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The impact of alternative sources of nicotine on oral cavity health

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ABSTRACT

From year to year, the popularity of alternative methods of using nicotine like smokeless tobacco, tobacco-free nicotine pouches, or e-cigarettes is increasing. Although they seem like a healthier alternative than cigarettes, they don't remain without impact on oral health. Because of their accessibility and comfort of use, they are gaining popularity, especially among young adults. The purpose of this review is to show how the abovementioned sources of nicotine influence oral mucosa, teeth, and periodontium.

Keywords: oral health, nicotine pouches, e-cigarette, snus, periodontium

1. INTRODUCTION

According to World Health Organization (WHO) report, tobacco kills more than 7 million people each year. The cause of this is the high content of chemicals in tobacco (approximately 7,000). According to list established by Food and Drug Administration in 2012, around 100 of them are classified by public health experts as causes or potential causes of smoking related diseases. According to a World Health Organization (WHO, 2024) report, the number of tobacco users reached 1.245 billion people in 2022. Alternative methods of nicotine delivery were created to minimize the negative impact of smoking tobacco. Considering them as a safe form of nicotine is, however, dangerous for general health.

In this review, 3 groups of alternative nicotine sources are considered. Among oral nicotine delivery systems, there are two categories of products. One of them is snus, a moist tobacco product placed under the lip. The second, new category consists of tobacco-free oral nicotine pouches that contain pharmaceutical-grade high-purity nicotine, either derived from tobacco or synthetic. The nicotine is either combined with a plant fibre-based substrate (e.g., wheat or bamboo) or in a dry powder format. (Grandolfo et al., 2024). They are also placed under the lip, which allows nicotine to be absorbed directly through the oral mucosa. The third group is e-cigarettes containing nicotine, carrier solution, and flavorings. They are handheld, battery-operated devices that heat a liquid. This process results in production of an aerosol inhaled by the user (Brown & Balk, 2020).

2. REVIEW METHODS

In this review, we analyzed studies found on PubMed and Google Scholar using keywords like: snus, nicotine pouches, oral mucosa, periodontium, e-cigarettes, candidiasis, oral cancer. We also used references from articles that contain essential information and were searched in the database. We found n=617 published between January 2016 and December 2025. We excluded n=1, as there were no available English translation. We also excluded n=163, because of the unavailability of full text. At the beginning of our research, we screened records identified from the database by titles and abstracts. After the screening, we analyzed the articles in their entirety. At the end, we included n=19 studies in this review. The studies focus on analyzed forms of nicotine and their influence on oral mucosa, teeth and periodontium. Clinical case reports were excluded. We focused on randomized controlled trials, clinical comparative studies, experimental research, narrative review, systematic reviews and meta-analyses. Studies about the impact of alternative sources of nicotine on general health were also excluded, and instead we focused only on their consequences on oral health (Figure 1).

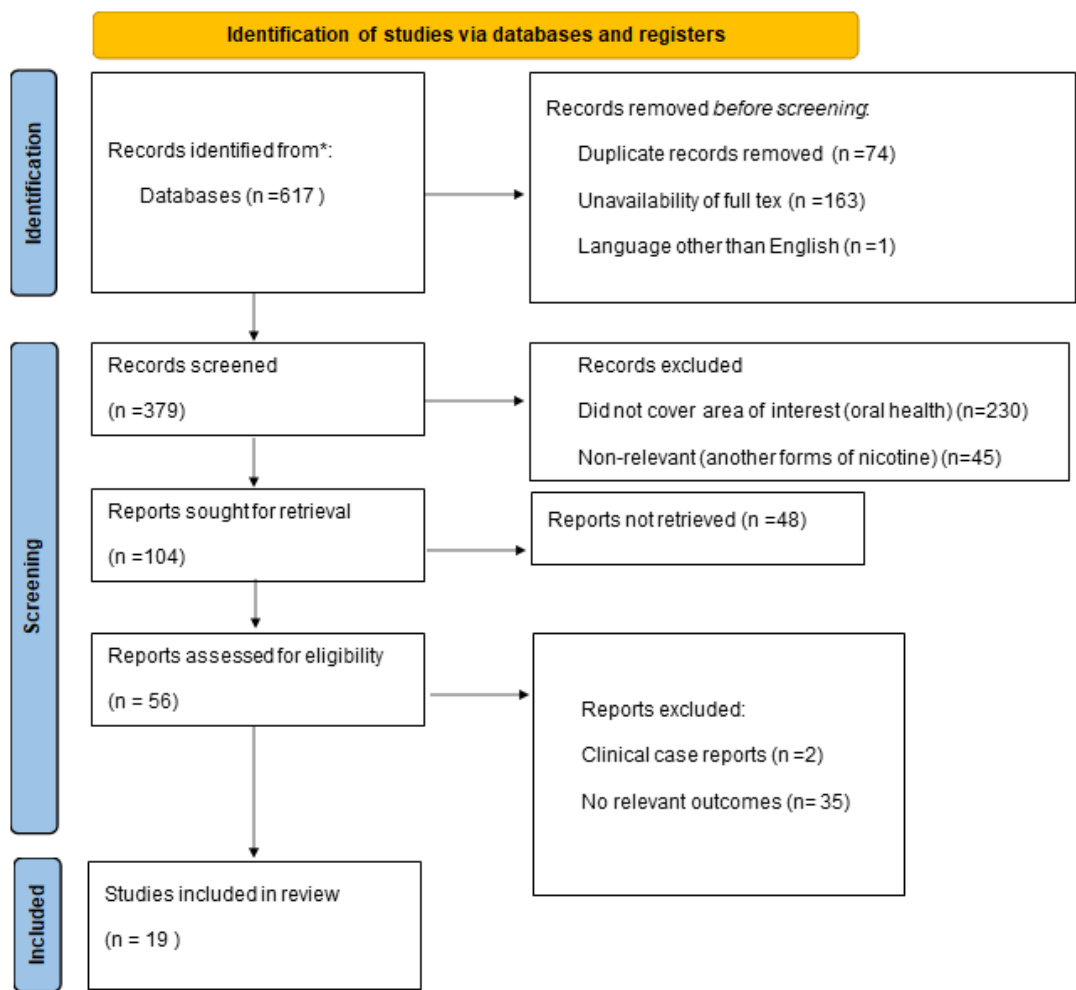


Figure 1. Flow chart

3. RESULTS & DISCUSSION

Oral mucosa lesions

Nicotine pouches called snus are repeatedly placed under the lip or in the buccal vestibule, which can damage the mucosa because of chemical and physical irritation or nicotine content. At the beginning, lesions are opalescent, white or gray with a wrinkled surface. At later stages they become keratotic with mucosal thickening and furrows (Müller, 2019). In the analyzed cohort study, 76 respondents were examined. 11,8% of them had mucosal changes in places, where respondents usually placed snuses. Lesions were white, localized, round, dot-like, or linear (Miluna et al., 2022). The study also showed a correlation between the number of tobacco units per day and the duration of using tobacco with mucosal lesions. Respondents who used 5-10 tobacco units for 5-10 years were more likely to have

mucosal changes. However, another study proved that the substitution of snus with a non-tobacco-based nicotine product can lead to a reduction of previous mucosal lesions. Over the course of 6 weeks, after substitution of snus with non-tobacco pouches, the number of patients suffering from mucosal changes decreased from 90% to 70%. The number of patients with no lesions increased from 9% to 30% after 6 weeks (Alizadehgharib et al., 2022). This may indicate that the tobacco content is causing changes to the oral mucosa, which can be eliminated by using tobacco-free nicotine pouches.

E-liquids used in e-cigarettes contain a lot of chemical substances and flavors. These compounds determine their taste, but also affect the oral mucosa. In another study, 90 patients were examined and divided into 2 groups: former smokers and electronic cigarette users. Oral mucosal lesions like: Nicotine stomatitis, a hairy tongue, and angular cheilitis were detected more frequently among electronic cigarette users than in former smokers (Bardellini et al., 2018). However, lesions connected with e-cigarette vapor are milder and more transient than those occurring in tobacco smokers. They also depend on the type of liquid in e-cigarettes. After switching from traditional tobacco smoking to e-cigarette use, oral mucosa condition improves (Zhang & Wen, 2023).

Cancer

Cancer is a disease that develops over a long period of time, and has multiple factors affecting its development. Because of that, nicotine pouches, which are relatively new products on the market, aren't fully evaluated. Studies show that the keratin surface of smokeless tobacco lesions is parakeratotic or orthokeratotic with no epithelial dysplasia, but with possible hyperchromatic nuclei in basal layer. Lesions resolve after 6 weeks without using smokeless tobacco, which can suggest a minor increased risk of oral cancer (Müller, 2019). On the contrary, globally 120,200 cases of oral cancers from 2022 were connectable to smokeless tobacco or areca nut consumption, which constitutes around 31% of all oral cancers (Rumgay et al., 2024). Smokeless tobacco products contain over 30 carcinogens, like tobacco-specific N-nitrosamines, nitrite, nitrate, heavy metals: nickel, cadmium, chromium. Due to carcinogens, mutations occur in K-ras, p53, and other genes, causing uncontrolled cell growth. Decreased apoptosis, increased angiogenesis and changes like chronic local inflammation, oxidative stress and formation of reactive oxygen species also contribute to tumor promotion (Gupta et al., 2018). However, there are no unequivocal studies indicating the connection between smokeless tobacco products and oral cancer.

In the second group of alternative nicotine sources, such as e-cigarettes, heated propylene glycol – one of liquid's ingredients – was identified as a carcinogen by The World Health Organization. Tobacco-specific nitrosamines (TSNA), significant carcinogens, were also detected in liquids and e-cigarette aerosols. The accelerated temperature generated during vaping causes an increase in the levels of TSNA. However, levels of TSNA are still lower in comparison to levels in traditional tobacco cigarettes. Using e-cigarettes can also damage endothelial cell barriers by inducing oxidative stress, inflammation, and cause genetic disorders connected with cancer (Zhang & Wen, 2023). It is difficult to assess direct impact of e-cigarettes on the risk of oral cancer, because of complicated pathogenesis of this disease. Another factor contributing to this is the crossover between various addictions such as vaping, traditional cigarette smoking, alcohol abuse and more.

Candidosis

Oral candidiasis is a common oral mucosa disease caused by *Candida* species, especially *Candida Albicans*. Patients with impaired immunity and smokers are more prone to candidosis. However, studies show that using e-cigarettes also affects *Candida albicans* growth. Results of Alanazi et al., (2019) study show that exposing cultures of *C. albicans* with e-cigarette vapors caused *Candida* growth and increased chitin production. E-cigarette vapor may also cause morphological changes in *Candida*, like increased hyphal length. This change may result in *C. albicans* attacking the patients. The study demonstrates that e-cigarettes increased the expression of genes such as SAP2, SAP3 and SAP9, which promote *C. albicans* growth and virulence. *Candida* exposed to e-vapor decreased growth and promoted morphological changes in epithelial cells. Besides that, they also had better adhesion to gingival epithelial cells. The study confirms that using e-cigarettes increases risk of oral candidiasis due to promoting pathogenesis of *C. albicans*.

Teeth caries

Caries is a common disease of the hard tissue of the tooth caused by bacterial biofilm. The oral bacteria, such as *Streptococcus mutans*, metabolize carbohydrates and produce acids. These metabolites decrease pH in oral cavity and lead to breaking down the hard tissue of the tooth (Kim et al., 2018). In an analyzed study, extracted teeth without caries were exposed to e-cigarette aerosol and incubated with *S. mutans*. Bacteria occurred more frequently in pits and fissures on the surface of extracted teeth, which were exposed to e-

cigarettes aerosol, than on unexposed teeth (Kim et al., 2018). This study may suggest that e-cigarette aerosol promotes caries. A study shows that *S. mutans* adheres to the e-cigarette-exposed teeth surface and forms biofilm, which is facilitated by viscous liquids made from propylene glycol and glycerin. It was proved that the increasing number of puffs of aerosol exposure increased bacteria adhesion to enamel. E-liquids also contain ingredients that are supposed to improve the taste, such as sweet flavors. Because of their chemical and physical similarity with sugary foods, which are the main reason for dental caries, their cariogenicity potential was searched. The research showed that out of five examined liquids, four of them: sucralose, ethyl butyrate, triacetin, hexyl acetate, increased biofilm formation. On the contrary, one of them, ethyl maltol, had the opposite effect, and decreased biofilm formation. In conclusion, e-cigarette aerosol caused increased bacteria adhesion four times, increased biofilm formation two times and decreased enamel hardness up to 27% (Kim et al., 2018). This contributes to the increased risk of caries for e-cigarette users.

Studies on the impact of nicotine pouches on tooth decay are inconclusive. Some studies show that nicotine pouches can stimulate growth of a bacteria, which is one of caries risk factor - *Streptococcus mutans*. However, in an analytical experimental lab trial after exposure to different nicotine pouch concentrations, biofilm formation and planktonic bacterial growth decreased, which may indicate an inhibitory effect on *Streptococcus mutans* (Henriksson & Bengtsson, 2025)

Teeth and restorations discoloration

A lot of chemical substances can influence teeth color. In vitro studies performed using spectrophotometry show that after exposure to e-liquid aerosol, enamel specimens change color. Another study proved that e-liquids can also alter the color of resin and ceramic restoration. However, changes in ceramic material were below clinically perceptible. In contrast, composite resins were very visible (Zhang & Wen, 2023). Smoking e-cigarettes affects the appearance of teeth, although the degree of color change may vary, depending on the flavor of e-liquids.

Periodontal disease

Periodontitis is a chronic, inflammatory disease of the tissue surrounding the tooth caused by groups of bacteria divided into complexes. Red complex bacteria like *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* are highly connected with periodontitis. The study, including 119 people, conducted using 16S rRNA high-throughput sequencing, shows that the presence of *Porphyromonas* and *Veillonella* was higher among vapers. A study also shows that e-cigarette aerosol changes levels of proinflammatory cytokines. In the first group, Fadu and Leuk-1 cells were exposed to e-cigarette vapor. In the second group, the cells were exposed to air. After the exposure, both groups were infected with *Porphyromonas gingivalis* and *Fusobacterium nucleatum*. After 2 hours, levels of IL-1 β , TNF- α , IFN- γ , IL-6, and IL-8 in e-cigarette exposed cells were significantly higher in comparison to air exposed cells. (Pushalkar et al., 2020). This result may suggest that e-cigarette aerosol changes oral microbiome and increases susceptibility to infection in cells, therefore increasing the risk of periodontitis among e-cigarette users. However, severity of periodontal disease and pocket depth was the highest in traditional smokers' group (72,5%) in comparison to e-cigarettes user (42,5%) and non-smokers (28,2%) (Pushalkar et al., 2020).

Nicotine pouches are placed directly on oral mucosa, near periodontal tissue. This kind of placement can indicate their influence on periodontitis, such as causing mechanical injury and irritation. Studies show that nicotine interacts with host cells, activating nicotinic acetylcholine receptor (nAChR) expression. and negatively affects viability of stem cells and fibroblast cells in periodontal ligament. It also causes increase in the number of cellular reactive oxygen species, contributing to DNA fragmentation and cell death, which can explain the relationship between nicotine pouches usage and periodontitis. Locally absorbed nicotine increases proinflammatory cytokines levels and number of osteoclastogenesis factors such as RANKL, RANK, TNF- α , and IL-1 β contribute to bone degradations. A lot of available flavors in nicotine pouches induce microbial dysbiosis, increase oxidative stress and proinflammatory and prosenescence responses, what can suggest that next to nicotine they are connected with increased risk for periodontal disease (Ye & Rahman, 2023). Even though in vitro studies provide evidence of the effect of oral nicotine pouches on periodontitis, there is a lack of unambiguous clinical studies confirming this connection.

Gingival recession

Gingival recession is a clinical condition related to periodontitis. It is defined as an apical displacement of the gingival margin to the cemento-enamel junction caused by loss of periodontal tissue (Imber & Kasaj, 2021). Nicotine pouches like snus are considered to be one of the risk factors of recession, because of the chemical and mechanical irritation of gum that they cause. In a cross-sectional study

among Norwegian adolescents, gingival retractions occur in 18,4% of snus users. Moreover, all recessions were observed in proximity to the upper incisors, where snus is placed most often. In most cases, recessions involve two or more teeth. Using a binary logistic regression model, the researchers proved that the odds for recessions increased by 34% for each year of using snus (Kopperud et al., 2023).

Halitosis and xerostomia

Halitosis is a chronic condition that causes the smell of breath to be altered and unpleasant. It is caused by several factors, such as poor oral hygiene, dry mouth, periodontitis, gastrointestinal diseases, dietary habits, and more. Malodor is connected with volatile sulfur compounds. These compounds are products of sulfur-containing amino acids degradation performed by anaerobic bacteria (Saleh et al., 2025). In the study, 7973 participants were divided into groups according to smoking habits. Results show that e-cigarette users and dual users of tobacco and e-cigarettes were more likely to experience halitosis than non-users (Saleh et al., 2025). It can be attributed to solvents in e-cigarette solutions like propylene glycol and vegetable glycerin, as they may cause xerostomia due to their hydrophilic properties and ability to absorb water from saliva (Woodall et al., 2020).

Xerostomia is the sensation of dry mouth caused by decreased salivary production. Guo et al., (2023) study shows the prevalence of xerostomia in different groups. It was present in 26% of overall society, in 24% of tobacco users and in 33% of e-cigarette users. E-cigarette users suffer from xerostomia more often than non-smokers. Apart from hydrophilic ingredients in e-cigarette solutions, it may also be caused by the reduction in saliva production. Saliva neutralizes acids and flushes out bacteria from the oral cavity. A decreased amount of saliva contributes to tooth decay and halitosis due to decreased pH level and increased number of bacteria causing bad breath (Saleh et al., 2025). Table 1 summarizes the impact of alternative nicotine sources on oral health.

Table 1. Summary of the oral health effects of alternative nicotine sources in included studies.

Author	Nicotine Source	Oral Health Outcome	Key Findings
Miluna et al., (2022)	Snus	Oral mucosal lesions	Mucosal lesions were observed in 11.8% of users; the incidence increased with duration and intensity of use.
Alizadehgharib et al., (2022)	Snus / Nicotine pouches	Oral mucosal lesions	Replacing snus with tobacco-free nicotine pouches resulted in a reduction of mucosal lesions from 90% to 70%
Bardellini et al., (2018)	E-cigarettes	Oral mucosal lesions	Nicotine stomatitis, hairy tongue and angular cheilitis are more common among e-cigarette users than former smokers.
Alanazi et al., (2019)	E-cigarettes	Oral candidiasis	E-cigarette vapor stimulates Candida albicans growth, chitin production, morphological changes, virulence, and adhesion to epithelial cells.
Kim et al., (2018)	E-cigarettes	Dental caries	Exposure to e-cigarette aerosol increases bacterial adhesion, biofilm formation and reduces enamel hardness.
Zhang & Wen, 2023	E-cigarettes	Teeth and restorations discoloration	E-liquids can alter the color of resin, ceramic restoration and enamel
Pushalkar et al., (2020)	E-cigarettes	Periodontal disease	E-cigarette use alters the oral microflora and increases the expression of proinflammatory cytokines
Ye & Rahman (2023)	Nicotine pouches	Periodontal disease	Flavors in nicotine pouches induce microbial dysbiosis, increase oxidative stress and proinflammatory response
Kopperud et al., (2023)	Snus	Gingival recession	Gingival recessions occur in 18.4% of snus users; risk increased by 34% with each year of use.
Woodall et al., 2020	E-cigarette	Xerostomia	Solvents in e-cigarette solutions may cause xerostomia
Guo et al., (2023)	E-cigarettes	Xerostomia	Xerostomia prevalence was higher among e-cigarette users (33%) than tobacco users (24%).

Saleh et al., (2025)	E-cigarettes	Halitosis/xerostomia	E-cigarette users suffer from xerostomia and halitosis more often than non-smokers
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4. CONCLUSION

The influence of alternative sources of nicotine on oral health is becoming an increasingly important problem in public health. They are considered safer and healthier alternatives than traditional cigarettes; however, a lot of studies indicate their negative impact on oral health. Nicotine pouches usage leads to potentially procancerous lesion on oral mucosa. It also causes microbial dysbiosis, increased levels of proinflammatory cytokines and oxidative stress. E-cigarettes contribute to increased risk of tooth caries and periodontitis. They also cause halitosis, xerostomia and candidiasis. Studies indicate their potential carcinogenic effects due to the presence of carcinogenic substances in e-liquids. Although there are in vitro studies indicating the negative impact of alternative sources of nicotine on oral health, there is still a lack of direct clinical evidence regarding their long-term effects, so further research is needed.

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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