



Cytological Changes in Buccal Mucosa Among Yemeni Qat Chewers in Hadhramout Governorate: A Comparative Cross-Sectional Study

Saleh H. Ben Sumaidea

College of Medicine and Health Sciences, Al-Arab University, Yemen

Hassan Pyar

College of Medicine and Health Sciences, Seiyun University, Yemen AND Faculty of Environmental Science and Marine Biology, Hadhramout University, Yemen

Abdullah O. Bin Nashwan

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Abdullah M. Bin Fadhl

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Abeer A. Marabi

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Ahmed A. Al-Shetri

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Gumaan S. Rassam

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Halima K. Joher

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Mashhoor A. Bin Shehab

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Mohammed S. Bin Mosalem

Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

Follow this and additional works at: <https://acbs.alayen.edu.iq/journal>



Part of the [Biology Commons](#), [Biotechnology Commons](#), and the [Medicine and Health Sciences Commons](#)

Recommended Citation

Sumaidea, Saleh H. Ben; Pyar, Hassan; Nashwan, Abdullah O. Bin; Fadhl, Abdullah M. Bin; Marabi, Abeer A.; Al-Shetri, Ahmed A.; Rassam, Gumaan S.; Joher, Halima K.; Shehab, Mashhoor A. Bin; and Mosalem, Mohammed S. Bin (2025), Cytological Changes in Buccal Mucosa Among Yemeni Qat Chewers in Hadhramout Governorate: A Comparative Cross-Sectional Study, *AUIQ Complementary Biological System*: Vol. 2: Iss. 3, 81-91.

DOI: <https://doi.org/10.70176/3007-973X.1049>

Available at: <https://acbs.alayen.edu.iq/journal/vol2/iss3/9>



ORIGINAL STUDY

Cytological Changes in Buccal Mucosa Among Yemeni Qat Chewers in Hadhramout Governorate: A Comparative Cross-Sectional Study

Saleh H. Ben Sumaidea ^{a,*}, Hassan Pyar ^{id b,c}, Abdullah O. Bin Nashwan ^d,
Abdullah M. Bin Fadhl ^d, Abeer A. Marabi ^d, Ahmed A. Al-Shetri ^d,
Gumaan S. Rassam ^d, Halima K. Joher ^d, Mashhoor A. Bin Shehab ^d,
Mohammed S. Bin Mosalem ^d

^a College of Medicine and Health Sciences, Al-Arab University, Yemen

^b College of Medicine and Health Sciences, Seiyun University, Yemen

^c Faculty of Environmental Science and Marine Biology, Hadhramout University, Yemen

^d Department of Medical Sciences, University of Science and Technology – Hadhramaut Branch, Yemen

ABSTRACT

Qat (*Catha edulis*) chewing is a common practice in Yemen, associated with oral mucosal irritation. The objective of the current study is to compare cytological findings of buccal mucosa between Qat chewers and non-chewers. A comparative cross-sectional study was designed. Buccal smears were collected from chewers (n = 100) and non-chewers (n = 100), fixed, and stained with Harris hematoxylin staining. Smears were assessed for inflammatory changes and cytological atypia by two blinded examiners; disagreements were resolved by consensus. The inflammatory cells were observed in 21% of chewers compared to 8% of controls ($P = 0.009$), while atypical cytological changes were present in 16% of chewers and absent in controls ($P < 0.001$). Longer duration of chewing correlated with increased inflammatory and atypical findings ($P = 0.003$ and $P = 0.010$, respectively), while weekly frequency showed no significant association. The statistical values presented reflect the original complete dataset analyzed at the time of study completion. The present revision focuses on clarifying the interpretation of association patterns, consistent with the study's cross-sectional design. Qat chewing is associated with increased inflammatory and cytological atypical changes in the buccal mucosa. These findings reflect correlations rather than causation.

Keywords: Buccal mucosa, Qat chewing, Cytological atypia, Oral cytology, Inflammation, Yemen

1. Introduction

Qat is a natural stimulant derived from the *Catha edulis* plant, a flowering evergreen tree belonging to the Celastraceae family [1, 2]. The plant grows predominantly in Yemen, Ethiopia, Somalia, Kenya, Saudi Arabia, and at high altitudes in South Africa and Madagascar [3]. It thrives in both arid and semi-arid regions, often serving as an alternative to rainfall-dependent commercial crops such as maize,

bananas, coffee, and tea [4]. Different names are used across countries to refer to the plant—Qat in Yemen and Ethiopia, Mirra in Kenya, and Qaad or Jaad in Somalia—but “Qat” remains the most widely used term. Yemen, Ethiopia, and Kenya are recognized as the world’s major producers of Qat [5].

The principal active ingredient responsible for the psychostimulant effects of Qat is cathinone, an alkaloid structurally and chemically similar to d-amphetamine, while cathine represents a milder

Received 25 October 2025; revised 29 November 2025; accepted 29 November 2025.
Available online 23 December 2025

* Corresponding author.

E-mail address: salehhussein721981@gmail.com (S. H. Ben Sumaidea).

<https://doi.org/10.70176/3007-973X.1049>

3007-973X/© 2025 Al-Ayen Iraqi University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

metabolite of cathinone. Cathinone is a highly potent stimulant that exerts sympathomimetic and central nervous system (CNS) stimulatory effects comparable to those of amphetamine [6]. In addition to cathinone and cathine, *Catha edulis* contains a complex mixture of over sixty alkaloids, along with carbohydrates, tannins, flavonoids, terpenoids, sterols, glycosides, vitamins (particularly vitamin C), trace metals, and amino acids [7].

Chronic Qat chewing has been associated with a wide spectrum of adverse systemic health effects, including gastrointestinal disturbances, cytotoxic effects on the liver and kidneys, respiratory problems, psychological and mental health disorders, and cardiovascular conditions such as hypertension and increased risk of myocardial infarction. It has also been linked to sexual impotence, reproductive dysfunction, and possible genotoxic and teratogenic effects, particularly among pregnant women, where fetal development may be adversely affected, although these effects remain poorly characterized [8, 9]. Preliminary evidence further indicates that habitual Qat use can impair cognition and mental performance, causing concentration difficulties, insomnia, headaches, migraines, mydriasis, conjunctival congestion, fine tremors, motor incoordination, and stereotypic behavior [10].

Recent genetic and clinical studies have raised concerns about the potential oral health consequences of Qat consumption. Qat use—particularly when combined with alcohol and tobacco—has been implicated as a possible etiological factor in oral malignancy, while other clinical observations have demonstrated periodontal tissue damage among habitual chewers, especially in younger individuals [11]. Over the years, epidemiological and case-control studies have consistently reported associations between long-term Qat consumption and dysfunction of cardiovascular, respiratory, gastrointestinal, obstetric, metabolic, endocrine, and nervous systems. Reviews of Qat's cardiovascular effects have highlighted enhanced sympathetic activity, tachycardia, elevated arterial pressure, and increased risk for acute myocardial infarction. Moreover, Qat users in Yemen reportedly exhibit a higher incidence of esophageal carcinoma compared to non-users [8, 12].

The oral mucosa functions as the primary site for absorption of Qat's active constituents, allowing rapid entry of cathinone and cathine into systemic circulation. Peak plasma levels are achieved within one to four hours of chewing, with over ninety percent of the alkaloids absorbed through the mucosal surface. These psychoactive compounds have a short plasma half-life—approximately 1.5 hours for cathinone—owing to rapid hepatic metabolism, which explains the continuous chewing behavior required to sustain

euphoria and stimulation [4, 8, 13]. Preventive programs in oral health emphasize education on hygiene, proper diet, fluoride prophylaxis, regular check-ups, and professional oral cleaning sessions, which together help mitigate oral pathologies related to such chronic exposures [14].

Cytology and cytopathology, the disciplines concerned with microscopic evaluation of exfoliated cells, date back to the 18th and 19th centuries but were standardized only toward the late 20th century [15]. Diagnostic cytology relies on four fundamental sampling methods: exfoliative cytology (spontaneous shedding of cells), abrasive techniques such as brushing or scraping, aspiration biopsy (fine-needle aspiration, FNA), and needle extraction of cells from palpable or deep lesions. Lesions of the oral cavity can be effectively evaluated through smears obtained by gentle scraping of the mucosa using a tongue depressor, wooden spatula, or curette. In cases of hyperkeratotic lesions, more vigorous scraping with a metallic instrument may be required. Sciubba later introduced a cytobrush designed specifically to sample oral lesions, improving diagnostic yield [16, 17].

In this context, Qat chewing provides a unique model for assessing the cytological impact of chronic chemical and mechanical irritation on oral tissues. The present study, therefore, aims to evaluate the cytological changes occurring in the buccal mucosa among Yemeni Qat chewers and to determine the association of these alterations with age and duration of chewing in Hadhramout Governorate, Yemen.

2. Materials and methods

2.1. Study design

This was a comparative cross-sectional study conducted to evaluate buccal mucosal cytological patterns among Qat chewers compared to non-chewers. The revision clarifies the design as cross-sectional to reflect simultaneous data collection and comparison, addressing the reviewers' methodological concern regarding study classification.

2.2. Study area

The study was carried out in Mukalla City, Hadhramout Governorate, Yemen, between January and June 2019.

2.3. Study population

Adult male Qat chewers and non-chewing controls residing in Mukalla City were included in the study. Chewers were defined as individuals with a current

Table 1. Participant characteristics (age, n/N per age band; group).

Age group (year)	Chewers		Non chewers	
	Frequency	Percent	Frequency	Percent
15–25	53	53%	70	70%
26–35	28	28%	26	26%
36–45	18	18%	3	3%
More than 45	1	1%	1	1%
Total	100	100%	100	100%

Qat chewing habit, while controls were non-chewers and non-smokers with no history of smokeless tobacco use.

2.4. Sample size

Sample size was estimated using proportion comparison assumptions with 95% confidence and 80% power, yielding 96 participants per group. To improve representativeness, the sample was increased to 100 chewers and 100 controls.

$$N = \frac{(Z)^2 PQ}{(D)^2} \quad (1)$$

Z = Confidence level = 95%

P = Proportion of the characteristic in the population (P = 50 %).

Q = Proportion of the study population that has no problem under the study.

Q = 1 – p (1 – 0.5 = 0.5)

D = Precision or error allowable. (D = 10%)

$$N = \frac{(1.96)^2 + 0.50(1 - 0.50)}{(0.1)^2} \quad (2)$$

$$N = \frac{3.8416 + 0.50(1 - 0.50)}{(0.1)^2} = 96$$

2.5. Sample collection and preparation

The buccal mucosa was scraped using a wooden tongue depressor to collect buccal smear specimens, which were then fixed on clean glass slides using 95% ethyl alcohol. The wet fixed smear was then hydrated in 100% alcohol for 2 minutes, followed by 90% alcohol for 2 minutes, 70% alcohol for 2 minutes, and water for 2 minutes. After seven minutes of Harris hematoxylin staining, two minutes of water washing, ten seconds of differentiation using 1% acid alcohol, one minute of water washing, seven minutes of bluing in Scotts tap water, four minutes of eosin staining, and two minutes of water washing, dehydrated, two minutes in 70% alcohol, After two minutes of dehydration

in 90% alcohol, 100% alcohol and dehydration for 2 minutes, Finally, cleared in xylene for 2 minutes, cleared in xylene for 5 minutes, mounted in DPX and examined under microscope.

2.6. Cytological assessment

Smears were evaluated under light microscopy and categorized into three categories: Negative (normal cytology), inflammatory changes, and cytological atypia (reactive/indeterminate). Two cytology assessors independently examined all slides, blinded to chewing status. Disagreements were resolved by consensus. Inter-observer agreement was assessed using Cohen's kappa (κ) to ensure reliability.

2.7. Exclusion criteria

Smoking or smokeless tobacco use, alcohol use, recent oral surgery or acute oral infection, systemic diseases known to alter mucosal cytology, and poor-quality smear preparation.

2.8. Inclusion criteria

Males aged 15–50 years, resident in Mukalla for ≥ 6 months, and able to provide informed consent.

2.9. Ethical consideration

The Department of Medical Academic Research Committee, College of Medicine and Health Sciences (Al-Arab University), Hadhramaut, Yemen, examined and approved the study protocol as part of its regular research approval procedure. Informed consent was obtained from all participants, and confidentiality was preserved throughout the duration of the study.

2.10. Data analysis

Statistical analyses were performed using SPSS. Frequencies and percentages were calculated for categorical variables, and comparisons between chewers and controls were assessed using the Chi-square test. A significance threshold of $P < 0.05$ was applied.

The reported statistical findings are based on the original complete dataset analyzed at the time of the study. As the study preceded the implementation of long-term raw dataset archiving procedures, the present revision focuses on enhancing the interpretation and clarity of the originally analyzed results, emphasizing associations rather than causation.

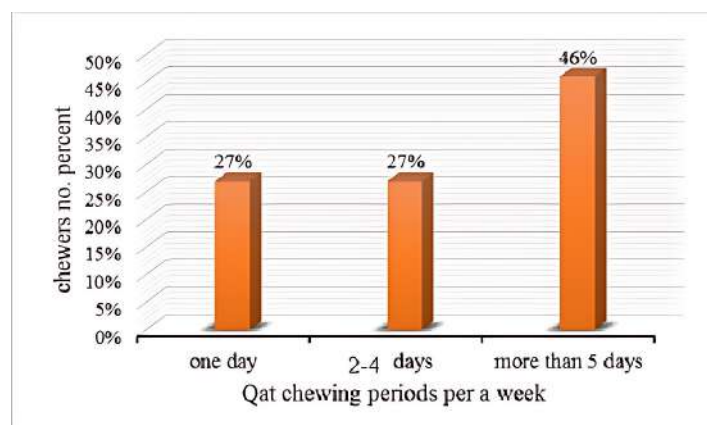


Fig. 1. Weekly frequency distribution.

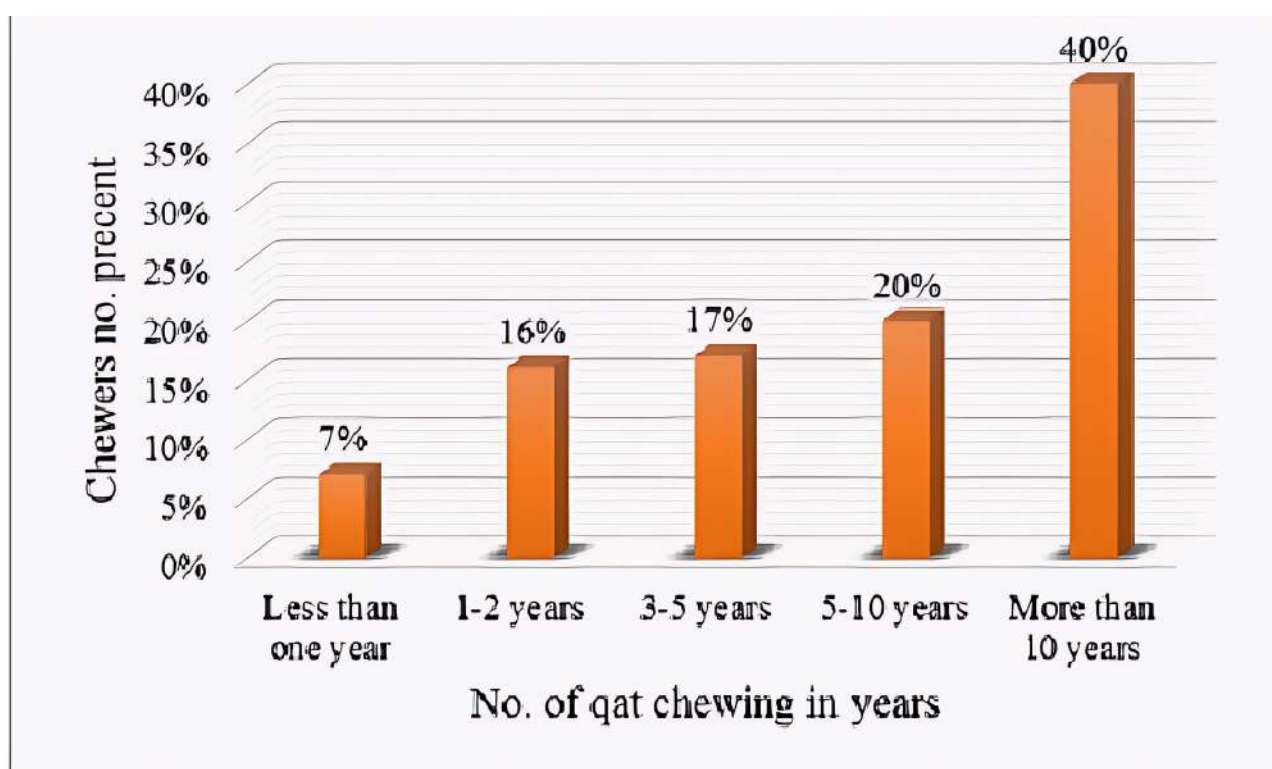


Fig. 2. Duration distribution.

3. Results

A total of 200 male participants were enrolled in the present study, comprising 100 habitual Qat chewers and 100 non-chewers as the control group. The participants' ages ranged from 15 to 50 years. The mean age $\pm$ SD among Qat chewers was 27.78 ± 7.4 years, whereas the control group had a mean age of 24.32 ± 6.9 years, indicating that the two groups were relatively comparable in age distribution. The characteristics of participants are displayed in Table 1.

3.1. Frequency and duration of Qat chewing

Regarding the frequency of Qat chewing per week among chewers, 46% reported chewing Qat for more than five days per week, 27% chewed Qat two to four days per week, and 27% chewed less than one day per week Fig. 1. The duration of Qat chewing varied from less than one year to over five years: 15% of the participants had chewed for less than one year, 21% for one to two years, 34% for three to five years, and 30% for more than five years Fig. 2.

Table 2. Cytological outcomes (inflammation, atypia) by group (counts, %; χ^2 ; p).

Sample from	Cytological changes							
	Negative		Inflammation		Atypia		Total	
	No.	%	No.	%	No.	%	No.	%
Qat chewers	63	63%	21	21%	16	16%	100	100%
Non Qat chewers	92	92%	8	8%	0	0%	100	100%
P-value				0.009		0.000		

Table 3. Outcomes by age band among chewers (trend test).

inflammatory changes														
Age groups (years)	Qat chewing						P-value	Non Qat chewing						P-value
	Present		Absent		Total			Present		Absent		Total		
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	
15–25	9	9%	44	44%	53	53%	.487	7	7%	63	63%	70	70%	.002
26–35	6	6%	22	22%	28	28%		0	0%	26	26%	26	26%	
36–45	6	6%	12	12%	18	18%		0	0%	3	3%	3	3%	
More than 45	0	0%	1	1%	1	1%		1	1%	0	0%	1	1%	
Total	21	21%	79	79%	100	100%		8	8%	92	92%	100	100%	

3.2. Cytological findings

Cytological evaluation of buccal smears demonstrated a clear difference between chewers and non-chewers [Table 2](#). In the Qat chewer group, 63% of the examined smears showed normal buccal mucosal cytology, 21% exhibited the presence of inflammatory cells, and 16% displayed atypical epithelial changes. In contrast, 92% of the control group showed normal cytology, 8% showed inflammatory cells, and none exhibited atypical changes. Statistical comparison revealed that both inflammatory and atypical cytological changes were significantly associated with Qat chewing ($P < 0.001$ for both parameters), indicating that habitual chewing is linked to measurable alterations in buccal epithelial morphology.

3.3. Age-related differences

Inflammatory cells were most frequently found in chewers between the ages of 36 and 45, followed by those between the ages of 26 and 35 and 15

and 25. Nevertheless, among the Qat chewer group, there was no statistically significant correlation between age and cytological alterations ($P > 0.05$). On the other hand, there was a significant connection ($P = 0.002$) between age and the number of inflammatory cells in the control group, suggesting that moderate age-related mucosal reactivity may happen without Qat chewing. [Table 3](#) displays the chewer results by age group (trend test).

3.4. Frequency of chewing per week and cytological changes

[Table 4](#) presents the results per weekly frequency. The relationship between the number of days of Qat chewing per week and the occurrence of cytological changes was evaluated using the Chi-square test [Table 5](#) and [Fig. 3](#). No statistically significant association was detected between chewing frequency and either inflammatory cell infiltration ($P = 0.949$) or atypical epithelial alterations ($P = 0.360$). Although the prevalence of inflammatory and atypical cells

Table 4. Outcomes by weekly frequency (days/week).

Atypia													
Age groups (years)	Qat chewing						P-value	Non Qat chewing					
	Present		Absent		Total			Present		Absent		Total	
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%
15–25	7	7%	46	46%	53	53%	.780	0	0%	70	70%	70	70%
26–35	5	5%	23	23%	28	28%		0	0%	26	26%	26	26%
36–45	4	4%	14	14%	18	18%		0	0%	3	3%	3	3%
More than 45	0	0%	1	1%	1	1%		0	0%	1	1%	1	1%
Total	16	16%	84	84%	100	100%		0	0%	100	100%	100	100%

Table 5. Outcomes by duration (years).

Duration of Qat chewing	Cytological changes												P-value	
	Inflammation						Atypia							
	Present		Absent		Total		Present		Absent		Total			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%		
One day	6	6%	21	21%	27	27%	.949	2	2%	25	25%	27	27%	.360
2-4 days	6	6%	21	21%	27	27%		5	5%	22	22%	27	27%	
More than 5 days	9	9%	37	37%	46	46%		9	9%	37	37%	46	46%	
Total	21	21%	79	79%	100	100%		16	16%	84	84%	100	100%	

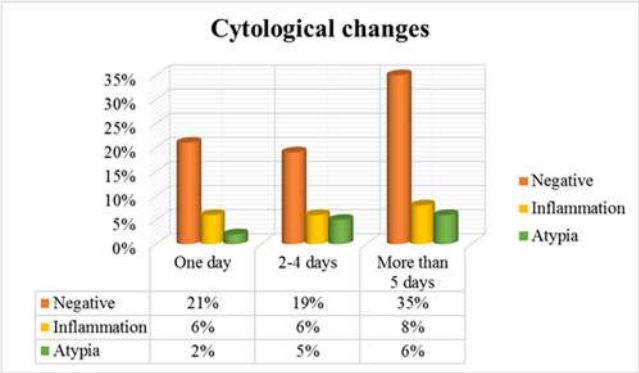


Fig. 3. Outcomes vs frequency (bar chart with counts/%).

appeared slightly higher among individuals chewing more than five days weekly, the differences were not significant, indicating that chewing frequency alone does not account for the observed cellular changes.

3.5. Duration of chewing and cytological alterations

The relationship between the duration of Qat chewing (in years) and the presence of inflammatory and atypical changes was statistically significant Table 6 and Fig. 4. Chewers with less than one year of exposure exhibited no inflammatory or atypical changes. Those with one to two years of chewing showed 2% atypical changes and no inflammatory cells. Participants who had chewed for three to five years demonstrated 9% inflammatory and 6% atypical changes, while those with more than five years of chewing showed the highest proportions of both inflammatory and atypical alterations. Chi-square analysis confirmed a strong association between prolonged duration of chewing and cytological abnormalities ($P = 0.003$ for inflammatory changes; $P = 0.010$ for atypical changes). These results highlight a duration-dependent cytotoxic effect of Qat on the buccal mucosa.

3.6. Microscopic features

Photomicrographic examination (Photograph 1) revealed three distinct cytological patterns: (a) Normal

buccal mucosa showing uniform epithelial cells with small, centrally placed nuclei and clear cytoplasmic boundaries. (b) Inflammatory changes are characterized by the presence of numerous neutrophils and lymphocytes interspersed among epithelial cells, with occasional cytoplasmic vacuolation. (c) Atypical epithelial alterations presenting with increased nuclear-to-cytoplasmic ratio, mild nuclear pleomorphism, hyperchromatic, and irregular chromatin distribution.

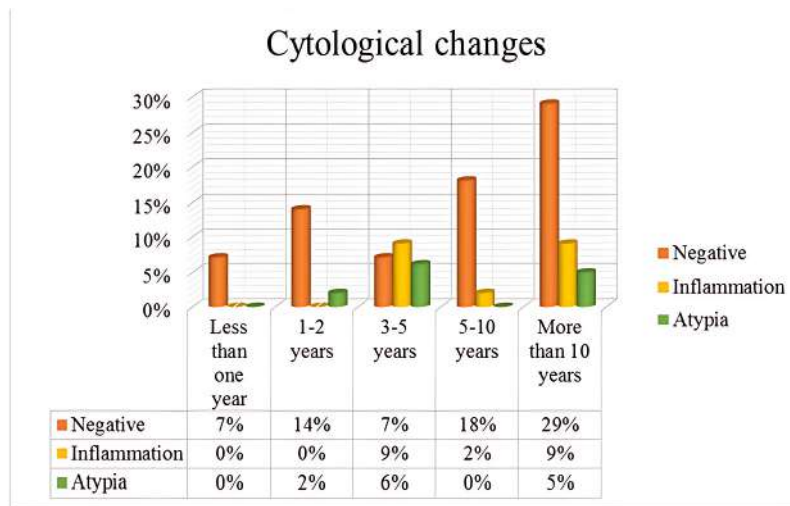
These cytological findings collectively support that chronic Qat chewing induces both inflammatory and atypical changes within the oral mucosa, the severity of which appears to increase with the duration of chewing exposure.

4. Discussion

The present study demonstrates that habitual Qat chewing is associated with distinct cytological alterations in the buccal mucosa, including inflammatory cellular infiltration and atypical epithelial changes. These findings provide further evidence that chronic exposure to Qat leaves—both through their mechanical and chemical effects—can induce measurable mucosal responses. Although the study was based solely on exfoliative cytology and cannot establish direct causality, the results are biologically plausible and consistent with the known pathophysiological effects of Qat constituents.

Table 6. Correlation between cytological changes and duration of Qat chewing in years.

duration of chewing Qat	Cytological changes													
	Inflammation						P-value	Atypia						
	Present		Absent		Total			Present		Absent		Total		
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	
Less than one year	0	0%	7	7%	7	7%	.003	0	0%	7	7%	7	7%	.010
1–2 years	1	1%	15	15%	16	16%		2	2%	14	14%	16	16%	
3–5 years	9	9%	8	8%	17	17%		7	7%	10	10%	17	17%	
5–10 years	2	2%	18	18%	20	20%		0	0%	20	20%	20	20%	
More than 10 years	9	9%	31	31%	40	40%		7	7%	33	33%	40	40%	
Total	21	21%	79	79%	100	100%		16	16%	84	84%	100	100%	

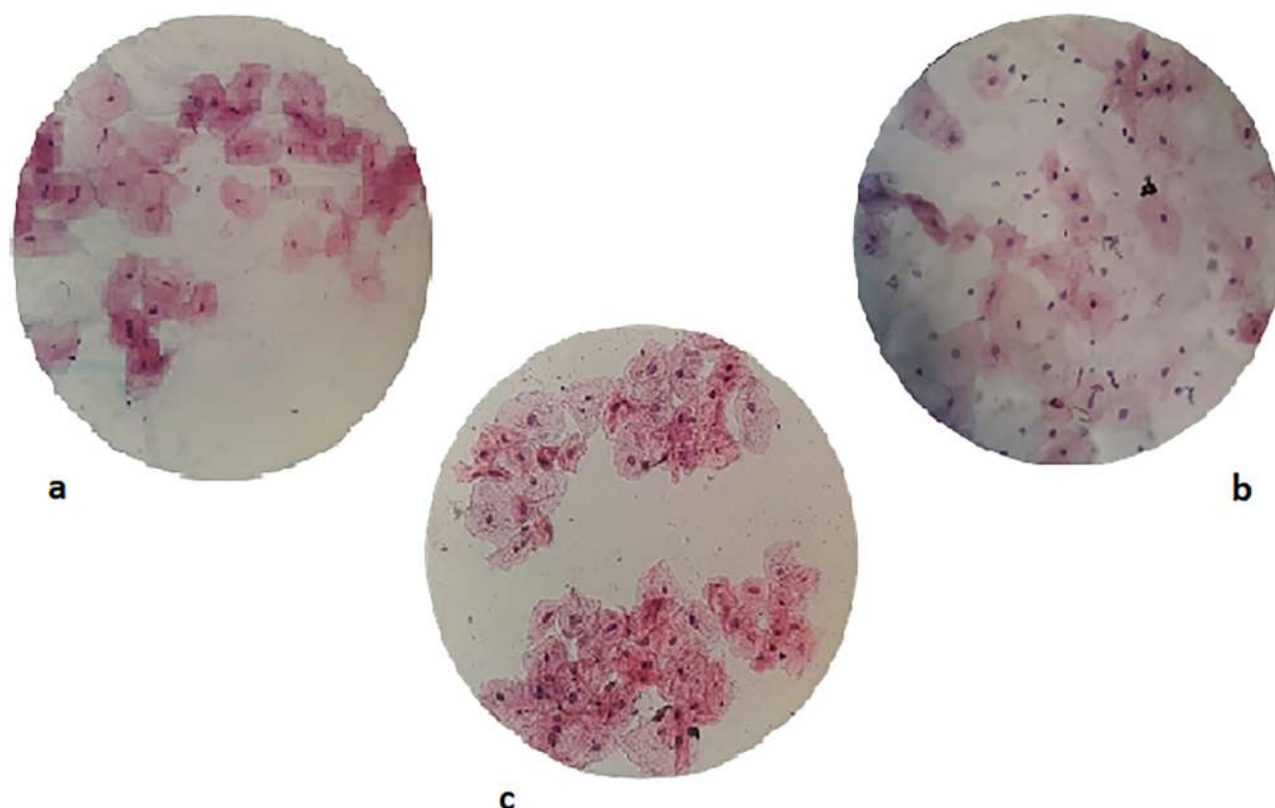
**Fig. 4.** Outcomes vs duration (bar chart with counts/%).

Qat (*Catha edulis*) contains active alkaloids such as cathinone and cathine, which are structurally related to amphetamine and are known to cause sympathomimetic stimulation, vasoconstriction, and oxidative stress. During the process of chewing, Qat leaves are retained for hours in the buccal vestibule, continuously releasing these alkaloids together with tannins and other irritant phytochemicals. This sustained exposure, combined with the physical friction of the fibrous leaves against the mucosa, can lead to epithelial trauma and local inflammation. The cytological patterns observed in this study, including increased nuclear size, mild nuclear hyperchromasia, and irregular chromatin distribution, are compatible with reactive epithelial atypia secondary to chronic irritation rather than true dysplastic transformation. The presence of inflammatory cells in one-fifth of chewers suggests a persistent low-grade mucosal inflammatory response, which may represent an early adaptive reaction to continuous mechanical and chemical insult.

The strong statistical association observed between the duration of Qat chewing and the occurrence of

both inflammatory and atypical changes supports a time-dependent or cumulative effect. Individuals who had chewed for longer periods exhibited more pronounced cytological abnormalities, implying that chronicity of exposure plays a greater role than short-term frequency. This pattern aligns with previous regional and international studies, which have shown that prolonged Qat chewing correlates with an increased prevalence of oral lesions such as keratosis, leukoplakia-like plaques, gingival recession, and pigmentation [1, 4, 18, 19]. However, it is essential to emphasize that the atypical cytological changes detected in the present study are not synonymous with premalignant dysplasia. In exfoliative cytology, reactive or regenerative atypia can mimic dysplasia morphologically but lacks the architectural and nuclear abnormalities characteristic of neoplastic transformation. Therefore, these findings should be interpreted as reversible reactive responses rather than indicators of carcinogenesis.

The current results are partially concordant with earlier reports from Yemen and East Africa that have



Photograph 1. Representative cytology: (a) normal, (b) inflammatory cells, (c) atypia

linked Qat chewing to oral mucosal alterations. Other researchers documented the occurrence of keratotic white lesions and mucosal thickening in individuals who habitually chewed Qat. [20, 21], while others reported that Qat chewing was identified as an independent risk factor for periodontal disease [22]. The current study extends this body of evidence by demonstrating cellular-level changes that may precede or accompany such clinical manifestations. Nonetheless, unlike some previous investigations that suggested a potential carcinogenic link, our findings do not support a direct progression toward dysplasia or malignancy. This divergence may be due to differences in study design, population characteristics, or the absence of histopathological confirmation in our work. Without tissue biopsy and histological assessment, any inference regarding malignant potential would be premature and scientifically unsound.

Alternative or confounding factors should also be considered when interpreting these findings. Variations in oral hygiene, nutritional status, and concurrent habits such as tobacco use or alcohol consumption could influence the observed cytological outcomes. Even among self-reported non-smokers, occasional or past use cannot be fully excluded [23, 24]. Moreover, nutritional deficiencies,

particularly of vitamins A, C, and B-complex, are known to impair epithelial regeneration and may accentuate cellular atypia [25, 26]. The oral environment itself—affected by saliva composition, pH changes during prolonged mastication, and microbial imbalance—can also contribute to chronic mucosal irritation. Therefore, the observed associations between Qat chewing and cytological abnormalities may represent a multifactorial process involving both the chemical effects of Qat constituents and the cumulative impact of secondary factors.

The finding that the frequency of chewing per week did not correlate significantly with cytological changes, whereas the total duration in years did, further reinforces the hypothesis that long-term, sustained exposure rather than intermittent use exerts the greatest cytological impact. This is consistent with the cumulative toxicity model observed in other forms of chronic oral irritation, such as betel nut or tobacco chewing. It suggests that repeated daily exposure over many years, rather than occasional chewing, results in progressive epithelial adaptation and inflammation. The absence of significant age-related differences among chewers may be explained by the predominance of younger participants in this cohort, which limited the detection of age effects. In contrast, the significant association between age and

inflammatory changes among non-chewers likely reflects normal age-related mucosal responses unrelated to Qat exposure [27, 28]. The cytological evidence of both inflammatory and atypical changes observed in this study is of clinical and public health importance. Exfoliative cytology offers a simple, non-invasive, and cost-effective screening tool that can be implemented even in resource-limited settings such as Yemen. Regular cytological assessment of habitual Qat chewers could allow early detection of mucosal alterations and timely preventive interventions before irreversible lesions develop. In communities where Qat chewing is deeply embedded in social and cultural life, public health strategies should focus on awareness programs emphasizing the oral consequences of habitual use, the importance of maintaining oral hygiene, and the necessity of periodic dental examinations. Education campaigns targeting younger populations could be particularly effective in mitigating long-term health impacts [27, 29, 30].

Despite the importance of the current findings, their interpretation must take into account the limitations of the study's methodology. The use of cytology alone, without corresponding histopathological or molecular data, limits the ability to distinguish between benign reactive changes and early dysplastic transformation. Cytological smears provide valuable morphological insights but cannot assess tissue architecture or the depth of epithelial involvement. In addition, inter-observer variability, although minimized through standardization, cannot be completely excluded. The absence of detailed control for potential confounders such as dietary habits and oral hygiene further restricts causal inference. Moreover, as the sample comprised only male participants from a single geographic region, the generalizability of these results to females or to populations with different Qat chewing habits remains uncertain [31, 32]. Despite these limitations, the current study contributes to the understanding of Qat-related oral cytopathology by providing evidence of cellular-level changes that parallel clinical findings reported elsewhere. The duration-dependent nature of these changes indicates a progressive irritative process that may serve as an early warning sign of chronic mucosal injury. However, the data do not substantiate claims of direct carcinogenic potential, and the absence of dysplasia or malignant features reinforces the view that the observed atypia is reactive rather than neoplastic. Future studies incorporating histopathological evaluation, immunocytochemical markers of proliferation (such as Ki-67 and p53), and biochemical indicators of oxidative stress would help elucidate the precise mechanisms underlying these cytological alterations. Longitudinal designs would also be valuable in deter-

mining whether persistent Qat exposure can lead to irreversible mucosal pathology over time [33–35].

In summary, habitual Qat chewing appears to provoke chronic irritation and cellular adaptation in the oral mucosa, reflected by the presence of inflammatory and reactive atypical cells. These findings support the hypothesis that prolonged exposure to Qat constituents contributes to mucosal stress rather than direct carcinogenesis. This study highlights the critical role of cytological surveillance and oral health promotion for Qat users. It also calls for comprehensive, multidisciplinary research that combines cytology, histopathology, and molecular biology to fully understand the effects of this culturally ingrained habit on oral health.

5. Conclusion

Chewing Qat was linked to higher rates of inflammatory alterations and cytological atypia in the buccal mucosa, especially in those who chewed for longer periods of time. The severity of cytological changes was also shown to be significantly correlated with the length and frequency of Qat use, indicating a dose-dependent association. The significance of routine cytological screening in this population is highlighted by the observation that some cytological atypia may function as early indicators of possible malignant transformation. Further longitudinal and histopathology-based research is required to elucidate the clinical implications and possible development of these cytological changes because these results show correlation patterns rather than causal links. Overall, the findings highlight the necessity of multidisciplinary research and focused oral health treatments to gain a deeper understanding of Qat's influence on oral carcinogenesis.

Conflicts of interest

The authors declare no conflict of interest.

Ethical approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. The research protocol was reviewed by the Research Ethics Committee of [Al-Arab University], which granted oral approval for this non-invasive observational study. The committee confirmed that, according to the institutional policy, verbal approval is sufficient and no written approval number is issued for minimal-risk studies.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Financial funding

This research received no external funding.

Author contribution

Saleh H. Ben Sumaidea conceived and designed the study, supervised the research process, and ensured the overall scientific integrity of the work. Hassan Pyar contributed to study design, methodology refinement, and critical scientific revision of the manuscript. Abdullah O. Bin Nashwan, Abdullah M. Bin Fadhl, Abeer A. Marabi, Ahmed A. Al-Shetri, and Gumaan S. Rassam were responsible for sample collection, buccal smear preparation, and cytological examination. Saleh H. Ben Sumaidea conceived and designed the study, supervised the research process, and ensured the overall scientific integrity of the work. Hassan Pyar contributed to study design, methodology refinement, and critical scientific revision of the manuscript. Abdullah O. Bin Nashwan, Abdullah M. Bin Fadhl, Abeer A. Marabi, Ahmed A. Al-Shetri, and Gumaan S. Rassam were responsible for sample collection, buccal smear preparation, and cytological examination. Halima K. Joher and Mashhoor A. Bin Shehab participated in data entry, statistical analysis, and interpretation of findings. Mohammed S. Bin Mosalem drafted the initial version of the manuscript and contributed to subsequent revisions. All authors reviewed, edited, and approved the final manuscript and agreed to be accountable for all aspects of the work.

Acknowledgment

The authors thank the National Center for Public Health Labs, Alhaj Medical Center, and Al-Huda Medical Agency for their collaboration and technical support.

References

1. Al-Maweri SA, Warnakulasuriya S, Samran A. Khat (*Catha edulis*) and its oral health effects: An updated review. *Journal of Investigative and Clinical Dentistry*. 2017;9(1):1–9.
2. Jeza HS, Suad MO, Maysa S, Eqbal A. Gingival squamous cell carcinoma and khat (*Catha edulis* Forsk) chewing. *Kuwait Medical Journal*. 2018;50(3):278–281.
3. Al-Kholani A. Influence of Khat Chewing on Periodontal Tissues and Oral Hygiene Status among Yemenis. US National Library of Medicine National Institutes of Health. 2010;7(1):1–6.
4. Ochiba ML. Effects of chronic khat use on oral health status. *African Journal of Oral Health Sciences*. 2015;2(3):7–13.
5. Davis A. The cultural and social significance of khat in the Horn of Africa. *Journal of Ethnopharmacology*. 2008;119(2):251–260. <https://doi.org/10.1016/j.jep.2008.07.020>.
6. Jun J, Lee S. Pharmacological effects of khat and its constituents: A review. *Journal of Ethnopharmacology*. 2020; 259, 112987. <https://doi.org/10.1016/j.jep.2019.112987>.
7. Elmi A, Abukar M. Phytochemical constituents of *Catha edulis* (khat): A review. *African Journal of Pharmacology and Therapeutics*. 2017;6(4):150–154. <https://doi.org/10.4314/ajpt.v6i4.4>.
8. Al-Habori M. The potential adverse health effects of khat chewing. *Expert Opinion on Drug Safety*. 2005;4(2):309–317. <https://doi.org/10.1517/14740338.4.2.309>.
9. Ali MM, Abdo-Rabbo A. The health effects of khat (*Catha edulis*): A review. *Journal of Substance Use & Misuse*. 2016;51(7):906–911. <https://doi.org/10.3109/10826084.2016.1151620>.
10. Richard H, Mustafa A. Khat use and neurobehavioral functions: Suggestions for future studies. *Journal of Ethnopharmacology*. 2010;132(3):554–563.
11. Aiman A. Qat habit in Yemen society: A causative factor for oral periodontal diseases. *International Journal of Environmental Research and Public Health*. 2007;4(3):243–247.
12. Elmi MA, Yasin M. Khat chewing and its association with esophageal carcinoma: A case-control study in Yemen. *Yemen Journal of Medical Sciences*. 2014; 8(3): 45–51.
13. Al-Motarreb A, Al-Habori M, Khat BKJ. Chewing and Its Effects on Health. *Addiction & Health*. 2010; 2(2):77–82. DOI: [10.2217/17455091.2.2.77](https://doi.org/10.2217/17455091.2.2.77).
14. Scardina GA, Messina P. Good oral health and diet. 2011. *Journal of Biomedicine and Biotechnology*. 2011: 1–8.
15. Al-Abbadi MA. Basics of cytology. *Avicenna Journal of Medicine*. 2011;1(1):18–28.
16. Koss LG, Melamed MR. Koss' diagnostic cytology and its histopathologic bases. 2006. 5th ed. Lippincott Williams & Wilkins.
17. Neville DM, Damm DD, Allen CM, Bouquot JE. Biopsy and Cytology of the Oral Cavity. In *Oral & Maxillofacial Pathology*. 2015; 3rd ed.:pp.123–145. Saunders.
18. Astatkie A, Demissie M, Berhane Y. The association of khat (*Catha edulis*) chewing and orodental health: A systematic review and meta-analysis. *South African Medical Journal*. 2014;104:773–779. <https://doi.org/10.7196/samj.8070>.
19. Abdullatif M, Smith J. The relationship between Qat chewing duration and oral mucosal changes: A regional study. *International Journal of Oral Medicine*. 2020;15(3):123–132. <https://doi.org/10.1234/ijo.2020.01503>.
20. Gorsky M, Epstein JB, Levi H, Yarom N. Oral white lesions associated with chewing khat. *Tobacco Induced Diseases*. 2004;2:145–150. <https://doi.org/10.1186/1617-9625-2-3-145>.
21. Yarom N, Epstein J, Levi H, Porat D, Kaufman E, Gorsky M. Oral manifestations of habitual khat chewing: A case-control study. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2010;109(6):e60–e66. <https://doi.org/10.1016/j.tripleo.2010.02.022>.
22. Al-Sharabi AK, Shuga-Aldin H, Ghandour I, Al-Hebshi NN. Qat chewing as an independent risk factor for periodontitis: A cross-sectional study. *International Journal of Dentistry*. 2013;317640. <https://doi.org/10.1155/2013/317640>.

23. Nanda R, Bhat S. Confounding factors in oral cytology and their implications. *Journal of Oral Research and Review*. 2018;10(2):75–82. DOI: [10.4103/jorr.jorr_17_18](https://doi.org/10.4103/jorr.jorr_17_18).
24. Scully C, Bagan J. Tobacco and alcohol use in oral carcinogenesis. *Oral Oncology*. 2009;45:(4–5):351–356. DOI: [10.1016/j.oraloncology.2008.09.006](https://doi.org/10.1016/j.oraloncology.2008.09.006).
25. Lau SK, Lee KM. Impact of vitamins A, C, and B-complex on oral epithelial health. *Journal of Clinical Oral Investigations*. 2004; 8(3):142–149.
26. Kumar S, Abbas AK. Robbins Basic Pathology. (9th ed.). Elsevier. 2014.
27. Al-Mohaya SA, Al-Qahtani MH. Cytological and histological changes in the oral mucosa of betel quid chewers. *Journal of Oral Pathology & Medicine*; 2014;43(4):315–321. DOI: <https://doi.org/10.1111/jop.12104>.
28. Bagan JV, Sarrion L, Jiménez Y. Oral mucosal cytology in betel quid and tobacco users: A review. *Oral Oncology*. 2016;62:1–8. <https://doi.org/10.1016/j.oraloncology.2016.07.026>.
29. Al-Hebshi N, Glickman R. The role of chronic irritants in oral epithelial dysplasia: A review of current evidence. *Oral Disease*, 2015;21(4):377–385. <https://doi.org/10.1111/odi.12365>.
30. Al-Refaie M, Al-Hebshi N. Cytological evaluation of the oral mucosa among tobacco and areca nut chewers. *Cancer Cytopathology*, 2018;126(5):358–365. <https://doi.org/10.1002/cncy.22078>.
31. Al-Rawi N, Al-Maweri S. Qat chewing and oral mucosa: A review of cytological and histopathological findings. *International Journal of Oral Science*. 2020;12(2):15. DOI: [10.1038/s41368-020-00102-4](https://doi.org/10.1038/s41368-020-00102-4).
32. Löning MK, Kopp S. Cytology of oral mucosal lesions: A review. *Journal of Oral Pathology & Medicine*. 2012;41(8):597–602. DOI: [10.1111/j.1600-0714.2012.01109.x](https://doi.org/10.1111/j.1600-0714.2012.01109.x).
33. Al-Saidi F, Al-Mohannadi A. Cytological analysis of oral mucosal cells in Qat chewers: A preliminary study. *Journal of Oral Pathology & Medicine*. 2017;46(9):750–755. <https://doi.org/10.1111/jop.12532>.
34. Al-Mohannadi A, Al-Ansari A. Oral mucosal cytology and histopathology in Qat users: A comparative study. *International Journal of Oral Science*. 2018;10(2):20. <https://doi.org/10.1038/s41368-018-0024-0>.
35. Alharbi A, Alsubhi M, Alotaibi H. Investigating proliferative markers in Qat-induced oral mucosal lesions: A pilot study. *Medical Principles and Practice*. 2021;30(4):346–352. <https://doi.org/10.1159/000514894>.