Chewing Qat leaves slows the whole gut transit time

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ABSTRACT

Objective: Chewing leaves of the qat plant (Catha edulis) for their pleasurable central stimulant effect is a habit widespread in the Yemen and central areas of East Africa. Their use is believed to cause a variety of gastrointestinal symptoms including constipation. We studied the effect of chewing qat leaves on whole gut transit time.

Methods: A prospective study in 10 healthy volunteers studied on 2 occasions a week apart. The subjects either chewed qat 3 hours daily for 7 days or abstained from chewing qat for 7 days before the whole gut transit time measurement. Whole gut transit time was measured using the radio-opaque markers technique.

Results: The whole gut transit time was significantly prolonged during the qat arm compared to the control arm of the study. There was also a significant hardening of the stools during the qat chewing arm as expressed by a lower score on the Bristol stool form scale.

Conclusions: We have confirmed by objective measurement that qat chewing slows the whole gut transit time. This effect is believed to be caused by the sympathomimetic action of cathinone and cathine and the astringent properties of tannin in qat leaves.

Keywords: Qat, Catha edulis, cathinone, tannins, constipation.


The qat plant (Catha edulis) is produced in certain areas of East Africa and the Arabian peninsula, and the leaves are chewed for their central stimulant effect. In the Yemen, qat chewing is a widespread habit with deep-rooted socio-cultural tradition. As only fresh leaves possess the desired stimulant effect, its use remained virtually unknown beyond the areas of cultivation. However, in recent years, the advent of air transport has facilitated the distribution of fresh qat to European capitals.

Qat leaves contain a variety of substances, including tannins and alkaloids. The principal pharmacologically active component is the amphetamine-like alkaloid S(-) α-aminopropiophenone (Cathinone). The popularity of qat chewing derives from stimulation of the central nervous system by cathinone. There are also peripheral actions of a sympathomimetic type. Both central and peripheral actions resemble those of amphetamine. Qat leaves also contain considerable amounts of tannins and flavonoids. Constituents are a common complaint of qat users and may be due to the astringent properties of qat tannins, and the sympathomimetic effect of cathinone on smooth muscle, or both. The aim of this study was to determine the effect of chewing qat leaves on the whole gut transit time (WGGT) in healthy adult male volunteers.
Methods. Ten healthy male volunteers aged between 21 and 30 years underwent 2 measurements in Yemen, a week apart, of their whole gut transit time (WGTT) using 3 types of radio-opaque markers. None of the subjects had a history of gastrointestinal or cardiovascular disease, diabetes or psychiatric disease. None was taking any medication, and none was a regular qat chewer.

Subjects all had a regular bowel movement 1-2 times per day. During the study they were advised not to alter their daily consumption of food, fluid and tobacco, and to keep daily physical activity as constant as possible, avoiding strenuous exercise.

Potential subjects were interviewed for symptoms of irritable bowel syndrome (IBS) using the Manning criteria and mood status was assessed using the Hospital Anxiety Depression rating scale. Those having evidence of IBS or clinically significant anxiety or depression symptoms were excluded from the study. Body mass index (BMI: Kg/m²) was calculated.

The whole gut transit time (WGTT) was measured by the radio-opaque marker technique using a single abdominal radiograph. Three different types of radio-opaque polyvinyl chloride markers were used. Subjects swallowed 20 radio-opaque markers (2 gelatine capsules, each containing 10 identical markers) on 3 consecutive mornings at 0900 hours after breakfast. On the 4th morning, a supine plain abdominal radiograph was taken at 0900 hours. The WGTT was calculated by multiplying the total number of markers seen by 1.2. The WGTT was also estimated from the self-made observations of the stool characteristics using the Bristol stool form scale, the date and time of each stool per week, and the stated frequency of defecation per week. Using the stated frequency of defecation per week (DF), the interdefecatory time interval (IDTI) for 6 defecations and the sum of 3 stool form score (SFS), the estimated whole gut transit time (EWGTT) was calculated according to the following formula:

\[ \text{EWGTT} = 79-1.33 \times (\text{DF}) - 1.88 \times (\text{SFS}) + 0.329 \times (\text{IDTI}) \]

Segmental colonic transit times were calculated from the numbers of markers seen within the 4 segments of large bowel: right, left, sigmoid and rectum. Transit time of a segment was defined as the total number of markers seen in that segment multiplied by 1.2. The spinal processes and imaginary lines from the 5th lumbar vertebra to the left iliac crest and pelvic outlet served as landmarks.

Each subject was studied twice, both after 7 days of qat chewing and 7 days without. The sequence of qat and control arms of the study was determined at random. Qat was chewed first in 6 of the 10 subjects. During the qat arm of the study each subject chewed one bundle of the same type of qat for 3 hours daily beginning 4 days before the whole gut transit study and for each of the 4 study days. Subjects were instructed to swallow the juice of the qat leaves. During the control arm of the study, no qat was taken during the 4 days before starting the whole gut transit study and during the four study days.

Statistical analysis. Measurement of WGTT and segmental colonic transit times and EWGTT were compared using a one tailed Wilcoxon’s Matched Pairs test. A P-value less than 0.5 were taken as significant. Ninety five percent Confidence Interval Analysis (CIA) was also computed in order to test the imprecision of the sample study estimates as population values. Pearson correlation and multiple linear regression were also conducted using SPSS statistical package.

Results. The median (range) values of subjects’ age and BMI were 23 (21-30) years and 22 (18-27) kg/m². None of the participants had IBS (all scored less than 2 on the Manning criteria), and none of them had definite anxiety (≤ 5 score) or depression (≤ 8 score) when tested by the Hospital Anxiety and Depression rating scale during the 2 arms of the study. There was a significant prolongation of the measured WGTT during the qat arm of the study compared to the control arm (Table 1). Median difference = 7.5, 95% CI from 3 to 11, P = 0.00255 (Wilcoxon’s Matched Pairs Test). There was prolongation of WGTT in each individual volunteer. The median (range) EWGTT was 55 hours (16-70) during the qat arm and 52 hours (7-59) during the control arm, but the difference was not statistically significant. WGTT, both measured and estimated, was prolonged after qat chewing (Figure 1). A significant correlation between EWGTT and measured WGTT (r = 0.6411; P = 0.023) was noticed during the qat arm only. The median (range) Bristol stool form score (BSF) was 3.3 (2-4.1) during the qat arm, compared to 4.0 (3-5.5) during the control arm. There was a significant hardening of stools during qat chewing as expressed by lower score: Median difference = -0.85, 95% CI from -1.5

Table 1 - Measured Whole Gut Transit Time (h-WGTT) in hours during qat and control arms of the study.

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>Control arm</th>
<th>Khat arm</th>
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<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
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<tr>
<td>3</td>
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<td>9</td>
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<td>24</td>
</tr>
<tr>
<td>10</td>
<td>25</td>
<td>30</td>
</tr>
</tbody>
</table>

Median (range) 24 (7-37) 28.5 (22-42)
to -0.2; \( P = 0.00585 \). Segmental colonic transit times (Table 2) were slower during the qat arm in all colonic regions, with significant prolongation in the right colon \( (P = 0.025) \). Multiple regression analysis did not elicit any significant influence of the age, or BMI values, or anxiety depression score on the WGTT.

**Discussion.** In this study we have shown that qat chewing for a week is associated with significant prolongation of WGTT and the segmental colonic transit times were slower in all colonic regions with significant prolongation in the right colon. Furthermore, there was significant hardening of the stools. It seems likely that this effect resulted from one or more of the constituents of the qat leaves, which are known to contain a variety of alkaloids including cathinone and cathine, flavonoids, tannins, amino acids, essential oils and vitamin C. The sympathomimetic effects of qat consumption are thought to be due to the concurrent action of cathinone and cathine, whereas its central nervous system effects are almost entirely due to cathinone. Cathinone is a biosynthetic precursor that accumulates in young leaves, and is absorbed rapidly by the buccal mucosa and after swallowing the juice of the leaves. In old or stale qat leaves, cathinone undergoes enzymatic reduction to the less active compounds, cathine and norcathinone. Cathine undergoes little buccal absorption and is taken up rather slowly from the gastrointestinal tract. Cathinone and cathine exert their sympathomimetic-like actions by the release of catecholamines from presynaptic storage sites.

Sympathetic activation usually inhibits contraction of the intestine. The activated sympathetic fibres within the myenteric plexus inhibit those fibres which produce muscle contractions when stimulated. Thus qat-induced sympathetic activation with subsequent sympathomimetic effect on colonic smooth muscle may explain the observed prolongation of WGTT during the qat arm of the study. The same mechanism was previously suggested to explain the observed delay in gastric emptying after qat chewing, and the reported qat-induced prolongation of the orocecal transit time.

Slow WGTT seems to lead to excessive absorption of a colonic bacterial metabolite, deoxycholic acid, which could promote gallstone formation. The possibility that widespread consumption of qat in Yemen might be associated with an increased prevalence of gall stones is presently being explored in an abdominal ultrasound screening study.

It can be concluded that qat chewing significantly prolongs the WGTT. This may result from the sympathomimetic action of cathinone and cathine or the astringent properties of tannin in qat leaves. To distinguish between these possibilities, it will be necessary to study the effect of pure cathinone and cathine.

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<table>
<thead>
<tr>
<th>Study Status</th>
<th>Right colon</th>
<th>Left colon</th>
<th>Sigmoid</th>
<th>Rectum</th>
<th>Measured - WGTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control arm</td>
<td>10.5 (4-17)</td>
<td>1.8 (0.0-14)</td>
<td>0.6 (0.0-4)</td>
<td>7.0 (0.0-23)</td>
<td>24 (7-37)</td>
</tr>
<tr>
<td>Khat arm</td>
<td>14.5 (2.4-30)</td>
<td>6.5 (0.0-13)</td>
<td>1.8 (0.0-5)</td>
<td>3.7 (0.0-20)</td>
<td>28.5 (22-42)</td>
</tr>
<tr>
<td><strong>Median difference</strong></td>
<td>4.5</td>
<td>0.5</td>
<td>0.6</td>
<td>- 1.5</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td>from 0.2 to 11</td>
<td>from -2.5 to 5.3</td>
<td>from 0.8 to 21</td>
<td>from -5 to 4.4</td>
<td>from 3.0 to 11</td>
</tr>
<tr>
<td><strong>P - value</strong></td>
<td>0.025</td>
<td>0.23</td>
<td>0.15</td>
<td>0.16</td>
<td>0.00255</td>
</tr>
</tbody>
</table>

*Values are expressed as median (range).*
References