbidden by Islam [1].

Qat belongs to the plant species of *Catha edulis* Forsks, of the family Celastraceae. This plant is grown in some countries of East Africa and South Arabia, mainly in Yemen [2].

It appears that chewing Qat was first used by Ethiopians in the 14th century [3], and probably it was first introduced to Yemen in the 15th century [4].

It has been brought into the USA and UK by emigrants from the source countries. The pleasurable central stimulant properties of Qat are commonly believed to improve work capacity, so it is used on journeys and by students preparing for examinations and to counteract fatigue.

Qat active constituents were extensively studied by many investigators including, United Nation Narcotic Laboratories [5–7]. They found that Qat contains groups of alkaloids called cathedulins. The most important one is cathinone, "cathinone," which accumulates in young leaves, whereas in old leaves, it undergoes enzymatic reduction to the less active compounds cathine and norephedrine. Cathinone is relatively unstable and

rapidly metabolized to norpseudoephedrine (cathine) and norephedrine [8]. This finding explains why Qat chewers prefer to chew the young leaves from the tips of the branches, suggesting the highest cathinone content and its highest stimulating effect [9].

Early clinical observations had suggested that Qat has amphetamine-like properties, and subsequent chemical analysis confirmed that the fresh leaves contain alkaloids such as cathine and cathinone, the latter being structurally related and pharmacologically similar to amphetamine [10]. Qat leaves also contain considerable amounts of tannins (7–14% in dried material), vitamins, minerals, and flavonoids. Cathinone is currently believed to be the main active ingredient in fresh Qat leaves.

Chewing is the most common route of administration of Qat and its constituent. Cathinone is rapidly absorbed after oral administration and rapidly distributed in the blood in contrast to cathine, which is slowly absorbed [11].

Cathinone is released within 15–45 min during chewing, and peak plasma levels of it are obtained 1.5–3.5 h after the onset of chewing Qat. Cathinone is detectable in plasma for up to 24 h after Qat consumption [12].

Cathinone is highly lipid soluble, and this characteristic facilitates its access to the central nervous system as well as to other central and peripheral neurotransmitters [11]. Cathinone is metabolized in the liver into norephedrine, and it is excreted almost exclusively in this form; only about 2% of the cathinone absorbed appears unchanged in the urine [11].

Dependence induced by cathinone has been extensively studied by WHO experts group on drug dependence. They concluded that cathinone does not induce physical dependence or addiction [13–15].

In Yemen, the habit of Qat chewing is widespread as a deep-rooted socio-cultural tradition. It is estimated that up to 90% of adult Yemeni males chew Qat 3–4 h daily, and the number of females may be as high as 50% [16].

On the contrary, Qat is considered a big problem in Yemen, because its trade expansion is replacing coffee crops, and estimates suggest that one-half to two-thirds of arable land is being cultivated with Qat.

Advocates of Qat claim that it eases the symptoms of diabetes and asthma.

The general belief among the Yemeni diabetics is that Qat chewing helps to lower their blood glucose. In recent study done by Atef and Assabry [17], they found that 61.5% of diabetic patients admitted to the emergency departments in Sana'a hospitals were Qat chewers, and 53% of them believe that chewing Qat is useful for diabetics. Opponents claim that Qat damages health and affects many aspects of life, with adverse social, economic, and medical consequences.

The fact that Qat chewing is a deeply rooted habit in our society motivated us to embark on this research.

In the local literature that has been reviewed, there are controversial reports on the effect of the Qat chewing on carbohydrate metabolism and insulin secretion.

The aim of this study is to assess the effect of chewing Qat on diabetes control and lipids metabolism among Yemeni patients with type 2 diabetes mellitus (DM) on oral antidiabetic agents.

Study justification

We chose this study for the following reasons:

(1) Qat chewing is a rooted problem in our country which affects all population life.
(2) There are widely spread concepts that Qat chewing has a beneficial effect on diabetes control.
(3) Lack of knowledge in our society about the disadvantages of chewing Qat on human health, including cardiovascular disease and diabetes (direct or indirect).

Objective

The objective is to study the effect of Qat on glucose level and lipids metabolism among patients with type 2 DM on oral therapy.

Materials and methods

Study design

This is a comparative case–control study.

Study population

The study consisted of 260 patients with type 2 diabetes who were previously diagnosed of having the disease for duration of not less than 2 years.

All cases were randomly selected from the Diabetes Center in Al-Thawra Hospital, Sana'a city, during the period from the 1 January 2010 to 30 June 2010.

Adults with type 2 DM on oral therapy, as a combination of sulfonylurea and biguanide, were included in the study, whereas patients with brittle diabetes cases and acute complicated cases and any cases complicated by other diseases, mainly liver diseases, renal diseases, heart failure, and hypertension, were excluded from the study.

The study patients were divided into two groups: G1, which included 130 non-Qat chewers with type 2 diabetes, and G2, which included 130 Qat chewers with type 2 diabetes with the duration of chewing Qat being not less than 2 years with regular daily chewing of at least 4 h per sitting.

All study cases were subjected to the following:

(1) History taking, including age, sex, and duration of DM.
(2) Clinical examination including: body weight, height, BMI following WHO formula, heart rate (HR), and arterial blood pressure (HR and blood pressure were measured before and after Qat chewing).
(3) Same laboratory technique estimating using glucometer of (Accu-Chek Active; Roche made in Ireland) a member of Roche Diagnostic Group, with measuring principle of glucose–dye-oxidoreductase and indicator dye; photometric endpoint measurement.
(4) Four blood samples were collected from each patient for blood glucose test:
    (a) Fasting blood glucose.
    (b) Postprandial blood glucose.
    (c) Mid-day blood glucose estimations – that is, 2 h after lunch meal, before chewing Qat, random blood glucose (R1BG), and 4 h later 'post-chewing Qat' blood glucose (R2BG) for both Qat chewers and nonchewers.
    (d) Glycated hemoglobin (HbA1c).
(5) Serum lipids profile.

All cases were informed to take their medications, which were sulfonylurea and metformin, without any changes in the dose or timing. All patients were asked to eat regular meals of restricted high glycemic index foods and were instructed not to eat following the lunch before the third and fourth samples of blood glucose.

Ethical approval and inform consent were obtained from all patients.

Statistical analysis

The results were expressed as mean±SD and analyzed using Software Package for Social Sciences (SPSS) V.20.0 computer program, per significant differences.

Results

Of 260 patients with type 2 diabetes who gave consent to participate in the study, 146 (56.15%) were males and 114 (43.85%) were females (Table 1).

It was noticed that there were no significant differences between both groups regarding the basic characteristics such as sex, age, BMI, and duration of diabetes (Table 1).

Regarding vital signs, we found that there was no significant difference in the pulse, systolic blood pressure, and diastolic blood pressure before Qat chewing among the two groups.

After 4 h, we found that there were no significant differences in pulse, systolic blood pressure, and diastolic blood pressure in group 1 (non-Qat chewers), whereas there were significant differences among group 2 (Qat chewers) before and after Qat chewing, as pulse, systolic blood pressure, and diastolic blood pressure increased from 88.31±7.16, 128.080 ±13.25, and 84.31±9.27 to 99.92±10.09, 143±14.46, and 91.62±12.63, respectively (Table 2).

Regarding the effect of Qat on glucose level, we found that there were no significant differences in fasting blood glucose, postprandial blood glucose, random blood glucose, and HBA1c in both groups (Table 3).

On comparison between the levels of blood glucose, we found that among non-Qat chewers (G1), there was a

Table 1 Patients' basal characteristics in both groups

	Sex [*n* (%)]		Age average	Duration	BMI [*n* (%)] (mean=26.56)		
	Male	Female			Normal	Overweight	Obese
G1	62 (23.82)	68 (26.23)	51.46±12	9.03	50 (19.2)	64 (24.6)	16 (6.2)
G2	84 (32.33)	46 (17.62)	47.42±6.8	8.5	38 (14.6)	64 (24.6)	28 (10.8)
SD			12			4.7	
P	0.052		0.075	1.03		0.293	

Table 2 Pulse and arterial blood pressure before and after 4 h (Qat sitting)

	Heart rate		Syst.BP		Diast.BP	
	P1	P2	Sys.BP1	Sys.BP2	Dias.BP1	Dias.BP2
G1						
Mean	87.450	89.400	128.310	130.770	81.230	82.150
SD	7.481	8.512	15.719	17.661	5.231	5.794
G2						
Mean	88.310	99.920	128.080	143.000	84.310	91.620
SD	7.159	10.092	13.249	14.464	9.265	12.628
P	0.504	0.000	0.928	0.000	0.021	0.000

Dias.BP1, diastolic blood pressure before Qat chewing in G1 and G2; Dias.BP2, diastolic blood pressure 4 h later for non-Qat chewing (G1) and after 4 h of Qat chewing (G2); P1, pulse before Qat chewing in G1 and G2; P2, pulse 4 h later for non-Qat chewing (G1) and after 4 h of Qat chewing (G2); Sys.BP1, systolic blood pressure before Qat chewing in G1 and G2; Sys.BP2, systolic blood pressure after 4 h for non-Qat chewing (G1) and after 4 h of Qat chewing (G2).

Table 3 Levels of blood glucose in both groups

	Variables				
	FBG	PPBG	R1BG	R2BG	HbAlc
G1					
Mean	149.570	225.910	210.150	191.570	8.350
SD	42.095	79.546	82.396	90.376	1.561
G2					
Mean	157.750	236.630	208.600	211.000	8.460
SD	74.694	94.949	69.793	72.802	1.240
P	0.443	0.478	0.908	0.179	0.668

FBG, fasting blood glucose in both groups; HbA1c, glycated hemoglobin; PPBG, postprandial blood glucose in both groups; R1BG, random blood glucose 2 h after lunch in both groups (before Qat chewing in G2); R2BG, random blood glucose 4 h after lunch in both groups (after Qat chewing in G2).

Table 4 Levels of lipid profile in both groups

	T.Ch	TG	LDL	HDL
G1				
Mean	196.310	224.600	117.370	31.570
SD	44.720	75.360	31.849	8.031
G2				
Mean	181.320	211.290	109.710	35.580
SD	33.148	82.184	24.236	8.803
P	0.072	0.338	0.087	0.088

HDL, high-density lipoprotein; LDL, low-density lipoprotein; T.Ch, total cholesterol; TG, triglyceride.

nonsignificant decrease in R1GB and R2GB, as the levels were 210.15±82.34 and 191.57±90.37, respectively.

In contrast, among Qat chewers (G2), there was a nonsignificant increase in R2BG, as it increased from 208.60±69.79 R1BG to 211±72.80 after Qat chewing. There was no significant difference in the level of HbA1c in both groups (Table 3).

On comparison of both groups regarding the effect of Qat on lipid level, it demonstrated that there were no significant differences between G1 and G2 in the levels of total cholesterol (196.310±44.72 and 181.320±33.140, respectively) and triglyceride (224.600±75.360 and 211.290±82.184, respectively). However, a nonsignificant decrease was noticed in the levels of low-density lipoprotein and a nonsignificant increase in the levels of high-density lipoproteins among Qat chewers in comparison with the non-Qat chewers, as the values were 117.370 ±31.849 and 31.750±8.031, respectively, among G1 and 99.710±24.236 and 35.580±8.803, respectively, among G2 (Table 4).

Discussion

In this study, we found that there was a significant increase in pulse, systolic blood pressure, and diastolic blood pressure among Qat chewers with type 2 diabetes, whereas there were no significant changes among non-Qat chewers with type 2 diabetes. These findings are in agreement with Al Motarreb *et al.* [18] who investigated the effects of Qat chewing on blood pressure and cardiac rhythm among Yemeni patients with hypertension and ischemic heart disease using 24 h ECG Holter monitoring and ambulatory blood pressure monitoring. The study showed the expected progressive increase in blood pressure and HR (18). Similar findings also have been found in a recent work by Hassan *et al.* [19] on healthy Yemeni adult volunteers, which provided evidence that Qat chewing induced a significant increase in arterial systolic and diastolic blood pressure and pulse rate in comparison with the baseline values [20].

Similar changes have been observed in a smaller number of patients when pure cathinone in gelatin capsules were taken orally [21] or when Qat leaves were chewed [22].

These observations support the suggestion that cathinone is the constituent that is mainly responsible

for the increase in arterial blood pressure and pulse rate during Qat chewing.

A possible mechanism of these results can be explained also by the effect of amphetamine-like and ephedrine-like substances in Qat. Amphetamines work by triggering the release of dopamine molecules from their storage vesicles in the neurons in the brain [10,23].

Stimulation of Qat can occur within the first 15 min of chewing, though the peak is reached in the third hour, and effects can remain for up to 24 h [10]. These changes run parallel with the changes in plasma cathinone levels during and after Qat chewing [24].

In our study, there was a nonsignificant decrease in the level of random blood glucose among non-Qat chewers with type 2 diabetes in the fourth sample (6 h after lunch) when compared with the third sample, which was taken 2 h after lunch.

This decrease of glucose level can be explained by the decrease in the hepatic production and increased glucose utilization in response to released insulin that was stimulated by food.

In contrast, serum glucose level increased nonsignificantly among Qat chewers with type 2 diabetes in the fourth sample (6 h after lunch or after 4 h of Qat chewing). These findings can be explained by the fact that Qat chewers with diabetes exhibit increased glycemic responsiveness to catecholamines owing to their ability to decrease insulin secretion and insulin sensitivity [24,25] and also can be explained by the effects of resistin and cortisol as it had been demonstrated that Qat chewing resulted in significant increase of resistin and cortisol levels in both diabetic and healthy patients, while it significantly decreases serum insulin level in Qat chewers with diabetes [26] and can be explained also by delayed stomach empty during Qat chewing [27,28].

On the contrary, the sympathetic action of Qat may increase glucose production through activation of glycogenolysis especially that of muscles, which leads to increase in the level of blood glucose by an indirect mechanism through increased glycolysis and subsequently release of lactate, which is transported to the liver where it serves as a gluconeogenic substrate [29].

Our findings are in agreement with the results presented by Ali *et al.* [30] who revealed a significant decrease of serum glucose level at the third and the fourth hour after lunch among non-Qat chewers with type 2 diabetes, whereas there were nonsignificant differences of serum glucose levels either at the second, third, or fourth hours after lunch among Qat chewers with type 2 diabetes.

In this study, we found that there were no significant difference in the level of HbA1c among both groups.

Moreover, we found that there were no significant difference in the levels of total cholesterol and triglyceride in both groups, whereas there were a nonsignificant decrease in the level of low-density lipoprotein-cholesterol and nonsignificant increase in the level of high-density lipoprotein-cholesterol among the Qat chewers (G2) in comparison with the nonchewer (G1). These findings are in agreement with that presented by Al-Habori and Al-Mamary [31] who demonstrated the same findings on the levels of plasma lipids on experimental animals who were fed Qat. These changes may occur because of ACTH activation, which increases cathinone [22,24,32,33].

Stimulatory effect of ACTH are believed to be mediated by the activation of adenyl cyclase with subsequent increase in the cyclin AMR concentration. The latter may then stimulate the conversion of cholesterol to cortisol by activation of various enzyme systems involved [34]. The changes may also be because of the sympathomimetic action of Qat which favors lipolysis and activation of β3 receptors, which result in activation of adenyl cyclase [34].

In conclusion, in contrast to the general concept among Yemeni population that Qat chewing helps to lower the level of blood glucose, we found that there are no significant changes in the level of blood glucose level before and after Qat chewing. Moreover, there is no significant effect of Qat on the levels of plasma lipids. The only effect, which leads to that wrong belief, is that Qat chewing produces feeling of euphoria, stimulation, heightened awareness, increased confidence, alertness, and energy, resulting in temporary alleviation of fatigue, which patients with diabetes experience. All these effects occur because of cathinone and moderate sympathetic effects [10].

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Almaqrami A, editor. Qat between politics and sociology (Arabic). Beirut, Lebanon: Azal Publication House; 1987. pp. 158–200.

2 Al-Hipshi A. Qat in Yemeni Art (in Arabic). ALyaman ALgdid, Sana'a Yemen 1972; 3:143–157.

3 Dillman A. The War Attitudes of the King's 'Amda-sion against the Muslims'. Meeting reports of the Royal Prussian AKad. Of the sciences to Berlin 1884..

4 Schopen A, editor. Das Qat (German): research reports of the ethnology depart. Wiesbaden, GFR: University of Frankfort Publications, Franz Stiener Verlag; 1987.

5 Cias M, Gins Berg D, Mandelbaum A. Constituents of Catha edulis. Tetrahedron 1975; 31:2727–2731.

6 Braenden O. Research on the chemical composition of Qat. NIDA Res Monogr 1979; 27:320–321.

7 Szendrei K. The chemistry of Qat. Bull Narc 1980; 32:5–35.

8 Al-Motarreb A, Al-Habori M, Broadley KJ. Khat chewing, cardiovascular diseases and other internal medical problems: the current situation and directions for future research. J Ethnopharmacol 2010; 132:540–548.

9 U.N. Narcotic Laboratory Reports No 8S9; 1979. Reports on the botany and chemistry of Qat 1979.

10 Kalix P. Pharmacologial properties of the stimulant Khat. Pharmacol Ther 1990; 48:397–416.

11 Brenneisen R, Geisshusler S, Schorno X. Metabolism of cathinon. J Pharm Pharmacol 1986; 38:298–300.

12 Graziani M, Milella MS, Nencini P. Khat chewing from the pharmacological point of view: an update. Subset Use Misuse 2008; 43:762–783.

13 Adam F, Hasselot N. Qat from traditional usage to the risk of drug addiction. Med Trop (Mars) 1994; 54:141–144.

14 WHO Expert Committee on Drug Dependece. Thirty-third report. Geneva, World Health Organization 2003.

15 Giannini AJ, Burge H, Shaheen JM, Price WA. Qat: another drug of abuse. J Psychoactive Drugs 1986; 18:155–158.

16 Al Mugahed L. Qat chewing in Yemen: turning over a new leaf. Bull WHO 2008; 86:741–742.

17 Atef ZA, Assabry AM. Pattern of diabetes emergencies among adult Yemeni diabetic patients. Tanta Med J 2008; 36:730–738.

18 Al-Motarreb A, Al-Kebsi M, Al-Adhi B, Broadley KJ. Qat chewing and acute myocardial infarction. Heart 2002; 87:279–280.

19 Hassan NAGM, Gunaid AA, El-Khally FMY, Al-Noami MY, Murray Lyon IM. Qat chewing and arterial blood pressure. A randomized controlled clinical trail of selective alpha and beta-1 adrenoreceptor blockades. Saudi Med J 2005; 26:537–541.

20 Hassan NA, Gunaid AA, Abdo-Rabbo AA, Abdel-Kader ZY, Al-Mansoob MA, Awad AY, Murray-Lyon IM The effects of Qat chewing in arterial blood pressure and heart rate in healthy volunteers. Trop Doct 2000; 30:107–108.

21 Benneisen R, Fisch HU, Koelbing U, Geisshüsler S, Kalix P Amphetamine-like effects in human after Qat alkaloid cathinone. Br J Clin Pharmacol 1990; 30:825–828.

22 Nencini P, Ahmed AM, Amiconi G, Elmi AS Tolerance develops to sympathetic effects of Qat in humans. Pharmacology 1984; 28:150–154.

23 Goth A, editor. Medical pharmacology principls and concepts. 9th ed. Saint Louis: The C.V. Mosby Company; 1978. pp. 310–311.

24 Halket JM, Karusu Z, Murray-Lyon IM. Plasma cathinone level following chewing Qat leaves. J Ethnopharmacol 1995; 46:111–113.

25 Cryer PE. Diseases of the sympathochromaffin system. In Felig P, Baxter TD, Broadns AE, Frohman LA, eds. Endocrinology and Metabolism. 2nd ed. New York: Mc Graw-Hill; 1987. pp.651–692.

26 El-Sayed MIK, Al-Kordy Amin H. Effect of Catha edulis on insulin, resistin and cortisol levels in type-2 diabetics and non-diabetics. Am J Biochem Biotech 2012; 8:157–163.

27 Gunaid AA, El-Khally FMY, Hassan NAGM, Murray-Lyon IM. Chewing Qat leaves slows the whole gut transit time. Saudi Med J 1999; 20:444–447.

28 Heymann TD, Bhupulan A, ZrieQat NEK, Bomanji J, Drinkwater C, Giles P, Murray-Lyon IM. Qat chewing delays gastric emptying of a semisolid meal. Aliment Pharmacol Ther 1995; 9:81–83.

29 Shafrir E, Bergman M. The endocrine pancease: diabetes mellitus. In Felig P, Baxter TD, Broadns AE, Frohman LA, eds. Endocrinology and Metabolism. 2nd ed. New York: Mc Graw-Hill; 1987. pp. 1043–1178.

30 Ali S, Qirbi AA, Al-Geiry A, Al-Habori M. Effect of *Catha edulis* on plasma glucose and c-peptide in both type 2 and non-diabetics. J Ethnopharmacol 2003; 86:45–49.

31 Al-Habori M, Al-Mamary M. Long-term feeding effects of *Catha edulis* leaves on blood constituents in animals. Phytomedicine 2004; 11:639–644.

32 Nencini P, Fraioli S. Environment specific reinstatement of amphetamine-mediated hyperdipsia by morphine and nor-pseudoephedrine. Pharmacol Biochem Behav 1994; 47:339–343.

33 Roberts MF, Wink M. Utilization of alkaloids in modern medicine. In Roberts MF, Wink M, eds. Alkaloids biochemistry, ecology and medicinal applications. New York: Plenum Press; 1998. pp. 435–459.

34 John FL, Peter HW. Control of cortisol release. In John FL, Peter HW, eds. Essential endocrinology. 2nd ed. Oxford: Oxford University Press; 1983. p. 99.