


IMPACT OF ELECTRONIC CIGARETTES ON THE ORAL CAVITY: SCOPING REVIEW

IMPACTO DOS CIGARROS ELETRÔNICOS NA CAVIDADE ORAL: REVISÃO DE ESCOPO

IMPACTO DE LOS CIGARRILLOS ELECTRÓNICOS EN LA CAVIDAD BUCAL: REVISIÓN EXPLORATORIA

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ABSTRACT

Electronic Nicotine Delivery Systems (ENDS) are devices that vaporize a liquid containing nicotine and other potentially toxic substances, such as heavy metals, aldehydes, and carcinogenic compounds. Popular among younger populations, their use has been associated with adverse health effects, particularly in the oral cavity, the first site of contact with aerosols. This study aims to identify conceptual categories and gaps related to the effects of e-cigarettes on the oral cavity. A scoping review was conducted following the Joanna Briggs Institute (JBI) protocol and the PRISMA-ScR checklist. The research question, based on the PEO (Participants, Exposure, Outcome) strategy, investigated the effects of e-cigarette use on oral health. Pilot studies, randomized clinical trials, controlled and non-randomized studies, and case reports were included without restrictions on language or publication date. A total of 68 studies were identified, of which 7 met the inclusion criteria. The results revealed cytotoxic, inflammatory, infectious, and carcinogenic effects associated with e-cigarette use, even in the absence of nicotine. Lesions such as nicotine stomatitis, hairy tongue, and hyperplastic candidiasis were more frequent, along with a higher prevalence of Human Papillomavirus (HPV). Therefore, e-cigarette use may cause significant damage to the oral mucosa, altering its integrity, microbiota, and metabolism, and may contribute to the development of neoplasms. These findings reinforce that e-cigarettes are not a safe alternative to smoking and highlight the need for clinical attention, especially among young users.

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Keywords: Electronic Nicotine Delivery Systems. Vaping. Mouth Neoplasms. Smokers. Mouth Mucosa.

RESUMO

Os Sistemas Eletrônicos de Administração de Nicotina (SEAN) são dispositivos que vaporizam um líquido contendo nicotina e outras substâncias potencialmente tóxicas, como metais pesados, aldeídos e compostos cancerígenos. Popular entre o público mais jovem, seu uso tem sido associado a efeitos adversos à saúde, especialmente na cavidade oral, o primeiro local de contato com os aerossóis. Este trabalho tem como objetivo identificar categorias conceituais e lacunas relacionadas aos efeitos dos cigarros eletrônicos na cavidade oral. Foi realizada uma revisão de escopo seguindo o protocolo Joanna Briggs Institute (JBI) e a lista de verificação PRISMA-ScR. A questão de pesquisa, baseada na estratégia PEO (Participants, Exposure, Outcome), investigou os efeitos do uso de cigarros eletrônicos na saúde bucal. Estudos piloto, ensaios clínicos randomizados, estudos controlados e não randomizados e relatos de caso foram incluídos sem restrições de idioma ou data de publicação. Um total de 68 estudos foram identificados, dos quais 7 atenderam aos critérios de inclusão. Os resultados revelaram efeitos citotóxicos, inflamatórios, infecciosos e cancerígenos associados ao uso de cigarros eletrônicos, mesmo na ausência de nicotina. Lesões como estomatite nicotínica, língua pilosa e candidíase hiperplásica foram mais frequentes, juntamente com uma maior prevalência do Papilomavírus Humano (HPV). Portanto, o uso de cigarros eletrônicos pode causar danos significativos à mucosa oral, alterando sua integridade, microbiota e metabolismo, e pode contribuir para o desenvolvimento de neoplasias. Esses achados reforçam que os cigarros eletrônicos não são uma alternativa segura ao tabagismo e destacam a necessidade de atenção clínica, principalmente entre os usuários jovens.

Palavras-chave: Sistemas Eletrônicos de Liberação de Nicotina. Vaporização de Nicotina. Neoplasias Bucais. Fumantes. Mucosa Oral.

RESUMEN

Los Sistemas Electrónicos de Administración de Nicotina (SEAN) son dispositivos que vaporizan un líquido que contiene nicotina y otras sustancias potencialmente tóxicas, como metales pesados, aldehídos y compuestos cancerígenos. Populares entre los jóvenes, su uso se ha asociado con efectos adversos para la salud, especialmente en la cavidad oral, primer sitio de contacto con los aerosoles. Este trabajo tiene como objetivo identificar categorías conceptuales y vacíos relacionados con los efectos de los cigarrillos electrónicos en la cavidad oral. Se realizó una revisión de alcance siguiendo el protocolo del Joanna Briggs Institute (JBI) y la lista de verificación PRISMA-ScR. La pregunta de investigación, basada en la estrategia PEO (Participants, Exposure, Outcome), investigó los efectos del uso de cigarrillos electrónicos en la salud bucal. Se incluyeron estudios piloto, ensayos clínicos aleatorizados, estudios controlados y no aleatorizados y reportes de caso, sin restricciones de idioma ni fecha de publicación. Se identificaron 68 estudios, de los cuales 7 cumplieron con los criterios de inclusión. Los resultados revelaron efectos citotóxicos, inflamatorios, infecciosos y cancerígenos asociados al uso de cigarrillos electrónicos, incluso sin nicotina. Lesiones como estomatitis nicotínica, lengua pilosa y candidiasis hiperplásica fueron más frecuentes, junto con mayor prevalencia del Virus del Papiloma Humano (VPH). El uso de cigarrillos electrónicos puede causar daños significativos en la mucosa oral, alterando su integridad, microbiota y metabolismo, y contribuir al desarrollo de

neoplasias. Estos hallazgos refuerzan que no son una alternativa segura al tabaquismo y destacan la necesidad de atención clínica, especialmente en usuarios jóvenes.

Palabras clave: Sistemas Electrónicos de Liberación de Nicotina. Vapeo. Neoplasias de La Boca. Fumadores. Mucosa Oral.

1 INTRODUCTION

An electronic nicotine delivery system (ENDS), or electronic cigarette (EC), is a battery-operated device containing a cartridge filled with a high-concentration nicotine solution and other substances that make up the e-liquid. These include 4-(methylnitrosamino), N'-nitrosonornicotine (NNN), -1-butanone (NNK), -1-(3-pyridyl), aldehydes, phenolic compounds, polycyclic aromatic hydrocarbons, tobacco alkaloids, heavy metals, and various artificial fruit flavors. Studies have shown that these compounds are potent carcinogens that induce oxidative stress in cells. This inflammatory process is enhanced by nuclear factor kappa B (NF- κ B), which drives the transcription of pro-inflammatory cytokines, playing a key role in tumorigenesis by creating a favourable microenvironment for these cells (Cátala-Valentin *et al.*, 2022).

The widespread use of ENDS over the past decade can be attributed to their offering of flavors and aromas distinct from conventional cigarettes, while visually presenting themselves as a less harmful alternative for users (de Sousa *et al.*, 2023). In 2013, the United States Food and Drug Administration (FDA) authorized the commercial sale of ENDS as an alternative to traditional cigarettes. Since then, ENDS users have perceived electronic cigarettes as being less harmful than conventional ones. However, scientific evidence has shown that regular use of ENDS is a risk factor for respiratory, cardiovascular, and neurological diseases (Ali *et al.*, 2022).

Several cases of an acute, unknown, and fatal respiratory illness affected many young patients in the United States, according to studies by the Centers for Disease Control and Prevention (CDC). This illness was linked to vaping, that is, the use of electronic cigarettes, leading users to experience respiratory, gastrointestinal, and systemic symptoms, as well as acute lung injury following the use of these devices (Silva *et al.*, 2021).

Conventional cigarettes operate through combustion, exposing the user to carbon monoxide, unlike electronic cigarettes, which heat the e-liquid vapor, turning it into an aerosol (Filho *et al.*, 2021). As the oral cavity is the first part of the body to come into direct contact with the aerosols produced by ENDS, it is at a higher risk of exposure to tobacco's immunological, microbial, carcinogenic and clinical effects. It also makes the microbiota more susceptible to colonization by *Streptococcus mutans*, favoring the development of dental caries (Alhajj *et al.*, 2022). The use of ENDS also affects the plaque index, probing depth, clinical attachment loss, and marginal bone loss all of which are increased in electronic cigarette users (Ali *et al.*, 2022). Due to their popularity, ENDS have also become

a major concern because of their association with the development and exacerbation of conditions such as xerostomia, nicotine stomatitis, angular cheilitis, hyperplastic candidiasis, and hairy tongue (Machado *et al.*, 2023).

This scoping review is particularly important for investigating the impacts of ENDS on the oral cavity due to the emerging and multifaceted nature of the topic. Given the diversity in study designs, populations, and outcomes assessed, ranging from cellular changes to clinical manifestations, this type of review enables a systematic and comprehensive mapping of the existing scientific literature. The purpose of the study aims to clarify the extent and nature of existing research on the impact of ENDS on the oral cavity. It contributes by identifying patterns, gaps, and inconsistencies in current knowledge, thereby supporting future studies and informing public health strategies. Additionally, the findings can assist healthcare professionals, particularly in dentistry and public health, in better understanding the risks associated with ENDS use and in guiding preventive and educational efforts targeting users and vulnerable populations.

2 OBJECTIVE

This scoping review aims to identify conceptual categories and gaps related to the effects of electronic cigarettes on the oral cavity, to summarise the literature, and to provide conclusions that enhance the understanding of the topic.

3 METHODOLOGY

3.1 STUDY DESIGN

This is a scoping review study. The choice of this review method was based on its suitability for mapping the existing evidence on a broad topic, especially in areas where the literature is still emerging or heterogeneous. Unlike systematic reviews, which focus on answering specific and well-defined research questions, scoping reviews are particularly useful for identifying knowledge gaps, clarifying key concepts, and exploring the extent and nature of the available research. In this context, it was the most appropriate approach to investigate the effects of electronic cigarettes on the oral cavity.

3.2 METHODOLOGICAL FRAMEWORK

The methodological strategy proposed by the Joanna Briggs Institute (JBI) protocol was adopted, following a methodological plan organized into 11 sequential steps: 1 –

Preliminary literature review; 2 – Development of the research protocol; 3 – Collection of information from the authors of the selected studies; 4 – Definition of the title, objective, and research question; 5 – Inclusion criteria; 6 – Search strategy; 7 – Data collection and history; 8 – Theoretical discussion; 9 – Results extraction; 10 – Evidence analysis; 11 – Presentation of the findings. In addition, the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist was used.

3.3 RESEARCH QUESTION

The guiding research question was developed using the PEO mnemonic (Participants, Exposure, Outcome). Accordingly, the following elements were considered: (P) Individuals who use electronic cigarettes; (E) Electronic cigarette use; (O) Repercussions in the oral cavity. The research question, based on the PEO framework, was: “What are the effects of electronic cigarette exposure on the oral health of individuals who use them?”.

3.4 ELIGIBILITY CRITERIA

Pilot studies, randomized controlled trials, controlled and non-randomized studies, and case reports available in full text on the topic of interest were included. There were no restrictions regarding language or year of publication. Duplicated studies, literature reviews, systematic reviews, letters to the editor, editorials, commentaries, or expert opinions were excluded.

3.5 SOURCES OF INFORMATION AND SEARCH STRATEGY

The search for studies was conducted in the following electronic information sources: Latin American and Caribbean Health Sciences Literature (LILACS), Virtual Health Library (VHL), Scientific Electronic Library Online (SciELO), Medical Literature Analysis and Retrieval System Online (MEDLINE), PubMed, and the Cochrane Library. The search strategies were formulated based on the combination of controlled descriptors and/or keywords related to the topic (Table 1). To identify additional potentially eligible studies, a manual search was also performed in the reference lists of the initially selected articles.

Table 1

Search strategy in databases

Database	Search strategy
PubMed MEDLINE	((("Electronic Nicotine Delivery Systems"[Mesh] OR "Electronic Nicotine Delivery Systems" OR "Electronic Nicotine Delivery System" OR "Electronic Cigarettes" OR "Electronic Cigarette" OR "Cigarette, Electronic" OR "Cigarettes, Electronic" OR "E-Cigs" OR "E Cigs" OR "E-Cigarettes" OR "E Cigarettes" OR "E-Cigarette" OR "E Cigarette" OR "E-Cig" OR "E Cig") OR ("Vaping" OR "THC Vaping" OR "THC Vapings" OR "Vapings, THC" OR "Vaping, THC" OR "Ecigarette Use" OR "Ecigarette Uses" OR "Use, Ecigarette" OR "Uses, Ecigarette" OR "ECig Use" OR "ECig Uses" OR "Use, ECig" OR "Vape" OR "Vapes" OR "E-Cigarette Use" OR "E Cigarette Use" OR "E-Cigarette Uses" OR "Use, E-Cigarette" OR "Nicotine Vaping" OR "Nicotine Vapings" OR "Vaping, Nicotine" OR "Vapings, Nicotine" OR "E-Cig Use" OR "E Cig Use" OR "E-Cig Uses" OR "Use, E-Cig" OR "Electronic Cigarette Use" OR "Cigarette Use, Electronic" OR "Electronic Cigarette Uses" OR "Use, Electronic Cigarette") AND ("Mouth Neoplasms"[Mesh] OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth"))
LILACS BVS SciELO	((("Sistemas Eletrônicos de Liberação de Nicotina" OR "Sistema Eletrônico de Liberação de Nicotina" OR "Cigarro Eletrônico" OR "Cigarros Eletrônicos" OR "e-Cig" OR "e-Cigarro" OR "e-Cigarros" OR "e-Cigs") OR ("Vaping" OR "Uso de Cigarro Eletrônico" OR "Uso de E Cig" OR "Uso de E-Cig" OR "Uso de e-Cigarro" OR "Usos de Cigarros Eletrônicos" OR "Vape" OR "Vaping com THC" OR "Vaping da Nicotina" OR "Vaporização da Nicotina") AND ("Neoplasias Bucais" OR "Câncer Bucal" OR "Câncer Oral" OR "Câncer da Boca" OR "Câncer da Cavidade Bucal" OR "Câncer da Cavidade Oral" OR "Câncer de Boca" OR "Câncer de Cavidade Bucal" OR "Câncer de Cavidade Oral" OR "Neoplasia Bucal" OR "Neoplasia Oral" OR "Neoplasia da Boca" OR "Neoplasia da Cavidade Bucal" OR "Neoplasia da Cavidade Oral" OR "Neoplasia de Boca" OR "Neoplasia de Cavidade Bucal" OR "Neoplasia de Cavidade Oral" OR "Neoplasias Oraís" OR "Neoplasias da Boca" OR "Neoplasias da Cavidade Bucal" OR "Neoplasias da Cavidade Oral" OR "Neoplasias de Boca" OR "Neoplasias de Cavidade Bucal" OR "Neoplasias de Cavidade Oral" OR "Tumor Bucal" OR "Tumor Oral" OR "Tumor da Boca" OR "Tumor da Cavidade Bucal" OR "Tumor da Cavidade Oral" OR "Tumor de Boca" OR "Tumor de Cavidade Bucal" OR "Tumor de Cavidade Oral" OR "Tumores Bucais" OR "Tumores Oraís" OR "Tumores da Boca" OR "Tumores da Cavidade Bucal" OR "Tumores da Cavidade Oral" OR "Tumores de Boca" OR "Tumores de Cavidade Bucal" OR "Tumores de Cavidade Oral"))
MEDLINE via BVS	((("Electronic Nicotine Delivery Systems"[Mesh] OR "Electronic Nicotine Delivery Systems" OR "Electronic Nicotine Delivery System" OR "Electronic Cigarettes" OR "Electronic Cigarette" OR "Cigarette, Electronic" OR "Cigarettes, Electronic" OR "E-Cigs" OR "E Cigs" OR "E-Cigarettes" OR "E Cigarettes" OR "E-Cigarette" OR "E Cigarette" OR "E-Cig" OR "E Cig" OR "Vaping"[Mesh] OR "THC Vaping" OR "THC Vapings" OR "Vapings, THC" OR "Vaping, THC" OR "Ecigarette Use" OR "Ecigarette Uses" OR "Use, Ecigarette" OR "Uses, Ecigarette" OR "ECig Use" OR "ECig Uses" OR "Use, ECig" OR "Vape" OR "Vapes" OR "E-Cigarette Use" OR "E Cigarette Use" OR "E-Cigarette Uses" OR "Use, E-Cigarette" OR "Nicotine Vaping" OR "Nicotine Vapings" OR "Vaping, Nicotine" OR "Vapings, Nicotine" OR "E-Cig Use" OR "E Cig Use" OR "E-Cig Uses" OR "Use, E-Cig" OR "Electronic Cigarette Use" OR "Cigarette Use, Electronic" OR "Electronic Cigarette Uses" OR "Use, Electronic Cigarette") AND ("Mouth Neoplasms"[Mesh] OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth"))
Cochrane Library	((("Electronic Nicotine Delivery Systems" OR "Electronic Nicotine Delivery System" OR "Electronic Cigarettes" OR "Electronic Cigarette" OR "Cigarette, Electronic" OR "Cigarettes, Electronic" OR "E-Cigs" OR "E Cigs" OR "E-Cigarettes" OR "E Cigarettes" OR "E-Cigarette" OR "E Cigarette" OR "E-Cig" OR "E Cig") OR ("Vaping" OR "THC Vaping" OR "THC Vapings" OR "Vapings, THC" OR "Vaping, THC" OR "Ecigarette Use" OR "Ecigarette Uses" OR "Use, Ecigarette" OR "Uses, Ecigarette" OR "ECig Use" OR "ECig Uses" OR "Use, ECig" OR "Vape" OR "Vapes" OR "E-Cigarette Use" OR "E Cigarette Use" OR "E-Cigarette Uses" OR "Use, E-Cigarette" OR "Nicotine Vaping" OR "Nicotine Vapings" OR "Vaping, Nicotine" OR "Vapings, Nicotine" OR "E-Cig Use" OR "E Cig Use" OR "E-Cig Uses" OR "Use, E-Cig" OR "Electronic Cigarette Use" OR "Cigarette Use, Electronic" OR "Electronic Cigarette Uses" OR "Use, Electronic Cigarette") AND ("Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth")):ti,ab,kw

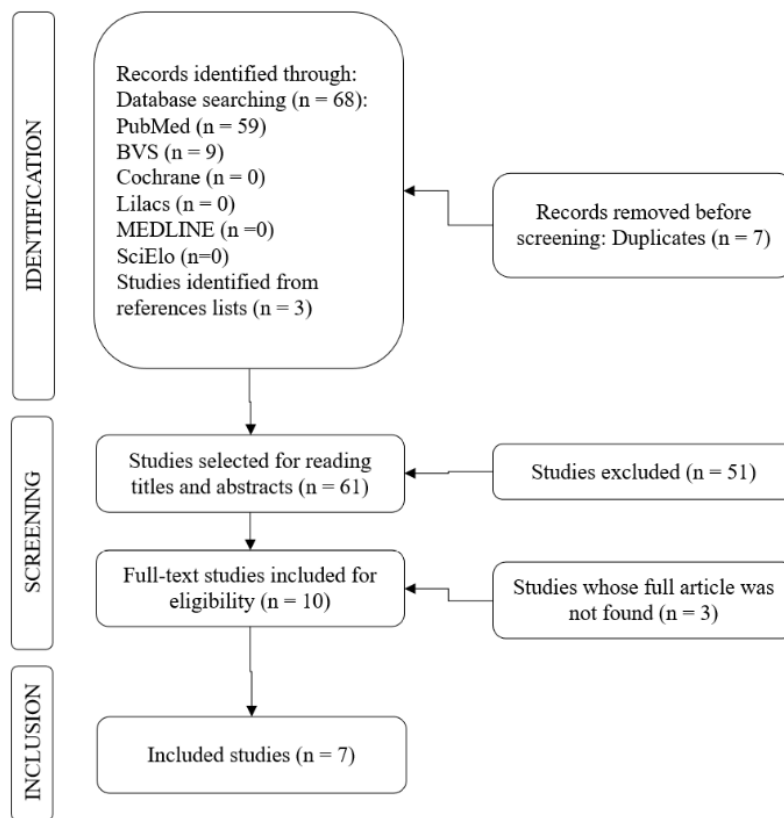
Source: author (2026).

3.6 STUDY SELECTION PROCESS

The initial screening and selection of the scientific documents retrieved from the databases were conducted independently by two researchers, with the aid of the online software Rayyan, a tool designed to facilitate the screening and selection of scientific articles. The identified articles were exported to the Rayyan interface in the RIS (Research Information Systems) format, where duplicate records were removed, and subsequently, the topic and study type were assessed (Phase 1) through title and abstract screening. Thereafter, the full texts of the remaining articles were reviewed to assess eligibility (Phase 2). Additionally, the reference lists of the studies selected in Phase 2 were examined to identify other potentially eligible studies for inclusion in this review. Throughout both phases, any disagreements among the two authors were resolved through a consensus meeting. If a consensus could not be reached, a third author was consulted to reach a final decision.

Figure 1

Flowchart of included studies



Source: author (2026).

4 RESULTS

A total of 68 articles were initially identified across the databases. After the removal of duplicates, 61 articles were screened based on titles and abstracts (phase 1). Following the application of inclusion and exclusion criteria, 7 articles were selected, distributed according to study design as follows: one comparative study, one prospective case-control study, one observational study, two cross-sectional case-control studies, two case reports. Table 2 shows the selected publications (n=7), according to authors, year of publication, country, objective, study type, participants, sex, age, main finding and conclusion.

Additional details concerning the excluded articles for exclusion rationales are detailed in Figure 1.

4.1 CHARACTERISTICS OF SOURCES OF EVIDENCE

Most of the included studies were concentrated in North America, with four studies conducted in the United States of America. In addition, three other studies were selected, each from a different country: Italy, Malaysia, and Saudi Arabia.

4.2 RESULTS OF INDIVIDUAL SOURCES OF EVIDENCE

One such investigation, conducted by Pandarathodiyil (2021) evaluated salivary levels of lactate dehydrogenase (LDH), an enzyme indicative of cellular damage, in three distinct groups: smokers, electronic cigarette users (vapers), and non-smokers/non-vapers. Standardized saliva collection yielded 5 mL of unstimulated whole saliva per participant, which was then analyzed using a colorimetric assay. The results showed significantly elevated LDH levels in both smokers (30.82 mU/mL) and vapers (35.15 mU/mL) compared to the control group (21.45 mU/mL). Although no significant difference was observed between smokers and vapers, the latter group had the highest mean LDH levels, suggesting relevant cytotoxic effects of e-cigarette use on the oral mucosa.

In a complementary approach, Elmahdi (2023) conducted a case-control study involving 500 Saudi men equally divided between e-cigarette users and non-smokers. Using exfoliative cytology and immunocytochemistry, they detected cytological atypia in 4.8% of e-cigarette users, compared to only 0.4% in non-users. Additionally, oral HPV infection was more prevalent among vapers (3.2%) than non-smokers (0.8%), and inflammation and keratinization were notably higher among long-term users, particularly those with over five years of exposure.

Similarly, Bardellini (2018) explored the prevalence and types of oral mucosal lesions (OMLs) in a prospective case-control study comparing former smokers and current e-cigarette users. Among the 90 participants, OMLs were identified in 55 individuals, 36 of whom were EC users. While the overall prevalence did not differ significantly between groups, specific lesions such as nicotinic stomatitis, hairy tongue, and hyperplastic candidiasis were significantly more frequent in the e-cigarette group. These findings point toward specific inflammatory changes associated with e-cigarette use.

In addition to cytological and clinical changes, molecular-level damage has also been reported. Guo (2021) employed high-resolution LC-NSI-HRMS/MS to quantify apurinic/aprimidinic (AP) sites in buccal cell DNA from cigarette smokers, e-cigarette users, and non-smokers. Surprisingly, AP site levels were significantly lower in e-cigarette users (3.3 per 10^7 nucleotides) than in both smokers (5.7) and non-smokers (6.0), although no difference was observed between the latter two groups. In vitro experiments failed to show protective effects of propylene glycol and glycerin, suggesting complex biological interactions. Despite the lower AP site formation, the results do not eliminate the risk posed by vaping and underscore the need for further investigation into the underlying mechanisms.

The study by Bustamante (2018) added to the evidence base by evaluating the endogenous formation of the carcinogen N'-nitrosonornicotine (NNN) in e-cigarette users. Analyzing saliva and urine from 59 participants, they detected salivary NNN in 80% of vapers (mean 14.6 ± 23.1 pg/mL), a level significantly lower than smokers but still higher than non-smokers. Importantly, e-cigarette liquids themselves contained negligible NNN, implying that its formation occurs locally in the oral cavity, likely from salivary nornicotine. These findings suggest a carcinogenic potential of vaping that is independent of direct product composition.

Case reports further reinforce this concern. In the report by Klawinski (2021), a 19-year-old male developed an aggressive, HPV-negative squamous cell carcinoma of the oral cavity after extensive e-cigarette use. Despite surgical and chemoradiotherapeutic interventions, the disease progressed rapidly, leading to metastasis and death within six months. This case underscores the potential carcinogenic effects of e-cigarette aerosols, as supported by in vitro studies showing DNA damage and oxidative stress in oral epithelial cells.

Likewise, Nguyen (2017) presented two case reports of men with no traditional risk factors who developed basaloid squamous cell carcinoma after over 13 years of exclusive e-cigarette use. Both cases emphasize the role of prolonged exposure to chemical

components and heavy metals in e-cigarette vapor as potential inducers of neoplastic transformations in the oral mucosa. The authors advocate for vigilant clinical monitoring of long-term users and call for further research on the long-term safety of electronic nicotine delivery systems.

5 DISCUSION

Table 2

Summary of characteristics of included studies (N=7)

Author, Year	Country	Objective	Study Type	Participants/Sex	Age	Main Finding	Conclusion
Nguyen et al. (2017)	USA	Report oral carcinoma cases in chronic EC users without risk factors.	Case report	2 male patients	66 and 59 years	Carcinoma in chronic EC users without traditional risk factors.	Chronic EC use may be linked to oral cancer.
Bardellina et al. (2018)	Italy	Evaluated prevalence of oral mucosa lesions in EC users vs ex-smokers.	Prospective case-control study	90 participants in 2 groups, mostly male years in EC group	Mean. 47	There was no statistically significant difference in the total prevalence of oral mucosa lesions between the groups.	E-cigarette users have a higher prevalence of oral mucosal lesions.
Bustamante et al. (2018)	USA	Investigated endogenous N-nitrosomethine (NNN) formation in saliva of EC users.	Cross-sectional case-control study	59 (20 smokers, 20 EC users, 19 non-smokers)	Specific ages not provided	N-nitrosomethine is formed endogenously in the mouths of e-cigarette users, with salivary levels detectable in 80% of cases.	Endogenous formation of NNN confirmed in EC users.
Guo et al. (2021)	USA	Analyze the impact of electronic cigarettes on the DNA integrity of oral cells and liver tissues.	Observational study	Human buccal cells and rat liver tissue	Humans: 23-55 years; Rats: 344 males	Both EC and traditional smoking had more DNA damage than non-smokers.	The use of e-cigarettes causes genetic damage comparable to that of traditional cigarettes.
Klavinski et al. (2021)	USA	Report rare oral cancer case in young EC user.	Case report	1 male	19 years	Aggressive tongue carcinoma, HPV-negative, resistant to treatment.	ECs may play a carcinogenic role in the oral cavity.
Pandarathody et al. (2021)	Malaysia	To evaluate the levels of the enzyme LDH in the saliva of electronic cigarette users and traditional cigarette smokers.	Comparative study	88 participants: 29 smokers, 29 vapers, 30 controls	26-32 years	Mean salivary LDH levels were significantly higher in the smokers (30.82 mU/ml) and vapers (35.15 mU/ml) groups.	Traditional and electronic smoking are associated with increased LDH activity in saliva.
Elmahdi et al. (2023)	Saudi Arabia	To investigate the association between e-cigarette use and HPV infection.	Cross-sectional case-control study	500 males: 250 EC users, 250 non-smokers	18 to 56 years	EC users had a higher prevalence of cellular atypia, oral HPV infection, inflammation and keratinization of the oral mucosa.	EC use increase the likelihood of contracting HPV and developing cytological atypia, which may contribute to the development of precancerous lesions.

Abbreviations: EC, Electronic Cigarette, HPV, Human Papillomavirus; LDH, Lactate Dehydrogenase.

Source: author (2026).

Several recent studies have highlighted the negative impacts of electronic cigarettes on oral health, raising concerns about their carcinogenic potential, even among young users without traditional risk factors.

In this context, Pandarathodiyil (2021) demonstrated that salivary LDH levels were significantly higher in smokers and e-cigarette users than in non-smokers. Notably, vapers showed the highest mean levels, suggesting that vaping induces cytotoxic effects in the oral mucosa. These findings reinforce that electronic cigarettes are not risk-free and highlight the usefulness of saliva as a non-invasive tool for monitoring oral changes associated with such habits.

Although Bardellini (2018) did not find a statistically significant difference in the overall prevalence of oral lesions between former smokers and electronic cigarette users, three types of lesions were significantly more common among vapers: nicotine stomatitis, hairy tongue, and hyperplastic candidiasis. These findings suggest that the use of such devices may be associated with specific inflammatory changes in the oral mucosa, mediated by factors such as altered oral pH, exposure to flavoring agents and aerosol chemicals, and possible reduction of local immunity.

Turning to aspects related to viral infections, Elmahdi (2023) demonstrated an association between electronic cigarette use and a significantly increased prevalence of oral human papilloma virus (HPV) infection, especially the high-risk subtype HPV-16, known for its oncogenic potential. This result indicates that, in addition to inflammatory effects, e-cigarettes may facilitate viral infections by compromising mucosal barriers and facilitating viral entry.

Still on the topic of carcinogenesis, although the article by Bustamante (2018) does not describe visible clinical lesions, the study demonstrated, for the first time, the endogenous formation of the carcinogen N'-nitrosonornicotine (NNN), a highly cancer-causing substance, in the saliva of electronic cigarette users, with detectable levels in 80% of participants, although significantly lower than those observed in smokers. This exposure, albeit subtle, may trigger silent cellular changes in the oral epithelium, representing a potential risk for the development of oral carcinoma over time. Although e-cigarette liquids contain very low levels of NNN, its formation in the oral cavity appears to occur primarily through the nitrosation of nornicotine, a nicotine metabolite. Urinary analysis performed in the study revealed that saliva is the most sensitive medium for detecting this form of exposure.

Supporting this concern, Klawinski (2021) reported a fatal case of oral squamous cell carcinoma in a 19-year-old man, linking the rapid progression of the disease and resistance to treatment to exposure to toxic substances found in aerosols, such as formaldehyde, heavy metals, and nitrosamines. Similarly, Nguyen (2017) described severe oral lesions in two patients with chronic use of electronic cigarettes for over 13 years, both without known risk factors for oral cancer. The lesions included exophytic masses with areas of hyperkeratosis, induration, and paresthesia on the tongue, as well as a persistent, painless, and indurated ulcer on the lower lip. These clinical changes are consistent with malignant neoplasms, and in both cases, biopsy confirmed the diagnosis of basaloid squamous cell carcinoma, an aggressive variant of squamous cell carcinoma. The occurrence of such lesions in individuals without a history of conventional tobacco use, alcohol consumption, or HPV infection suggests a possible association between continuous exposure to the toxic compounds in electronic cigarettes and the development of oral cancer. The authors also highlight the presence of substances such as acrolein, diethylene glycol, heavy metals (nickel, mercury, and aluminum), and volatile organic compounds, all with recognized carcinogenic potential.

Finally, Guo (2021) investigated the presence of apurinic/apyrimidinic (AP) sites in the DNA of oral cells from smokers, non-smokers, and electronic cigarette users. Interestingly, e-cigarette users showed a lower number of AP sites compared to the other groups, raising the hypothesis that the propylene glycol present in the devices might exert a moderate antimicrobial effect, reducing inflammation and, consequently, the formation of oxidative DNA damage. However, the authors caution that this isolated finding should not be interpreted as an indication of safety, as the long-term effects of vapor exposure remain unknown.

6 CONCLUSION

The evidence compiled in this review shows that electronic cigarette use can cause significant damage to the oral mucosa, even in the absence of nicotine. Observed effects include cytotoxicity, inflammation, metabolic alterations, increased susceptibility to viral infections, and the potential initiation and progression of oral neoplasms. Clinically, this damage may manifest as specific lesions such as hairy tongue, nicotinic stomatitis, and hyperplastic candidiasis. These results underscore the need for continued surveillance and further research to clarify the full extent of harm caused by vaping.

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