

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

A Astatkie,¹ BSc, MPH; M Demissie,² MD, MPH, PhD; Y Berhane,² MD, MPH, PhD

¹ School of Public and Environmental Health, College of Medicine and Health Sciences, Hawassa University, Hawassa, Ethiopia

² Addis Continental Institute of Public Health, Addis Ababa, Ethiopia

Corresponding author: A Astatkie (ayalewastatie@gmail.com)

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.

S Afr Med J 2014;104(11):773-779. DOI:10.7196/SAMJ.8070



Khat (*Catha edulis*) is a green shrub that grows in several countries in eastern and southern Africa and the Arabian Peninsula.^[1-3] The leaves and tender shoots are commonly chewed by people in these regions, and by ethnic minorities who have emigrated

from these areas to other parts of the world.^[3,4] Psychostimulation and euphoria result from the chewing and seem to reinforce the habit.^[5] While there are more than 40 chemical constituents in *khat*, the alkaloid called cathinone is the active principle and responsible for its stimulant effect.^[6,7]

Many health problems have been attributed to the *khat* chewing habit,^[4,7,8] including a range of orodental problems^[9] ranging from stomatitis^[10] and plasma cell gingivitis^[11,12] to oral cancer.^[13] However, much of the literature is inconclusive and contradictory. For example, Mengel *et al.*^[14] and Ali^[15] found *khat* chewing to have adverse effects on periodontal health, and Al-Sharabi *et al.*^[16] found that heavy chewing is associated with clinical attachment loss. In contrast, based on an experimental study of 17 people (eight *khat* chewers and nine non-chewers), Al-Hebshi and Al-Ak'hali^[17] showed *khat* chewing to have antiplaque and antigingivitis properties; similarly, Jorgensen and Kaimenyi^[18] found that the oral hygiene status of *khat* chewers was better than that of non-chewers, and that there was no evidence that *khat* chewing was detrimental to periodontal health.

Such contradictions in the literature call for a systematic qualitative and quantitative synthesis of the evidence in the literature available to date. We report a systematic review and meta-analysis of the evidence on the association between *khat* chewing and orodental health, which to our knowledge is the first such work.

Methods

Literature search strategy

To search the available literature for this review and meta-analysis, we carried out a web-based search using the advanced features of PubMed, Google Scholar, Embase, Scopus and the Directory of Open Access Journals (DOAJ). The PubMed search was carried out using the EndNote bibliographic software. In Google Scholar, search results were downloaded using the Zotero software and then exported to EndNote. Pertinent search results from Embase, Scopus and the DOAJ were individually downloaded and manually archived in EndNote.

We used various key words for the search. *Khat*, *Catha edulis*, *qat*, *qàt*, *qaat*, *kath*, *kat*, *gat*, *miraa*, *murungu*, *tohai*, *herari*, *jaad*, *kaad*, *oral*, *oral health*, *dental*, *dental health*, *periodontal*, *periodontal health*, *tooth*, *tooth loss*, *gingivitis* and *periodontal pocketing* were used as key words in various combinations using a Boolean search technique. For example, in PubMed we used the following combinations of key terms for the search: *khat* AND oral, *khat* AND dental, *khat* AND oral health, *khat* AND dental health, *khat* AND periodontal, *khat* AND periodontal health, *khat* AND periodontal pocketing, *khat* AND tooth, *khat* AND tooth loss, and *khat* AND gingivitis. The term *khat* was subsequently alternated with the search terms *Catha edulis*, *qat*, *qàt*, *qaat*, *kath*, *kat*, *gat*, *miraa*, *murungu*, *tohai*, *herari*, *jaad* and *kaad*. In Google Scholar, Embase, Scopus and the DOAJ, the following combination of search terms was used in one go: *khat* AND (oral OR dental OR 'oral health' OR 'dental health' OR periodontal OR 'periodontal health' OR 'periodontal pocketing' OR tooth OR 'tooth loss' OR gingivitis). As in PubMed, here also the term *khat* was alternated with other terms. We also used Google search, mainly

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 χ^2 -based test statistic (Q-test) and the I^2 test statistic. For three of the meta-analyses, the χ^2 tests were significant ($p<0.001$) and $I^2 \geq 95\%$ 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.

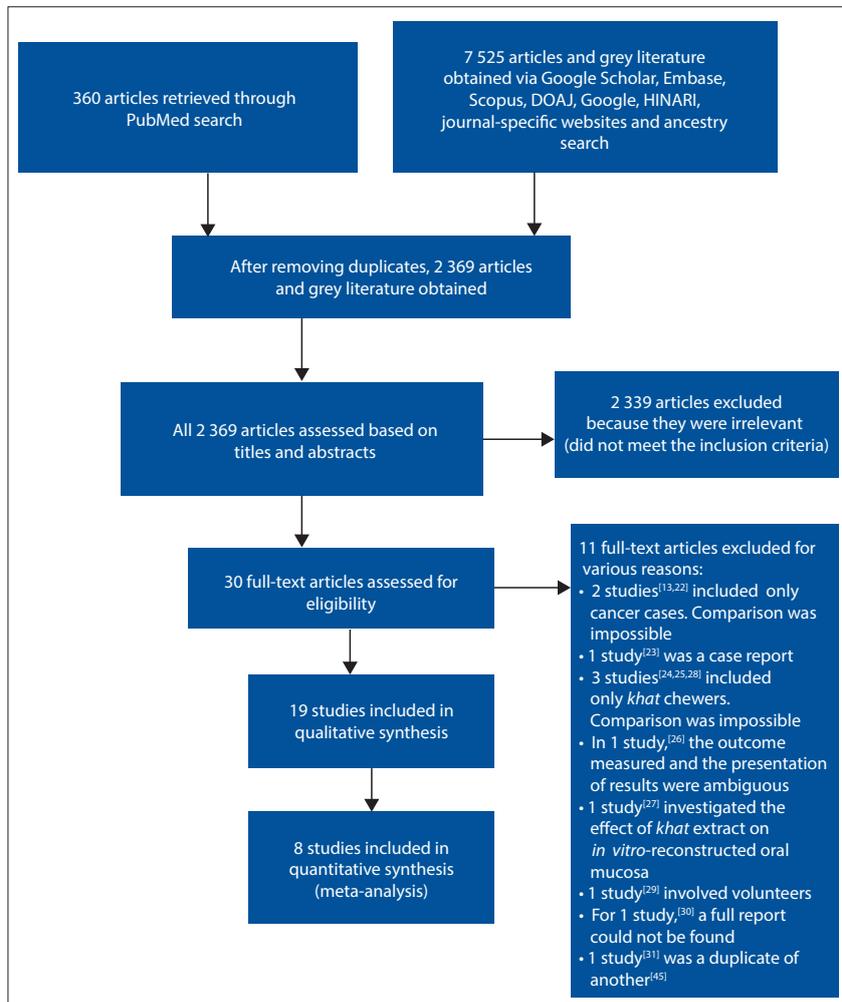


Fig. 1. Flow diagram showing article retrieval for this review. (DOAJ = Directory of Open Access Journals.)

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^[40] fell into the 'grey' category. Year of publication ranged from 1990^[18] to 2013.^[16] 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^[38,40,41,45] 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.^[43] 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^[15,39,41,42] 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^[15,39] 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^[15] of the studies used periodontal examination to establish the presence or absence of bleeding, while the other^[39] 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^[33-36] 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,^[33] 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.*^[35] 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,^[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.

Seven^[14,16-18,32,37,44] 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 male 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.

Table 1. Overview of the studies included in this systematic review and meta-analysis

Study (author, year)	Country	Study design	Sample size	Literature type
Ali <i>et al.</i> , 2004 ^[38]	Yemen	Cross-sectional	2 500	Journal article
Gorsky <i>et al.</i> , 2004 ^[45]	Israel	Cross-sectional	102	Journal article
Macigo <i>et al.</i> , 1995 ^[43]	Kenya	Case-control	226	Journal article
Al-Sharabi, 2011 ^[41]	Yemen	Cross-sectional	650	Journal article
Al-Sanabani, 2011 ^[40]	Yemen	Cross-sectional	162	Grey
Ali, 2007 ^[15]	Yemen	Cross-sectional	2 500	Journal article
Al-Kholani, 2010 ^[39]	Yemen	Cross-sectional	730	Journal article
Ali <i>et al.</i> , 2006 ^[37]	Yemen	Cross-sectional	50 (70 biopsies)	Journal article
Al-Bayaty <i>et al.</i> , 2011 ^[32]	Yemen	Cross-sectional	2 506	Journal article
Jorgensen and Kaimenyi, 1990 ^[18]	Kenya	Cross-sectional	430	Journal article
Mengel <i>et al.</i> , 1996 ^[14]	Yemen	Cross-sectional	1 001	Journal article
Al-Hebshi and Al-Ak'hali, 2010 ^[17]	Yemen	Experimental	17	Journal article
Al-Sharabi <i>et al.</i> , 2013 ^[16]	Yemen	Cross-sectional	500	Journal article
Al-Hebshi <i>et al.</i> , 2006 ^[33]	Yemen	<i>In vitro</i> experiment	33 oral microbial strains	Journal article
Al-Hebshi <i>et al.</i> , 2005 ^[35]	Yemen	<i>In vitro</i> experiment	1 bacterial strain (<i>Streptococcus mutans</i>)	Journal article
Al-Hebshi <i>et al.</i> , 2005 ^[36]	Yemen	Cross-sectional	51 (408 sub- and supra-gingival plaques)	Journal article
Al-Hebshi <i>et al.</i> , 2010 ^[34]	Yemen	Cross-sectional	20 (40 sub-gingival plaque)	Journal article
Amran and Ataa, 2011 ^[42]	Yemen	Cross-sectional	602	Journal article
Nyanchoka <i>et al.</i> , 2008 ^[44]	Kenya	Cross-sectional	167	Journal article

We tried to test the statistical significance of the mean differences, but it was not possible as the authors of the original study had not reported the standard deviations of the respective means. Nyanchoka *et al.*,^[44] in their study in Kenya ($N=162$), found a significantly higher caries rate, as measured by the decayed, missing and filled teeth (DMFT) index, in *khat* chewers than in non-chewers. They found the mean DMFT score in current chewers to be 8.778, while that in subjects who never chewed *khat* was 6.529. The authors suggested that the higher DMFT score in chewers could be a result of cariogenic substances such as soft drinks that are often consumed with *khat*. Al-Sharabi *et al.*^[16] also found that *khat* chewing significantly increased the odds of clinical attachment loss. However, they found 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 and Al-Ak'hali^[17] reported what could be considered a 'beneficial' effect of *khat* chewing on periodontal health. Jorgensen

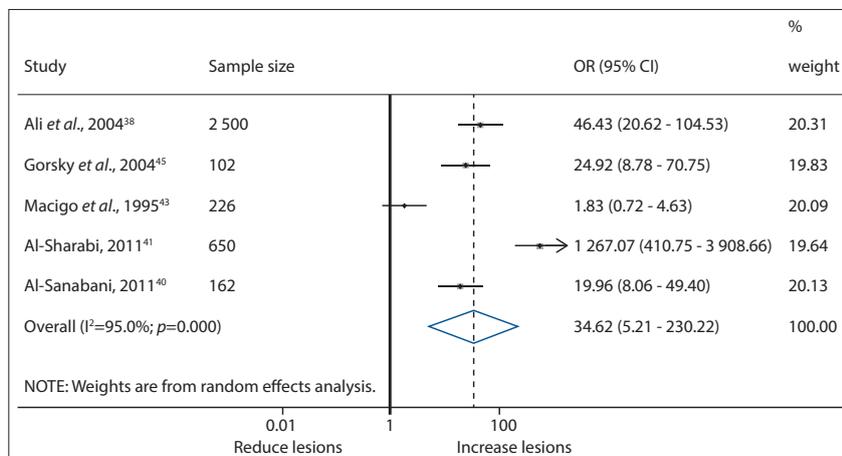


Fig. 2. Forest plot of the effect measure of khat chewing on oral mucosal white lesions. (OR = odds ratio; CI = confidence interval.)

and Kaimenyi^[18] reported lower mean gingivitis scores and lower mean surface plaque scores among *khat* chewers than among non-chewers, while documenting no significant difference in terms of attachment loss, while Al-Hebshi and Al-Ak'hali^[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

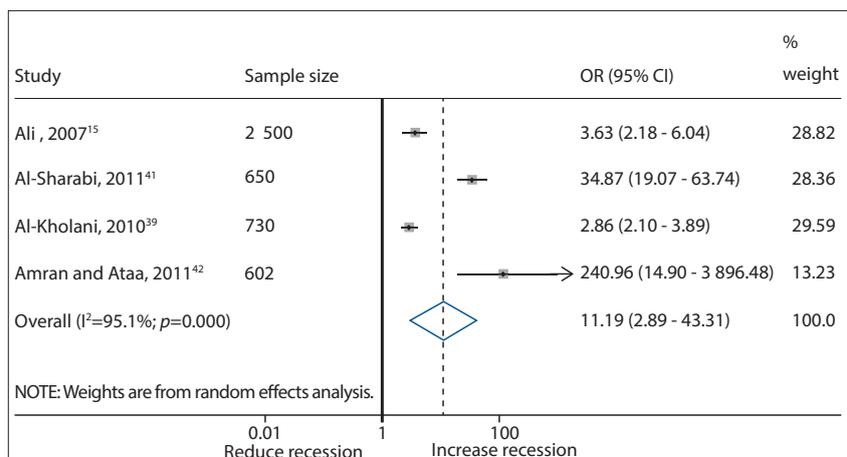


Fig. 3. Forest plot of the effect measure of khat chewing on gingival recession. (OR = odds ratio; CI = confidence interval.)

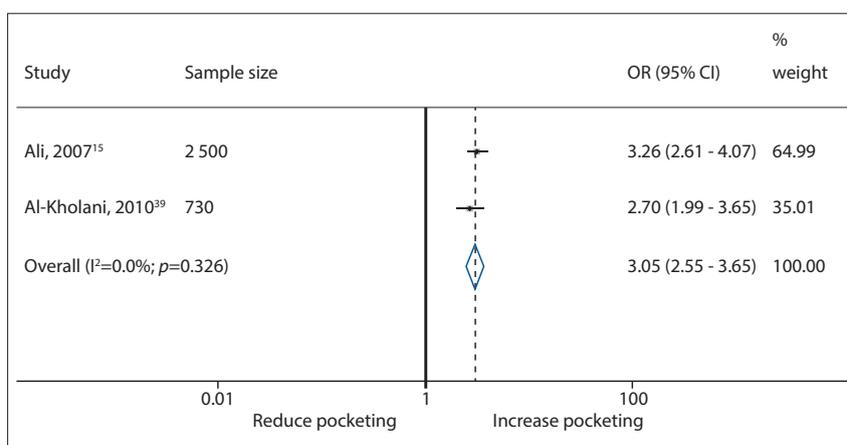


Fig. 4. Forest plot of the effect measure of khat chewing on periodontal pocketing. (OR = odds ratio; CI = confidence interval.)

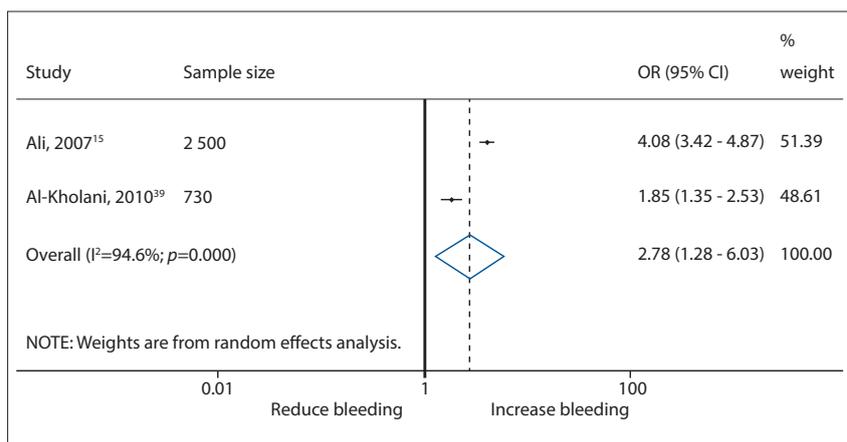


Fig. 5. Forest plot of the effect measure of khat chewing on gum bleeding. (OR = odds ratio; CI = confidence interval.)

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*^[46] may result in adverse consequences in the oral cavity. Continuous exposure of the oral mucosa to a high concentration of the alkaloids in *khat*^[47] could account for the effects on the oral mucosa observed. Date *et al.*^[48] 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^[17,18] 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

Table 2. Summary effect size of *khat* chewing on oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding

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

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,^[1-3] the fact that 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 asso-

ciation of *khat* chewing with orodental health, make synthesis of evidence and pooling effect measures problematic. We were therefore 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.

Acknowledgement. There was no funding support to conduct this review. We are grateful to the authors of the original studies upon which this review is based.

References

1. Fitzgerald J. *Khat*: A Literature Review. Centre for Culture, Ethnicity & Health, and Louise Lawrence Research, 2009. http://www.ceh.org.au/downloads/khat_report_final.pdf (accessed 25 September 2014).

2. Lemessa D. *Khat (Catha edulis)*: Botany, Distribution, Cultivation, Usage and Economics in Ethiopia. Addis Ababa: United Nations Development Programme, Emergencies Unit for Ethiopia (UNDP-EUE), 2001.
3. Advisory Council on the Misuse of Drugs (ACMD). *Khat (Qat): Assessment of Risk to the Individual and Communities in the UK*. London: Home Office, 2005.
4. Al-Motarrab A, Baker K, Broadley KJ. *Khat*: Pharmacological and medical aspects and its social use in Yemen. *Phytother Res* 2002;16(5):403-413. [<http://dx.doi.org/10.1002/ptr.1106>]
5. Brenneisen R, Fisch HU, Koelbing U, Geisslauer S, Kalix P. Amphetamine-like effects in humans of the *khat* alkaloid cathinone. *Br J Clin Pharmacol* 1990;30(6):825-828. [<http://dx.doi.org/10.1111/j.1365-2125.1990.tb05447.x>]
6. Kalix P, Khan I. *Khat*: An amphetamine-like plant material. *Bull World Health Organ* 1984;62(5):681-686.
7. Dhaifalah I, Santavý J. *Khat* habit and its health effect: A natural amphetamine. *Biomedical Papers* 2004;148(1):11-15. [<http://dx.doi.org/10.5507/bp.2004.002>]
8. Cox G, Ramesh H. Adverse effects of *khat*: A review. *Advances in Psychiatric Treatment* 2003;9(6):456-463. [<http://dx.doi.org/10.1192/apt.9.6.456>]
9. El-Wajeh YAM, Thornhill MH. *Qat* and its health effects. *Br Dent J* 2009;206(1):17-21. [<http://dx.doi.org/10.1038/sj.bdj.2008.1122>]
10. Halbach H. Medical aspects of the chewing of *khat* leaves. *Bull World Health Organ* 1972;47(1):21-29.
11. Marker P, Krogdahl A. Plasma cell gingivitis apparently related to the use of *khat*: Report of a case. *Br Dent J* 2002;192(6):311-313. [<http://dx.doi.org/10.1038/sj.bdj.4801364>]
12. Rawal SY, Rawal YB, Anderson KM, Bland PS, Stein SH. Plasma cell gingivitis associated with *khat* chewing. *Perio* 2008;5(1):21-28.
13. Soufi HE, Kameswaran M, Malatani T. *Khat* and oral cancer. *J Laryngol Otol* 1991;105(8):643-645. [<http://dx.doi.org/10.1017/S0022215100116913>]
14. Mengel R, Eigenbrodt M, Schunemann T, Flores-de-Jacoby L. Periodontal status of a subject sample of Yemen. *J Clin Periodontol* 1996;23(5):437-443. [<http://dx.doi.org/10.1111/j.1600-051X.1996.tb00571.x>]
15. Ali AA. *Qat* habit in Yemen society: A causative factor for oral periodontal diseases. *Int J Environ Res Public Health* 2007;4(3):243-247. [<http://dx.doi.org/10.3390/ijerph2007030008>]
16. Al-Sharabi AK, Shuga-Aldin H, Ghandour I, Al-Hebshi NN. *Qat* chewing as an independent risk factor for periodontitis: A cross-sectional study. *Int J Dent* 2013;2013: Article ID 317640. [<http://dx.doi.org/10.1155/2013/317640>]
17. Al-Hebshi NN, Al-Akhal MS. Experimental gingivitis in male *khat (Catha edulis)* chewers. *J Int Acad Periodontol* 2010;12(2):56-62.
18. Jorgensen E, Kaimenyi JT. The status of periodontal health and oral hygiene of Miraa (*Catha edulis*) chewers. *East Afr Med J* 1990;67(8):585-590.
19. Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. *Stat Med* 2000;19(22):3127-3131. [[http://dx.doi.org/10.1002/1097-0258\(20001130\)19:22<3127::AID-SIM784%3E3.3.CO;2-D](http://dx.doi.org/10.1002/1097-0258(20001130)19:22<3127::AID-SIM784%3E3.3.CO;2-D)]
20. Cohen J. A power primer. *Psychol Bull* 1992;112(1):155-159. [<http://dx.doi.org/10.1037/0033-2909.112.1.155>]
21. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *BMJ* 2009;339:b2535. [<http://dx.doi.org/10.1136/bmj.b2535>]
22. Sawari FA, Al-Mutwakel A, Al-Eryani K, et al. High relative frequency of oral squamous cell carcinoma in Yemen: *Qat* and tobacco chewing as its aetiological background. *Int J Environ Health Res* 2007;17(3):185-195. [<http://dx.doi.org/10.1080/09603120701254813>]
23. Fasanmade A, Kwok E, Newman L. Oral squamous cell carcinoma associated with *khat* chewing. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104(1):e53-e55. [<http://dx.doi.org/10.1016/j.tripleo.2007.01.010>]
24. Sultan M, Alhadad KA, Alsanaban E. Tooth lost and gingival recession as a risk factor of *khat* chewing in Yemen. *Cairo Dental Journal* 2008;24(2):171-176.
25. Cobián OG, Triguero RJP, Pérez HS, Salgado KMR. Trastornos temporomandibulares en adictos al qat [Temporomandibular disorders in qat addicted people]. *Rev Cubana Estomatol* 2012;49(4):268-275.
26. Halboub E, Dhaifullah E, Abdulhuk M. *Khat* chewing and smoking effect on oral mucosa: A clinical study. *Acta Medica (Hradec Kralove)* 2009;52(4):155-158.
27. Lukandu OM, Neppelberg E, Vintermyr OK, Johannessen AC, Costea DE. *Khat* alters the phenotype of in vitro-reconstructed human oral mucosa. *J Dent Res* 2010;89(3):270-275. [<http://dx.doi.org/10.1177/0022034509354980>]
28. Ali AA. Histopathologic changes in oral mucosa of Yemenis addicted to water-pipe and cigarette smoking in addition to *takhzeen al-qat*. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103(3):e55-e59. [<http://dx.doi.org/10.1016/j.tripleo.2006.10.008>]
29. Hill CM, Gibson A. The oral and dental effects of *qat* chewing. *Oral Surg Oral Med Oral Pathol* 1987;63(4):433-436. [[http://dx.doi.org/10.1016/0030-4220\(87\)90255-6](http://dx.doi.org/10.1016/0030-4220(87)90255-6)]
30. Ayagah IN, Dimba E, Macigo E, Wanzala P. Effect of *khat* chewing in the oral cavity. https://iadr.confex.com/iadr/afmrde05/preliminaryprogram/abstract_69180.htm (accessed 15 November 2012).
31. Yaron N, Epstein J, Levi H, Porat D, Kaufman E, Gorsky M. Oral manifestations of habitual *khat* chewing: A case-control study.

- Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109(6):e60-e66. [http://dx.doi.org/10.1016/j.tripleo.2010.02.022]
32. Al-Bayaty FH, Ali NAW, Bulgiba AM, Masood M, Hussain SF, Abdulla MA. Tooth mortality in khat and non khat chewer in Sana'a Yemen. *Scientific Research and Essays* 2011;6(5):1039-1045.
 33. Al-Hebshi N, Al-Haroni M, Skaug N. *In vitro* antimicrobial and resistance-modifying activities of aqueous crude khat extracts against oral microorganisms. *Arch Oral Biol* 2006;51(3):183-188. [http://dx.doi.org/10.1016/j.archoralbio.2005.08.001]
 34. Al-Hebshi NN, Al-Sharabi AK, Shuga-Aldin HM, Al-Haroni M, Ghandour I. Effect of khat chewing on periodontal pathogens in subgingival biofilm from chronic periodontitis patients. *J Ethnopharmacol* 2010;132(3):564-569. [http://dx.doi.org/10.1016/j.jep.2010.08.051]
 35. Al-Hebshi NN, Nielsen Ø, Skaug N. *In vitro* effects of crude khat extracts on the growth, colonization, and glucosyltransferases of *Streptococcus mutans*. *Acta Odontol Scand* 2005;63(3):136-142. [http://dx.doi.org/10.1080/00016350510019838]
 36. Al-Hebshi NN, Skaug N. Effect of khat chewing on 14 selected periodontal bacteria in sub- and supragingival plaque of a young male population. *Oral Microbiol Immunol* 2005;20(3):141-146. [http://dx.doi.org/10.1111/j.1399-302X.2004.00195.x]
 37. Ali AA, Al-Sharabi AK, Aguirre JM. Histopathological changes in oral mucosa due to takhzeen al-qat: A study of 70 biopsies. *J Oral Pathol Med* 2006;35(2):81-85. [http://dx.doi.org/10.1111/j.1600-0714.2006.00362.x]
 38. Ali AA, Al-Sharabi AK, Aguirre JM, Nahas R. A study of 342 oral keratotic white lesions induced by qat chewing among 2500 Yemeni. *J Oral Pathol Med* 2004;33(6):368-372. [http://dx.doi.org/10.1111/j.1600-0714.2004.00145.x]
 39. Al-Kholani AI. Influence of khat chewing on periodontal tissues and oral hygiene status among Yemenis. *Dent Res J* 2010;7(1):1-6.
 40. Al-Sanabani JSM. Oral white lesions due to qat chewing among women in Yemen. Doctor Medicinae Dentariae thesis. Berlin: Universitätsmedizin, 2011.
 41. Al-Sharabi AK. Conditions of oral mucosa due to takhzeen al-qat. *Yemeni Journal of Medical Sciences* 2011;5:1-6.
 42. Amran AG, Ataa MAS. Statistical analysis of the prevalence, severity and some possible etiologic factors of gingival recessions among the adult population of Thamar city, Yemen. *RSBO (Online)* 2011;8(3):305-313.
 43. Macigo FG, Mwaniki DL, Guthua SW. The association between oral leukoplakia and use of tobacco, alcohol and khat based on relative risks assessment in Kenya. *Eur J Oral Sci* 1995;103(5):268-273. [http://dx.doi.org/10.1111/j.1600-0722.1995.tb00025.x]
 44. Nyanhoka IN, Dimba EAO, Chindia ML, Wanzala P, Macigo FG. The oral and dental effects of khat chewing in the Eastleigh area of Nairobi. *Journal of the Kenya Dental Association* 2008;1(1):37-42.
 45. Gorsky M, Epstein JB, Levi H, Yarom N. Oral white lesions associated with chewing khat. *Tob Induc Dis* 2004;2(3):145-150. [http://dx.doi.org/10.1186/1617-9625-2-3-145]
 46. Hassan NAGM, Gunaid AA, Murray-Lyon IM. Khat (*Catha edulis*): Health aspects of khat chewing. *East Mediterr Health J* 2007;13(3):706-718.
 47. Al-Habori M. The potential adverse effects of habitual use of *Catha edulis* (khat). *Expert Opin Drug Saf* 2005;4(6):1145-1154. [http://dx.doi.org/10.1517/14740338.4.6.1145]
 48. Date J, Tanida N, Hobara T. Qat chewing and pesticides: A study of adverse health effects in people of the mountainous areas of Yemen. *Int J Environ Health Res* 2004;14(6):405-414. [http://dx.doi.org/10.1080/09603120400012884]

Accepted 3 July 2014.