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EFFECTS OF CHRONIC KHAT USE ON ORAL HEALTH STATUS. (REVIEW PAPER)

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Abstract

Background: The habit of khat chewing is common in many East African and Middle Eastern cultures and is slowly spreading to other parts of the world. Fresh leaves and twigs of the khat plant are chewed for various reasons, the main one being the stimulating amphetamine-like effects it induces among users. There is growing evidence linking chronic khat use to various medical and oral conditions.

Objectives: The review aimed to provide a summary of information drawn from various studies focusing on effects of chronic khat use on oral health, with special focus on dental hard tissues, the oral mucosa and the periodontium.

Methodology: This was a narrative desk review that looked at published literature focusing on aspects of oral health among khat chewers.

Results: The review revealed scientific evidence that chronic khat use was associated with adverse oral conditions such as oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding. There was also adequate research evidence linking chronic khat chewing to dental discoloration, excessive tooth wear and even tooth loss. There was however no adequate evidence linking khat chewing to serious oral conditions such as oral cancer.

Conclusion: From the published work reviewed here, chronic khat chewing appeared to have the potential to induce adverse effects on the oral mucosa and the periodontium.

Keywords; Khat, Oral, *Miraa*, Oral health, Adverse effects.

Introduction

Khat (*Catha edulis* Forsskal) also known in Kenya as *miraa*, is an evergreen flowering tree or shrub that grows in equatorial climates mainly in the Arabian Peninsula and the regions around the horn of Africa¹. The khat plant grows well both in arid and semi-arid areas making it an alternative to rainfall-dependent commercial crops such as maize, bananas, coffee and tea. Khat production has been on a rapid increase in khat growing regions replacing coffee, tea and food crops such as maize. Ethiopia, Yemen and Kenya are the three leading khat-growing countries in the world Figure 1. Whereas most of the khat grown in Yemen is for local consumption, Ethiopia and Kenya do export substantial amounts of their khat produce.

Fresh shoots and leaves of the khat plant are chewed mainly for their psycho-stimulant properties. Many khat

chewers believe the habit is useful in relieving fatigue and stress, boosting energy to enhance ability to work, staying alert to enhance performance of work, reducing hunger and enhancing self-esteem. Khat is therefore used by truck drivers and other workers who desire to keep awake and alert during the night. Khat is also thought to have nutritional and medicinal properties and is known to enhance social bond-



Figure 1. A photograph of a khat plant taken in the Meru County of Kenya.

ing among user communities. At present, khat is still largely used by communities in the regions where it is grown. Khat contains three main phenylpropylamine alkaloids; cathinone, cathine and norephedrine¹. Cathinone is the main psychoactive constituent in khat, but it is very unstable and rapidly decomposes into norpseudoephedrine and norephedrine as the leaves and shoots dry up.

Khat use has often been associated with various adverse effects that occur in almost all body systems². The most widely studied effects are those that lead to various psychological and reproductive conditions. A number of previous studies have also focused on the potential association between khat use and various cardiovascular and gastrointestinal effects.

The traditional method of using khat is through mastication, but historical narratives suggest that dry leaves of the

khat plant may have been used in a manner similar to tea leaves in the past periods³. Fresh leaves and barks of the plant are placed in the mouth and chewed continuously while left to accumulate in the lower vestibule as more khat is added creating a noticeable pouch in the cheek^{1,4}. Khat chewing often induces dryness of the oral mucosa and chewers tend to consume a variety of fluids such as water, coffee and sugary soft drinks⁵.

A session or duration of chewing khat could last anywhere between 2 and 10 hours every day, a factor that predisposes oral tissues to potentially toxic effects of khat. It has been shown that the psychoactive compounds in khat are adequately extracted into saliva during chewing while still in the oral cavity.

The oral mucosa serves as the first and key absorption surface of these constituents and this enables rapid entry of cathinone and cathine into the bloodstream to achieve peak plasma levels within 1 – 4 h of chewing khat⁶. Over 90% of the alkaloids could be absorbed in this manner. Once absorbed into the bloodstream, the psychoactive compounds have short half-life (1.5 hours for cathinone) due to rapid metabolism⁷. This is partly the reason why khat has to be chewed continuously in order to elicit prolonged stimulant and euphoric effects.

Effects of khat use on dental hard tissues

One of the earliest studies describing effects of khat on oral tissues was carried out in Yemen and was conducted among a group of 121 Yemeni males⁸. The study revealed a lower dental caries rate among khat chewers when compared to non chewers. The authors suggested that the diet rich in fiber used by Yemenis could partly explain the low caries rate. However, dental

hard tissues depicted severe wearing out due to abrasive forces experienced during chewing. One subsequent study demonstrated that the low caries rate did not have any link at all to the fluoride content in khat leaves⁹. Khat in itself is considered to be non cariogenic and the way it is used is suggested to have a cleansing effect on the teeth with a potential to lower dental caries rate among users⁴. A number of researchers have suggested that the high consumption of sugary drinks and frequent use of sugar to counteract the bitter taste of khat in the mouth during khat chewing could predispose to increased dental caries rate especially cervical caries⁴. This factor could explain the higher number of missing teeth found among khat chewers in some recent studies¹⁰.

In a study involving 167 Kenyans, khat chewers had a significantly higher dental caries rate than non chewers¹¹. The authors found the mean number of affected teeth (DMFT score) in current chewers to be about 8.8, compared with 6.5 among non chewers. The authors also noted an emerging trend where khat is used alongside sugary foods to mask the bitter taste of khat. They attributed the high dental caries rate among khat chewers to the soft sugary drinks that were often consumed together with khat.

Increased dental discoloration has often been reported in chronic khat chewers. The staining was noted to specifically affect teeth on the chewing side and adjacent to the point where the khat bolus is placed while chewing when compared with the non-chewing side^{11,12}. In one study¹², over 90% of the khat chewers had dental staining whereas no staining was noted in the control group, indicating a significant association between khat chewing and staining of teeth. Moreover, the observed dental staining among khat

chewers was found to be independent of the habit of smoking tobacco.

Effects of khat use on periodontal health status

Previous clinical studies that have compared periodontal health status of khat chewers with the status in non chewers have generally yielded conflicting results. In one study, Mengel *et al* studied the periodontal health of over 1000 Yemeni adults and found that the clinical loss of attachment and the calculus index were significantly higher among khat chewers¹³. Interestingly, among khat chewers, he found that khat chewing sides of their mouths had less clinical loss of attachment than did the non chewing sides. Whereas khat chewing was generally detrimental to periodontal health, the specific sides used for chewing had somewhat better periodontal health

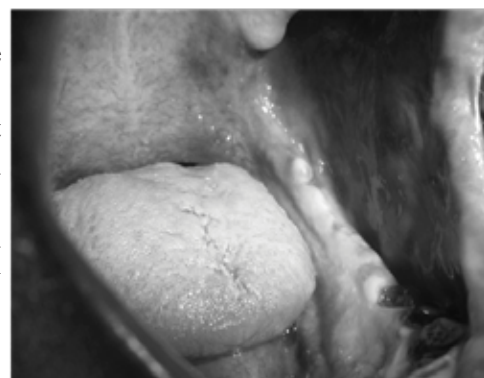


Figure 2. A clinical oral photograph of a chronic khat chewer from Meru County of Kenya. Notice the tooth loss and residual roots affecting both upper and lower jaws.

status. somewhat better periodontal health status.

Another clinical study by Yarom *et al* showed that the health of the gingiva among khat chewers was better than gingival health status among non chewers. In fact, even among individual chewers, gingival health was significantly better on the chewing side when compared to the non chewing side¹². In this study, periodontal

pocketing among khat chewers was also lower on the chewing side compared to the non chewing side. An earlier study by Hill and Gibson had also showed reduced periodontal pocketing both among khat chewers and on the

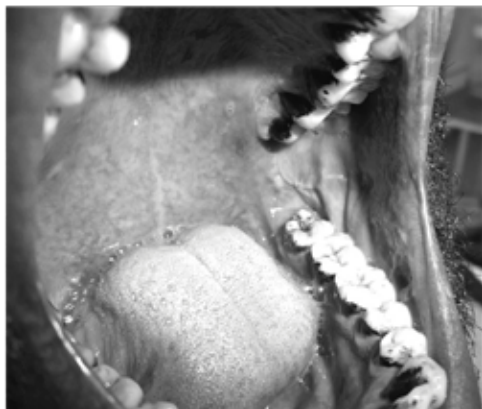


Figure 3. A clinical oral photograph of a chronic khat chewer and tobacco smoker from the Meru County of Kenya. Notice the heavy staining of the upper and lower teeth and the whitening of the oral mucosa that is specifically more severe on the buccal mucosa.

chewing side, when compared to non chewers and the non chewing side respectively⁸.

In a clinical study conducted in Kenya, Jorgensen and Kaimenyi¹⁴ did not find significant differences in the periodontal health status when they compared 131 khat chewers with 199 non chewers. However, khat chewers showed significantly lower plaque and gingivitis scores than did the non chewers. Following these findings, the authors suggested that there was no evidence from their study that khat chewing was detrimental to periodontal health. In yet another study, the findings suggested that the proportion of the population with severe periodontal disease in Yemen where prevalence of khat use is high was lower than the proportion in countries with a high level of dental health care¹³. The authors' conclusions implied that khat use could have beneficial effects on

periodontal health.

The findings described above appear to be in sharp contrast with those from a study involving 2500 Yemenis among which 1528 were khat chewers and 972 were non chewers. The study which had a cross-sectional design found that 31.8% of the khat chewers had periodontal pockets compared to a paltry 12% of the non chewers who had periodontal pocketing¹⁵. The study also found that over 79% of the khat chewers had gum bleeding whereas only 48.7% of non chewers had gum bleeding. Gingival recession was described in 10.4% of those who used khat daily and in 2.2% of those who chewed khat once per week. According to the study findings, the observed effects were more serious in those with higher frequency and longer duration of khat chewing. The authors concluded that khat could have a negative effect on periodontal health by predisposing to periodontal pocketing as well as gingival bleeding and recession.

The findings described earlier also contrast with those in another study in Yemen that compared periodontal health status among 336 khat chewers and 394 non-chewers¹⁶. According to the study, khat chewers depicted poor oral hygiene status when compared to non chewers. Furthermore, a higher proportion of khat chewers presented with gingival bleeding and a burning sensation in the soft tissues within their mouths. Oral mucosal ulcerations were present in about 7% of chewers compared to only 0.5% of the non-chewers while gingival recession was present in over 50% of the chewers compared to about 26% of the non chewers. Recently, a clinical study also from the Middle East demonstrated a significant association between khat chewing and adverse periodontal health status¹⁷. The effects manifested in form of increased periodontal, calculus and gin-

gival indices.

Data from laboratory studies has not helped resolve these controversies. In a series of *in vitro* studies, it was revealed that khat does have selective antibiotic effects that could be of significance for periodontal and dental health^{18,19}. It was not clear what active compounds in khat were responsible for the antibiotic activity. Aqueous crude extracts of khat were shown to interfere with formation of adherent biofilms by cariogenic bacteria in humans. Khat extracts were also shown to inhibit synthesis of molecules that are known to assist in bacterial attachment to dental hard tissues. All these effects were dose-dependent. According to these studies, periodontal bacteria in sub- and supragingival regions of khat chewers were not detrimental to the periodontium.

Aqueous crude extracts of khat were found to possess selective antibacterial properties against a majority of periodontal disease-associated bacteria. In general, findings from these studies suggested that, rather than increase bacterial colonization of gingival tissue, khat chewing could induce microbial profiles compatible with gingival health. In another recent study by the same researchers, khat chewing was shown to elicit an anti-plaque and anti-gingivitis effect²⁰. This was a 20 day experiment designed to investigate the effect of khat chewing on formation of dental plaque and development of gingivitis. Khat chewing was associated with lower plaque index scores, and khat chewing sides of the mouth also showed lower gingival index scores and bleeding scores.

In summary, whereas some researchers have found khat chewing to have adverse effects on periodontal health, other researchers found khat chewing to have anti-plaque and anti-gingivitis

properties, and that the oral hygiene status of khat chewers was better than that of non-chewers. These contradictions in the literature were noted in a recent systematic review and meta-analysis of available research with regard to effects of khat on oral health²¹. In the study, the pooled effect measure of khat chewing on oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding all showed 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). Assessment of possible presence of publication bias 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. Some meta-analyses used only two studies each, and additional regression tests for bias were not possible.

One proposed theory put forward in a recent study could help explain some of these contrasting findings²². In this study, khat chewing sides showed more periodontal destruction compared to the non chewing sides in heavy and chronic khat chewers, but no effect or even a beneficial effect in less chronic chewers. The authors theorized that the effects of khat on the periodontium could range from detrimental to no effect and further to beneficial effect depending on the chronicity of the habit. According to the proposed theory, other suggested predictors for the overall clinical effect included oral health status and concomitant use of tobacco.

Effects of khat use the oral mu cosa

In a case-control study conducted in Kenya which aimed to investigate the role of tobacco, alcohol and khat use in

the development of oral white lesions, the authors did not find a significant association between khat chewing and white lesions of the oral mucosa²³. This is contrary to several other studies that have reported khat chewing to be associated with specific effects of on oral mucosa, particularly induction of oral keratotic white lesions.

In a cross-sectional study involving 2500 people in Yemeni, 22.4% of khat chewers had oral keratotic white lesions compared to a paltry 0.6% of non chewers who had white lesions on their oral mucosa²⁴. According to the authors, khat chewing was responsible for the oral keratotic white lesions because the lesions occurred at specific sites of the mucosa consistent with the habit of chewing khat. The prevalence and severity of the lesions were found to be dependent upon the chronicity of khat chewing. In two follow up studies, the same authors reported that the oral lesions showed histopathological changes such as acanthosis, hyperkeratosis and mild dysplasia^{25,26}, and were especially severe among people who used tobacco products alongside khat chewing²⁶. The lesions induced by khat were however not considered to be potentially cancerous²⁵.

Oral keratosis has been described in many studies conducted among khat chewers. One of the earliest studies was carried out by Hill and Gibson who found that just under 50% of khat chewers had some degree of keratosis⁸. None of the lesions depicted features suggestive of dysplasia and malignancy. In another study, it was found that oral white lesions were more prevalent in khat chewers than in non chewers¹². This particular study also found that the lesions were mainly on the buccal aspect of the lower gingiva, the alveolar mucosa and the lower mucobuccal fold. However, contrary to other studies described earlier, this

study did not find any association between the occurrence of the white lesions and tobacco use.

Mucosal lesions resulting from khat use do vary according to the duration of khat chewing. According to one previous study, the mucosal lesions identified in khat chewers included mucosal whitening, whitening with mild corrugation, frictional keratosis and frictional keratosis with mild corrugation²⁷. These effects were less varied on the non chewing side and were confined to the mucosa of the vestibule and mucobuccal fold. The appearance of these lesions did not vary between smokers and non smokers.

In another study, oral white lesions were more prevalent in khat chewers (83%) compared to non chewers (16%) and the lesions were mainly on the lower buccal attached gingival mucosa, the alveolar mucosa and the lower mucobuccal fold on the chewing side²⁸. The authors of this study attributed the white lesions to chronic local mechanical and chemical irritation of the mucosa during khat chewing. However, in response to this study, one researcher felt the authors failed to consider the fact that chronicity in khat use is dependent on two factors; the duration of use in years and frequency of chewing per week²⁹.

Recently, a cross-sectional hospital based study observed that oral white lesions were present on the chewing side of over 75% of khat chewers compared to less than 10% on the non chewing side³⁰. The study also revealed a significant difference in the prevalence of white lesions between cases and controls. There was a positive correlation between presence of white lesions and duration of khat chewing but not with duration of water-pipe smoking and cigarette smoking.

To investigate molecular aspects of khat induced oral white lesions, an *in vitro* study where oral mucosal cells were exposed to an extract of khat found that the cells in culture expressed molecules that are known to indicate cellular stress, differentiation and senescence³¹. In a follow up study where they exposed a model of oral mucosa to an extract of khat, they were able to mimic the situation in the oral cavity of khat chewers by inducing premature and abnormal hyperkeratinization similar to what is seen in oral keratotic white lesions of khat chewers. From the two studies, the authors suggested that the effects induced by khat were partly due to the chemical constituents within khat and not merely frictional keratosis.

Oral mucosal pigmentation related to khat use has also been described¹². In this study, all khat chewers who were also non smokers had mucosal pigmentation, and the pigmentation was independent of pigmentation associated with tobacco use even among khat chewers who smoked tobacco. On the basis of evidence presented in a recent systematic review, it appeared that khat chewing was associated with various adverse oral and dental health outcomes such as oral mucosal white lesions, gingival recession, periodontal pocketing and gum bleeding. (Astatkie, Demissie et al. 2014). A meta-analysis in this review did summarize the commonest effects of khat in the oral cavity as follows in order of strength of association 1) oral mucosal white lesions, 2) gum recession, 3) periodontal pocketing and 4) gum bleeding.

Khat and oral cancer

A few studies have found a higher incidence of head and neck cancer among people who chew khat compared to non chewers^{32,33}. The cancers were shown to develop on the chewing side of the mouth at the very site where the users placed the khat bolus while

chewing. Gunaid *et al* also found a high frequency of khat chewing and smoking among Yemeni head and neck cancer patients, but the authors did not identify independent association with khat use³⁴. Case reports of oral cancer³⁵, oral verucous carcinoma and also plasma-cell gingivitis³⁶ have also been described in association with prolonged periods of khat use.

Given the small number of studies and their methodological weaknesses, khat use is not considered a risk factor for oral cancer. It is therefore generally agreed that larger well controlled studies are needed in this area^{3,5,37}. Data drawn from a recent systemic review⁵ appeared to firmly conclude that there was no sufficient evidence that khat chewing is an independent risk factor for development of head and neck cancers, and the authors attributed suggested associations to confounding factors such tobacco smoking and alcohol consumption. The review specifically noted the relatively few sound epidemiological studies on khat use and its association with potentially malignant or malignant oral disorders.

Conclusion

Despite the limited number of studies and limitation in the methodologies employed in the studies touching on aspects of khat and oral health, there is adequate evidence to link khat use to a number of oral and dental conditions. As pointed out earlier, the effects of chronic khat use in the oral cavity include oral mucosal white lesions, gum recession, periodontal pocketing and gum bleeding. There is also adequate research evidence linking khat chewing to dental discoloration and excessive tooth wear. Even though a number of studies arrived at contrary findings, the said studies did have methodological shortcomings that could discount their findings. For instance, a number of studies did report what appeared to be a 'beneficial' effect of khat chewing on periodontal health, but the findings were not substantiated by subsequent studies and could not counteract the

evidence that demonstrated khat chewing to be associated with adverse oral and dental health. From current understanding, the said beneficial effects of khat chewing could probably occur only in controlled chewing settings where there is a limit on amount of khat chewed, duration of chewing and an absence of associated habits such as smoking and drinking sugary diets. Even though there is overwhelming evidence linking chronic khat use to oral keratotic white lesions, there is currently no evidence that these lesions do indeed lead to increased cases of oral cancer among khat chewers.

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