The association of khat (Catha edulis) chewing and orodental health: A systematic review and meta-analysis

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Background. It has been claimed that chewing khat (Catha edulis), a plant common in parts of eastern and southern Africa and the Arabian Peninsula, is associated with a range of orodental problems.

Objective. To provide a synthesis of the evidence on the association between khat chewing and orodental health.

Method. A systematic review and meta-analysis of studies that reported on the association of khat chewing and outcomes related to orodental health identified through a systematic search using web-based electronic search engines.

Results. Nineteen studies were found suitable for this review. Of these, between two and five (based on the type of outcome measured) were suitable for meta-analysis. The rest were used only for qualitative synthesis. A meta-analysis of the association of khat chewing with mucosal white lesions, gum recession, periodontal pocketing and gum bleeding showed that chewing increased the odds of the respective oral problems. However, qualitative synthesis of the findings on the effect of khat chewing on oral micro-organisms showed no evidence that the practice favours the presence of pathogenic micro-organisms in the oral cavity – instead, it seems to favour the proliferation of micro-organisms compatible with orodental health.

Conclusion. Khat chewing is associated with adverse orodental health outcomes. While literature on the topic is scarce and there is a need for generation of more evidence from different countries, on the basis of the evidence accumulated to date, public health officials and health practitioners should consider khat a threat to orodental health and take appropriate action.

to identify ‘grey literature’; the World Health Organization (WHO) database (HINARI) and specific journal websites were also searched. The references of the relevant literature so obtained were consulted in order to locate additional literature (ancestry search). The literature identified through Google, HINARI, journal-specific websites and the ancestry search was manually entered into EndNote. Finally, the EndNote libraries created for the different search strategies were merged and duplicate retrievals removed.

The last literature search for this systematic review and meta-analysis was undertaken on 10 February 2014.

Inclusion and exclusion criteria
To be included into this systematic review and meta-analysis, the study had to be original, could be observational or experimental, had to include both khat chewers and non-chewers (except in studies designed to investigate the in vitro effect of khat extract on oral micro-organisms at varying concentrations of the extract), and should have measured oral health-related outcomes in both groups. In vitro experiments that investigated the potential effect of khat on orodental health were also included. Both articles published in peer-reviewed journals and unpublished research outputs such as theses (‘grey literature’) were included. Not only studies that reported the statistical association between khat chewing and oral health-related outcomes were included; studies were considered for inclusion as long as they presented the outcomes for khat chewers and non-chewers. No time limit was imposed for the search, in order to identify as much literature as possible, and there were no restrictions regarding the language in which articles were published.

Case reports and studies that included only khat chewers, those that did not report sufficient and clear findings on the association of the dependent and independent variables, those that used a purely convenience selection of study participants, commentaries, letters to the editor and debates were excluded. In the case of duplicate publications, later versions of the duplicated articles were excluded.

Selection of relevant references
For all studies identified through the search strategies described above, the title was examined first. Studies with irrelevant titles were excluded outright. For studies with titles that seemed relevant, the abstracts, and if necessary the objectives, methods and key variables, were examined. Subsequently, studies that failed to fulfil the inclusion criteria described above were excluded. In the case of unpublished reports that were relevant but where a full report could not be found online, an attempt was made to contact the authors; if no contact addresses of the authors could be found, the reports were excluded.

Data extraction
Required data were extracted from the studies selected, according to the criteria described above, using a format prepared for this purpose by one of the authors (AA). Various attributes of the studies selected such as the author(s), year of publication, country where the study was conducted, study design, sample size, cell frequencies for a 2 × 2 cross-tabulation of the relationship between the exposure of interest (i.e. khat chewing) and the presence or absence of the outcome of interest (i.e. a specific oral health-related outcome), etc. were extracted from the studies. When 2 × 2 cross-tabulations were not readily available in the studies, they were constructed based on the information provided in the text. As the oral health-related outcome/s measured differed from study to study, the data extraction was performed separately based on the type of outcome measured (oral mucosal white lesions, gingival recession, gum bleeding, etc.).

Data analysis and reporting
The extracted data that could be combined by means of meta-analysis were entered into a computer as separate data files based on the type of outcome measured using the statistical software IBM SPSS Statistics version 20 (IBM, USA) and then exported to Stata 12 (StataCorp LP, USA) for analysis. Generally, we performed four separate meta-analyses on the association of khat chewing and oral white lesions (n=5 studies), the association of khat chewing and gum recession (n=4), the association of khat chewing and periodontal pocketing (n=2) and the association of khat chewing and gum bleeding (n=2). Tests for heterogeneity in effect size among the original studies were carried out using the χ²-based test statistic (Q-test) and the I² test statistic. For three of the meta-analyses, the χ² tests were significant (p<0.001) and I² ≥95% in the fixed-effects model, and the random-effects model was therefore used to determine the DerSimonian and Laird summary effect (i.e. odds ratio (OR)). It is also logical to assume that the studies were heterogeneous, as they were carried out at different times, by different researchers, on different populations and in different settings. For the model for which the test of heterogeneity was not significant, the summary effect measure obtained from the fixed-effect model using the inverse-variance method was retained. To determine whether the effect sizes were small, medium or large, we converted the overall OR of each meta-analysis to effect size using the formula suggested by Chinn[19] and applied Cohen’s cut-offs.[20]

The possible presence of publication bias was investigated by visual inspection of funnel plot symmetry and by using a regression test (based on Egger’s test). However, the regression test could be performed only in the analyses that used three or more studies. For analyses that used only two studies, the possible existence of publication bias was based on visual inspection of funnel plot symmetry alone.

For studies that were relevant but could not be included in the meta-analysis, a synthesis of the findings is reported. Reporting of the present systematic review and meta-analysis is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline.[21]

Results
Description of the original studies
After removing duplicate retrievals, 2 369 articles, including ‘grey literature’, were obtained. Of these, 30 were eligible for full article reading. Eleven[13,22-31] of the 30 articles were excluded because they did not meet the inclusion criteria. Nineteen studies were therefore found appropriate for this systematic review and meta-analysis (only eight of the 19 studies were suitable for meta-analysis) (Fig. 1).

Based on the outcomes measured, the studies can be grouped into six categories: (i) studies that measured oral white lesions (n=5); (ii) studies that measured gingival recession (n=4); (iii) studies that measured periodontal pocketing (n=2); (iv) studies that investigated gum bleeding (n=2); (v) studies that investigated oral micro-organisms (n=4); and (vi) studies that measured other oral health-related outcomes (n=7). As some studies measured more than one outcome, the sum of the number of studies falling into the different categories was more than 19.

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Of the 19 studies, 15\(^{14-17,32-42}\) were carried out in Yemen, three\(^{18,43,44}\) were from Kenya and one\(^{45}\) was from Israel (conducted among people of Yemeni origin). In terms of design, 15 were cross-sectional, three were experimental (both in vivo and in vitro) and one was a case-control study. Eighteen of the 19 studies were journal articles and only one\(^{45}\) fell into the ‘grey’ category. Year of publication ranged from 1990\(^{18}\) to 2013.\(^{34}\) Details of the studies are given in Table 1.

### The association of khat chewing and orodental health

Of the 19 studies in this review, five investigated the association of khat chewing with oral mucosal white lesions. Four\(^{18,43,44,45}\) of the five studies showed a statistically significant association between khat chewing and oral mucosal white lesions (i.e. there was a higher relative frequency of occurrence of oral mucosal white lesions in chewers than in non-chewers). Only Macigo et al.\(^{45}\) reported an association that was not statistically significant. Although the point estimate of the effect size they reported is closer to 2, the 95% confidence interval (CI) embraced 1, rendering the association insignificant.

Of the 19 studies, four\(^{14,16,32,42}\) investigated the association between khat chewing and gum recession. In all four studies, khat chewing had a statistically significant positive association with the presence of gum recession.

Similarly, two\(^{14,45}\) of the 19 studies reported on the association between khat chewing and periodontal pocketing. Both studies documented that a significantly higher proportion of chewers than non-chewers were affected by periodontal pocketing. These same studies also investigated the association between khat chewing and gum bleeding. One\(^{14}\) of the studies used periodontal examination to establish the presence or absence of bleeding, while the other\(^{45}\) was based on participants’ self-report. Both showed that the occurrence of gum bleeding was significantly higher in khat chewers than in non-chewers.

Of the 19 studies included in this review, four\(^{15-17,32-42}\) investigated the *in vitro* effect of crude khat extracts on oral micro-organisms and the effect of khat chewing on periodontal bacteria identified from sub- and supra-gingival plaques. All four studies, undertaken by Al-Hebshi and colleagues, demonstrated a possible antimicrobial effect of khat on oral micro-organisms. In one of the *in vitro* studies,\(^{31}\) the authors showed a selective antimicrobial effect of crude khat extracts on oral micro-organisms. They demonstrated that while bacteria associated with periodontal disease were sensitive to the extracts, bacteria associated with periodontal health were less sensitive, and cariogenic bacteria were not susceptible. They further showed that the khat extracts resulted in a two- to four-fold potentiation of tetracycline and penicillin G activities against some oral bacterial strains. In another study, Al-Hebshi et al.\(^{31}\) showed that crude khat extracts interfered with the ability of *Streptococcus mutans* to form adherent biofilms, implying that khat may have anticariogenic effects. In two other studies,\(^{14,34,36}\) investigating the effect of khat chewing on sub- and supra-gingival bacteria from chewers and non-chewers, Al-Hebshi and colleagues showed that khat chewing did not seem to increase colonisation of gingival plaque by periodontal pathogens\(^{36}\) but rather decreased the total pathogen burden and increased the total sub-gingival bacterial count,\(^{34}\) implying that khat chewing may favour the presence of bacterial species compatible with periodontal health.

Seventeen\(^{14-16,32,37,40,42}\) of the 19 studies compared various oral health-related outcomes between khat chewers and non-chewers. Al-Bayaty et al.\(^{32}\) analysed the association between khat chewing and mean number of teeth lost, stratified by gender, and showed that among female chewers the mean was significantly higher than among female non-chewers. The mean difference was not statistically significant (at an alpha value of 0.05) between male chewers and non-chewers.

Similarly, Mengel et al.\(^{14}\) studied 1 001 subjects selected randomly from schools, clinics, university and private dental practice in four different areas of Yemen, and reported that the mean community periodontal index of treatment need (CPITN) index, mean attachment loss and mean calculus index were all higher in khat chewers than in non-chewers. However, these authors did not report on the statistical significance of the differences.
and Al-Ak’hali [17] reported what could not have reported the standard deviations of the mean differences, but it was not possible as the authors of the original study. We tried to test the statistical significance of the mean differences, found a significantly higher caries rate, as measured by the decayed, missing and filled teeth (DMFT) index, in chewers than in non-chewers. They found the mean DMFT score in current chewers to be 8.778, while it was 6.529. The authors suggested that the community periodontal index (CPI) was not significantly associated with khat chewing.

Ali et al.,[37] in a study of biopsies taken from the oral mucosa of khat chewers and non-chewers, showed clear histopathological changes in biopsies taken from the chewing side of the mouths of chewers, while such changes were almost non-existent in biopsies from non-chewers. On the other hand, Jorgensen and Kaimenyi [18] and Al-Hebshi et al. [17] reported lower mean scores for plaque index, gingival index and bleeding on probing among chewers than among non-chewers.

**Meta-analysis**

The effect measure (both in individual studies and in pooled form) of khat chewing on various oral health-related outcomes is shown in the forest plots in Figs 2 – 5. The pooled effect measure of khat chewing on oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding is summarised in Table 2. In all cases, the pooled effect of chewing is an increase in the odds of the outcome of interest. The effect sizes for oral mucosal white lesions and gum recession were large (1.95 and 1.33, respectively), while those for periodontal pocketing and gum bleeding were medium (0.61 and 0.56, respectively). Although the 95% CIs of two of the effect measures are very wide, signalling lack of robustness of

<table>
<thead>
<tr>
<th>Study (author, year)</th>
<th>Country</th>
<th>Study design</th>
<th>Sample size</th>
<th>Literature type</th>
</tr>
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<td>Gorsky et al., 2004[16]</td>
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<td>Cross-sectional</td>
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<td>Journal article</td>
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<tr>
<td>Al-Sharabi, 2011[40]</td>
<td>Yemen</td>
<td>Cross-sectional</td>
<td>650</td>
<td>Journal article</td>
</tr>
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<td>Al-Sanabani, 2011[41]</td>
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<td>Cross-sectional</td>
<td>162</td>
<td>Grey</td>
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<tr>
<td>Ali et al., 2006[33]</td>
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<td>Cross-sectional</td>
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<td>Journal article</td>
</tr>
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<td>Cross-sectional</td>
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<td>Experimental</td>
<td>17</td>
<td>Journal article</td>
</tr>
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<td>Cross-sectional</td>
<td>500</td>
<td>Journal article</td>
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<tr>
<td>Al-Hebshi et al., 2006[43]</td>
<td>Yemen</td>
<td>In vitro experiment</td>
<td>33 oral microbial strains</td>
<td>Journal article</td>
</tr>
<tr>
<td>Al-Hebshi et al., 2005[44]</td>
<td>Yemen</td>
<td>In vitro experiment</td>
<td>1 bacterial strain (Streptococcus mutans)</td>
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<tr>
<td>Al-Hebshi et al., 2005[44]</td>
<td>Yemen</td>
<td>Cross-sectional</td>
<td>51 (408 sub- and supra-gingival plaques)</td>
<td>Journal article</td>
</tr>
<tr>
<td>Al-Hebshi et al., 2010[35]</td>
<td>Yemen</td>
<td>Cross-sectional</td>
<td>20 (40 sub-gingival plaque)</td>
<td>Journal article</td>
</tr>
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<td>Amran and Ataa, 2011[36]</td>
<td>Yemen</td>
<td>Cross-sectional</td>
<td>602</td>
<td>Journal article</td>
</tr>
<tr>
<td>Nyanchoka et al., 2008[45]</td>
<td>Kenya</td>
<td>Cross-sectional</td>
<td>167</td>
<td>Journal article</td>
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</table>

<table>
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<tr>
<th>Study</th>
<th>Sample size</th>
<th>OR (95% CI)</th>
<th>weight</th>
</tr>
</thead>
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<tr>
<td>Gorsky et al., 2004[16]</td>
<td>102</td>
<td>24.92 (8.78 - 70.75)</td>
<td>19.83</td>
</tr>
<tr>
<td>Macigo et al., 1995[30]</td>
<td>226</td>
<td>1.83 (0.72 - 4.63)</td>
<td>20.09</td>
</tr>
<tr>
<td>Al-Sharabi, 2011[40]</td>
<td>650</td>
<td>1.267.07 (410.75 - 3,908.66)</td>
<td>19.64</td>
</tr>
<tr>
<td>Al-Sanabani, 2011[41]</td>
<td>162</td>
<td>19.96 (9.06 - 49.40)</td>
<td>20.13</td>
</tr>
<tr>
<td>Overall (I²=95.0%, p=0.000)</td>
<td>34.62 (5.21 - 230.22)</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 2. Forest plot of the effect measure of khat chewing on oral mucosal white lesions. (OR = odds ratio; CI = confidence interval.)**
the effect size estimates (probably owing to the small number of studies used for the meta-analyses), looking at the lower bounds of the intervals alone shows that the effects are considerable. Assessment of the possible presence of publication bias by visual inspection of funnel plots revealed no evidence of bias, though it was difficult to judge the symmetry reliably owing to the small number of studies included in the meta-analysis. A regression test using Egger’s test for the possible presence of publication bias showed no evidence of bias for the meta-analyses that pooled five and four studies. For the two meta-analyses that used two studies each, a regression test was not possible.

**Discussion**

This systematic review and meta-analysis presents a synthesis of the evidence regarding the association between *khat* chewing and various orodental health-related outcomes, based on the best studies available at the time the review was conducted.

On the basis of the evidence presented, *khat* chewing is shown to be associated with various adverse oral and dental health outcomes such as oral mucosal white lesions, gingival recession, periodontal pocketing and gum bleeding. The summary effect size of *khat* chewing on the various outcomes was shown to be considerable. It has been claimed that continuous mechanical friction and exposure to the chemical content in *khat* may result in adverse consequences in the oral cavity. Continuous exposure of the oral mucosa to a high concentration of the alkaloids in *khat* could account for the effects on the oral mucosa observed. Date et al. have suggested that pesticides on *khat* may cause acute and chronic adverse health outcomes, implying that pesticides applied to *khat* in the process of production could constitute an additional insult to the oral cavity.

Although two studies reported what appears to be a ‘beneficial’ effect of *khat* chewing on periodontal health, the findings were not substantiated by subsequent studies and could not counteract the evidence that demonstrated *khat* chewing to be associated with adverse orodental health.

Regarding the effect of *khat* chewing on oral micro-organisms, the available evidence consistently indicates that chewing did not favour the proliferation of pathogenic oral micro-organisms. Rather, it was shown to have selective antimicrobial effects and to favour the presence of micro-organisms compatible with oral health. This does not imply that its use should be encouraged, as two of these four studies were conducted under *in vitro* conditions and may not be replicable *in vivo*. Additionally, the mechanical and chemical insults to the oral tissues resulting from chewing *khat* may create fertile conditions for infection of tissues of the oral cavity, as abraded tissues can be susceptible to infection even by the normal flora of the oral cavity.

Given that only a few studies were identified for the present review, and that most of them were just from one country, there appears to be a paucity of evidence on the association of the dependent and independent variables that were the focus of the review. While *khat* chewing is common in several African regions, further research is needed to fully understand the health implications of this practice.
Table 2. Summary effect size of khat chewing on oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies included, n</th>
<th>Summary effect measure OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral mucosal white lesions</td>
<td>5</td>
<td>34.62 (5.21 - 230.22)</td>
</tr>
<tr>
<td>Gum recession</td>
<td>4</td>
<td>11.19 (2.89 - 43.31)</td>
</tr>
<tr>
<td>Periodontal pocketing</td>
<td>2</td>
<td>3.05 (2.55 - 3.65)</td>
</tr>
<tr>
<td>Gum bleeding</td>
<td>2</td>
<td>2.78 (1.28 - 6.03)</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval.

countries such as Ethiopia, Somalia, Eritrea, Kenya, Djibouti and Uganda, in countries of the Arabian Peninsula such as Yemen and Saudi Arabia, and in other parts of the world, the fact that the most of the evidence is based on studies conducted in one country (Yemen) suggests that the issue has not been prioritised as a subject for research in other countries where the habit is commonplace. Additionally, the fact that most (15/19) of the studies included in this review were conducted in Yemen may limit generalisability of the evidence to a broader context, as aspects of the chewing habit and its effects may differ from country to country. However, in spite of the possibility of contextual differences in the habit, we maintain that the mechanisms (chemical, mechanical or other) by which khat chewing may result in the aforementioned orodental outcomes do not change significantly. While the amount of khat chewed and the duration of chewing, as well as other habits such as smoking and concomitant use of sweet substances such as sugar, soft drinks, tea, coffee, etc., may modify the orodental effect of khat chewing in any direction, we consider that the net effect attributable to khat remains the same. We therefore believe that the findings of the present review may apply to contexts beyond those in which the original studies were conducted.

Most of the studies included in our meta-analysis did not control for the effects of possible confounding variables such as cigarette smoking and consumption of sweet substances. We therefore did a meta-analysis of the crude ORs. If adjusted effect measures were available and used, the effect sizes might have differed (at least might have been slightly lower).

Furthermore, different studies measured different orodental health-related outcomes. Even a single outcome was measured in different ways. Some authors measured the outcomes as ‘present/absent’ or ‘yes/no’, while others used scoring systems and reported outcomes numerically. These inconsistencies in reporting outcomes, coupled with the scarcity of studies investigating the association of khat chewing with orodental health, make synthesis of evidence and pooling effect measures problematic. We therefore were able to pool effect measures for only four outcomes (oral white lesions, periodontal pocketing, gingival recession and gum bleeding). The association of khat chewing with the multitude of other orodental health-related outcomes remains scant and unclear. This calls for proper investigation of the association of khat chewing with different oral and dental health-related outcomes in a consistent way.

**Conclusion**

Khat chewing has been shown to be associated with adverse orodental health outcomes such as oral mucosal white changes, gum recession, periodontal pocketing and gum bleeding, with effect sizes ranging from medium to large. It has also been shown that chewing is associated with other indicators of periodontal health and tooth loss. The evidence that khat chewing is associated with adverse orodental health consequences outweighs that of studies reporting what seemed to be beneficial effects of khat. Public health officials and health practitioners should therefore consider khat a threat to orodental health and take appropriate action. Further studies on the association of khat chewing and orodental health should come from countries that have overlooked the issue so far. High-powered cohort and/or case-control studies that control for the confounding effect of variables such as smoking are required to come up with stronger evidence of the association between khat chewing and orodental health. Finally, the present review should be updated in the light of studies that will emerge in the future.

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References


Amran AG, Atas M. Statistical analysis of the prevalence, severity and some possible etiologic factors of gingival recession among the adult population of Ta’izz city, Yemen. RBIO Online 2011;4(3):305-313.


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