



## The relationship between electronic cigarettes and potentially malignant lesions in the oral cavity: an integrative literature review

### *La relación entre los cigarrillos electrónicos y las lesiones potencialmente malignas en la cavidad oral: una revisión bibliográfica integradora*

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**Abstract:** Potentially malignant lesions can be defined as areas whose tissue is morphologically altered and where cancer, in that location, is more likely to occur. These lesions can be triggered by environmental and behavioral factors, and, in this sense, this study seeks a relationship between electronic cigarettes and potentially malignant oral lesions. The objective of this work is to present a relationship between electronic cigarettes and potentially malignant oral lesions. The search for scientific articles to compose the research sample took place in June and July 2023, using the Medline and Web of Science databases, with an advanced search feature, using the following descriptors: "Oral neoplasm"; "Oral cancer" and "Electronic cigarette". It was found that all articles analyzed in this study showed some relationship between electronic cigarettes and potentially malignant lesions in the oral cavity. It is possible to identify relationships between electronic cigarettes and potentially malignant lesions in the oral cavity. However, studies are still scarce. In this sense, there is an indisputable need for more studies that seek to delve deeper into this topic, as it is extremely relevant to health. Although the evidence is still developing and there are significant gaps in research, the studies analyzed in this review indicate that electronic cigarettes may pose a risk for the development of potentially malignant lesions in the oral cavity. Importantly, more research is needed to fully understand the relationship between e-cigarette use and potentially malignant lesions in the oral cavity.

**Keywords:** *Oral neoplasm; Oral cancer; Electronic cigarette.*

**Resumen:** Las lesiones potencialmente malignas pueden definirse como áreas cuyo tejido está morfológicamente alterado y en las que es más probable que se produzca un cáncer en esa localización. Estas lesiones pueden ser desencadenadas por factores ambientales y conductuales y, en este sentido, este estudio busca una relación entre los cigarrillos electrónicos y las lesiones orales potencialmente malignas. El objetivo de este trabajo es presentar una posible relación entre los cigarrillos electrónicos y las lesiones orales potencialmente malignas. La búsqueda de artículos científicos para componer la muestra de la investigación se realizó en junio y julio de 2023, utilizando las bases de datos Medline y Web of Science, con una función de búsqueda avanzada, utilizando los siguientes descriptores: "Oral neoplasm"; "Oral cancer" y "Electronic cigarette". Se comprobó que todos los artículos analizados en este estudio mostraban alguna relación entre los cigarrillos electrónicos y lesiones potencialmente malignas en la cavidad oral. Es posible identificar relaciones entre los cigarrillos electrónicos y las lesiones potencialmente malignas en la cavidad oral. Sin embargo, los estudios son todavía escasos. En este sentido, es indiscutible la necesidad de más estudios que traten de profundizar en este tema, ya que es extremadamente relevante para la salud. Aunque las pruebas aún están en desarrollo y existen importantes

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lagunas en la investigación, los estudios analizados en esta revisión indican que los cigarrillos electrónicos pueden suponer un riesgo para el desarrollo de lesiones potencialmente malignas en la cavidad oral. Es importante destacar que se necesitan más investigaciones para comprender plenamente la relación entre el uso de cigarrillos electrónicos y las lesiones potencialmente malignas en la cavidad oral.

**Palabras clave:** *Neoplasia oral; Cáncer oral; Cigarrillo electrónico.*

## **INTRODUCTION**

Oral cancer is the sixth most common malignant neoplasm in humans, with new cases reported every year all over the world. There is a wide variety of head and neck cancers and most of them occur in the oral cavity (lips, tongue, gums, hard palate, jugal mucosa and floor of the mouth), pharynx and paranasal sinuses (Flach, 2019).

The etiological factors of potentially malignant lesions are like the etiological factors of oral cancer itself, such as chronic exposure to ultraviolet radiation, alcoholism, smoking, nutritional deficiency, genetic inheritance and human papilloma virus (HPV) infection. Thus, the development of oral cancer is highly linked to environmental factors (Klawinski, 2021).

Potentially malignant lesions can be defined as areas where the tissue is morphologically altered and where cancer is more likely to occur, compared to other areas where the tissue is normal. These lesions have different prevalences in the population and are often related to environmental and behavioral factors. Among the potentially malignant lesions, leukoplakia, erythroplakia, actinic cheilitis and lichen planus are the most common in terms of their rate of involvement. Oral leukoplakia is a mostly white lesion that can have a smooth, rough or verrucous appearance. Erythroplakia, however, refers to a macule or plaque lesion that is red in color. Actinic cheilitis is more common on the lower lip and is manifested by dryness, erosions and loss of the lip border. Finally, lichen planus has an unknown etiopathogenesis (Maia, 2016).

Over the last ten years, e-cigarettes have become increasingly popular, and in some cases are being recommended as an alternative for people who cannot use conventional cigarettes. The use of e-cigarettes among adults in the UK in 2012 reached around 700,000 adults who used e-cigarettes. In 2017, this number increased dramatically, reaching around 2.9 million adults who used the electronic device, which corresponds to approximately 6% of the UK adult population (Flach, 2019).

Electronic nicotine delivery devices have emerged as an alternative to conventional cigarettes, arousing growing interest. To this end, the relationship between the use of these devices and the development of potentially malignant lesions in the oral cavity remains a field of study with significant gaps and needs substantial scientific deepening. Lima (2023) pointed out that existing research still lacks more refined scientific methodologies to clarify this potential link.

Although smoking is widely recognized as an exogenous factor associated with oral cancer, electronic cigarettes remain in a scientific limbo about their relationship with potentially malignant lesions in the oral cavity. This integrative review seeks to fill this gap by examining the current literature and evaluating the available evidence on the possible association between the use of electronic cigarettes and the risk of developing oral lesions with malignant potential.

In the course of this work, scientific studies will be reported which support the evidence that electronic cigarettes are harmful to health, for example by increasing the risk of cancer and potentially malignant lesions. The general aim of this study is to present an integrative literature review to investigate the relationship that may exist between electronic cigarettes and potentially malignant lesions in the oral cavity.

## **THEORETICAL BACKGROUND**

Electronic cigarettes, also called nicotine delivery systems, are devices usually powered by a battery that aerosolize a solution inside the device called e-liquid. This solution contains various flavoring chemicals, substances for inhalation purposes and, in addition, nicotine. This electronic nicotine delivery system works with the help of the battery inside. This battery, together with an atomizer, aerosolizes the solution in the device's cartridge. Once the aerosol is formed, it is inhaled by the user, causing them to inhale all the substances that were present in the cigarette (Manyanga, 2021).

The emergence of the electronic cigarette is marked by a great deal of commercial advertising that emphasizes that it is less aggressive than conventional cigarettes. This has led to an alarming increase in the number of e-cigarette users, including people who already had problems with conventional cigarettes in the expectation that this new device would not be harmful to their health. However, it is worth noting that e-cigarettes are not a less aggressive alternative to conventional cigarettes. Studies analyzing the effects of toxins present in electronic cigarettes on oral cells, conducted by Yu *et al.*, 2016; Holliday *et al.*, 2016; and Tommasi *et al.*, 2019, have shown a strong carcinogenic argument related to these cigarettes. These studies showed, *in vitro*, a deregulation of DNA chains and genes involved in carcinogenesis. This therefore provides a plausible argument for linking the use of e-cigarettes to potentially malignant lesions in the oral cavity (Raj, 2020).

The composition of electronic cigarettes contains numerous substances considered toxic or potentially toxic to the human body, such as volatile organic compounds like acrolein, acetaldehyde, formaldehyde, benzaldehyde, acetone and toluene; as well as free radicals and heavy metals considered carcinogenic, such as formaldehyde and cadmium. It is noteworthy that, given the presence of these compounds, studies have reported a certain resistance to chemotherapy during cancer treatment.

However, given the very few restrictions and the lack of guidelines regulating their use, electronic cigarettes are constantly used as a less aggressive form of combustible cigarettes (Manyanga, 2021).

There are more than 500 brands of these devices currently circulating on the market, which also means that there is a marked variability in the types of electronic cigarettes, the substances present in the e-liquid, the amount of nicotine and, most importantly, the toxin content. All this unpredictability regarding the composition of the product makes it even more difficult to regulate such products in accordance with safety parameters for human health. As a result, this device is now a product that is still uncertain about what it can do to the health of its users (Sultan, 2018).

The electronic cigarette is still a recent product that is circulating too widely among people. This reflects the lack of solid studies on the relationship between e-cigarettes and potentially malignant lesions in the oral cavity. On the other hand, there are studies that link this type of cigarette to increased chances of head and neck cancer. "One example is a pilot study in the *New England Journal of Medicine* showing that the aerosols released by electronic cigarettes during the *vaping* process contain hidden formaldehyde. Formaldehyde is a potent carcinogen, and, in this sense, it is likely that people who make chronic use of the product may have an increased risk of cancer of the upper digestive tract (Menicagli, 2020; Sultan, 2018).

Currently, there is little evidence to suggest a direct role for e-cigarettes in the pathogenesis of potentially malignant oral disorders. However, xerostomia is the most common chief complaint, and actinic stomatitis, hairy tongue and angular cheilitis have also been reported when related to the use of electronic nicotine delivery systems. *In vitro*, studies have found that the vapor from these devices induces changes in the DNA of normal and squamous cell carcinoma cells of the head and neck (Sultan, 2018).

Direct and frequent exposure of healthy oral mucosa to a variety of substances, including carcinogens from conventional and smokeless cigarettes, can lead to the formation of potentially malignant lesions in the oral cavity. However, it is difficult to quantify the rate of transformation of oral epithelial dysplasia (Wisniewski, 2018).

The constituents released by electronic cigarettes can be of various types, determined by the type of device, user behavior, power, e-liquid content and the materials that make up the heating element and reservoir. These products may or may not resemble conventional cigarettes. The substances released by the aerosol can include glycols, aldehydes, metals and volatile organic compounds, glyoxal and methyl glyoxal, formaldehyde and others. In addition, these substances can be modified during the aerosolization process, since heating can help form new substances through a variety of reactions. It is extremely

important to note that the flavorings contained in electronic cigarettes can be a source of toxins, given that each flavor has a different chemical profile and therefore different toxic emission profiles (Ramôa, 2017).

Nicotine is one of the main agents responsible for cigarette addiction today, but it cannot be said with certainty that it is a carcinogenic substance. Despite this, nicotine can function as a strong inducer of cell migration in dysplastic oral keratinocytes. Therefore, although nicotine is not a carcinogenic product, it can function as an inducer of proliferative and migratory responses in neoplastic cells (Wisniewski, 2018). The use of electronic cigarettes can damage cells in such a way as to cause many reactive oxygen species, promoting oxidative stress. It is not yet known exactly how these free radicals are formed, since unlike conventional cigarettes, e-cigarettes do not combust. In fact, the characteristics of these devices can be harmful to the oral cavity, but the studies that are currently available are mostly guesswork. In this sense, e-cigarettes can cause some harm to their users, but it is essential that this evidence is proven with more in-depth studies (Menicagli, 2020).

*In vitro*, several adverse effects of e-cigarette aerosols can be reported, such as decreased cell viability, increased apoptosis rates, increased DNA chain breaks, changes in cell morphology and increased production of inflammatory mediators (Ramôa, 2017). Thus, although studies on the long-term effects of aerosols are currently scarce, the literature has already established a strong association with their potential to alter physiological processes, which can contribute to an increase in the chances of cancer, including in the oral cavity. Researchers at the University of Oklahoma Health Sciences Center in 2021 showed that exposure to e-cigarettes during cisplatin-based cancer treatment induces cisplatin resistance in cancer cells, negatively impacting cancer treatment and decreasing patient survival. This scenario shows that e-cigarette use can not only cause cancer, but also make its treatment more difficult.

Tellez *et al.* (2017) demonstrated that the aerosols formed by electronic cigarettes are likely to induce stress and genotoxicity in the cells of the oral cavity. Based on this, there is a likelihood that this electronic device induces damage to oral health, including potentially malignant damage (Santana, 2022). As mentioned above, nicotine has been shown to promote the migration of dysplastic keratinocytes through the activation of epidermal growth factor dependent on the overexpression of fatty acid syntaxin (a key hepatic lipogenic enzyme), a common pro-oncogenic event (Winiewski, 2018).

Korrapati *et al.* (2016) showed that short-term treatment of normal epithelial cells with e-cigarette aerosols induced up to a 10-fold increase in cell death compared to untreated cells. This is important to mention, as the study reports a direct negative action of the device's substances on the cells that are part of the oral mucosa (Flach, 2019).

Human papillomavirus (HPV) is, like smoking, one of the most common etiological agents in head and neck cancer. That said, it is worth noting that e-cigarette smoking has been shown to be associated

with a decreased expression of genes related to the immune system, offering potential mechanistic support for HPV infection. This raises the need for more in-depth investigations to confirm these claims in a study with a larger sample size, because with the increased incidence of oropharyngeal cancer associated with HPV, this issue is extremely relevant to health in general (Herdone, 2022).

## **METHODOLOGY**

This work is characterized as an integrative literature review, the aim of which is to provide a synthesis of knowledge and to incorporate the applicability of the results of significant studies into practice (Souza, 2010). In this sense, this literature review aims to show the relationship between electronic cigarettes and potentially malignant lesions in the oral cavity.

The following methodological steps were used in this work: elaboration of the guiding question, establishment of inclusion and exclusion criteria, searches for references, reading of titles and abstracts or full text, delimitation of the sample for critical analysis of the texts and synthesis of the results. The guiding question used in this review was: "Is there a relationship between electronic cigarettes and potentially malignant lesions in the oral cavity?".

The search for scientific articles to make up the research sample took place in June and July 2023, using the Medline (*Medical Literature Analysis and Retrieval System Online*) databases, via the Virtual Health Library, and the *Web of Science*. As a search strategy, the advanced search feature was configured using the following search descriptors: "Oral neoplasm"; "Oral cancer" and "*Electronic cigarette*". In addition, the Boolean operator "AND" was used in the databases to select the articles and apply inclusion and exclusion criteria to delimit the sample. The search key used was: "*Oral neoplasm*" AND "Oral cancer" AND "*Electronic cigarette*".

The inclusion criteria were full texts with free access, available on the databases and related to the research question. The exclusion criteria were theses, dissertations, repeatedly indexed articles and articles that did not address the research question. All the articles extracted for this research are from the last 6 years and are available in English language databases. To conduct a critical analysis of the studies included in this study, tables were used which present aspects such as: research title, authors, databases, year of publication, type of research, objectives and main results.

## **RESULTS AND DISCUSSIONS**

The search, using the keywords described in the methodology, resulted in a total of 51 publications (n=51), of which 12 (n=12) were published in the *Medline* database and 39 (n=39) in the

Web of Science database. The inclusion and exclusion criteria were then applied, leaving a total of 12 publications (n = 12) that were close to the theme of this review, as described in Table 01.

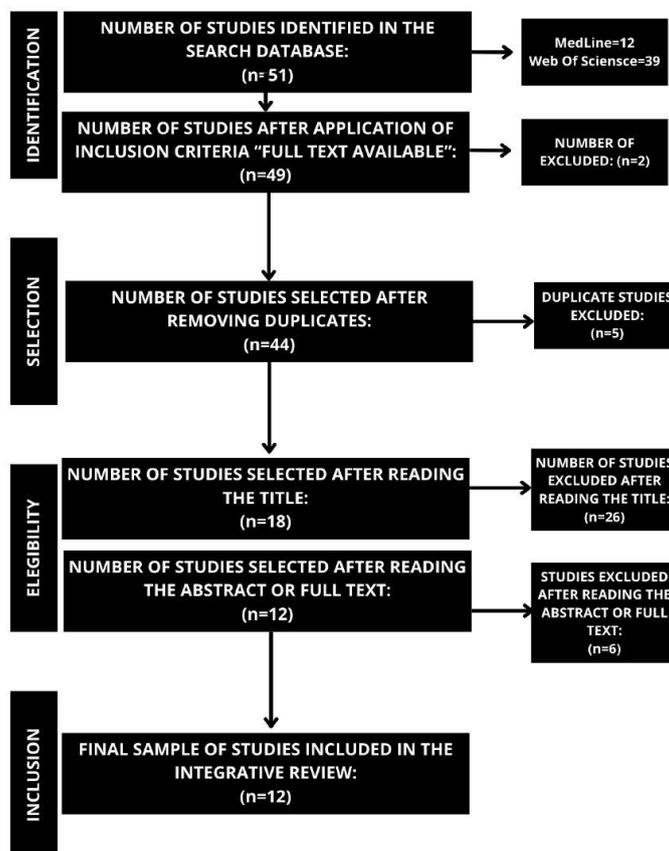
**TABLE 01:** Study design: delineation, identification and selection of publications, applying the inclusion and exclusion criteria.

Databases	N. of articles found	N. of articles filtered for the search
Medline	12	5
Web of Science	39	7
Total	51	12

SOURCE: Authors' data, (2023).

Figure 01 details the selection process for the final sample of publications included for full-text reading.

**FIGURE 01:** Flowchart of the publications found and included after applying the inclusion and exclusion criteria.



SOURCE: Authors' data, (2023).

All the publications included in this review are shown in **Table 02**, according to the information on the selected studies: title, authors, year, objectives and methodology used.

**TABLE 02:** Descriptive analysis of the publications included in the review that show a relationship between electronic cigarettes and potentially malignant lesions in the oral cavity.

N°	Title	Author/year	Objectives	Methodology
1	Electronic cigarette aerosols alter the expression of cisplatin transporters and increase drug resistance in oral cancer cells	Manynga <i>et al.</i> , 2021	To assess whether exposure to electronic cigarette aerosols modifies the body's response to cisplatin, a chemotherapy drug widely used in head and neck cancer treatment.	In vitro study
2	Increasing Popularity of Waterpipe Tobacco Smoking and Electronic Cigarette Use: Implications for Oral Health Care	Ramôa; Eissenberg; Sahingur, 2017.	To inform and highlight the emerging evidence on the biological effects of hookahs and e-cigarettes on the oral cavity.	Integrative literature review.
3	Nicotine induces oral dysplastic keratinocyte migration via Fatty Acid Synthase-dependent Epidermal Growth Factor Receptor Activation	Wisniewski; Ma; Schneider, 2018.	It provides new insight into the role of nicotine in signaling and cell migration in potentially cancerous cells.	In vitro study
4	Vaping the Venom: Oral Cavity Cancer in a Young Adult With Extensive Electronic Cigarette Use	Klawinski <i>et al.</i> , 2021.	To describe a case report of a student with an extensive history of electronic cigarette use who was diagnosed with squamous cell carcinoma (SCC).	Case report.

5	Electronic nicotine delivery systems: Oral health implications and oral cancer risk	Sultan; Jessri; Farah, 2018.	Discuss and review oral and systemic complications related to electronic nicotine delivery systems.	Integrative literature review.
6	Association between E-cigarette use and oral HPV-16 infection	Herndo; Jassal; Cramer, 2022.	To assess whether there is a relationship between electronic cigarettes and the increased risk of oral HPV-16 infection.	Cross-sectional comparative study.
7	Use of electronic cigarettes and the risk of developing potentially malignant disorders: What are we really supposed to know?	Santana <i>et al.</i> , 2022.	Report the main facts that electronic cigarettes can do when it comes to the risk of developing potentially malignant diseases.	Letter to the editor
8	E-cigarettes and head and neck cancers: A systematic review of the current literature	Flach; Maniam; Manickavasagam, 2019.	To explore the association between electronic cigarettes and head and neck cancer.	Qualitative systematic review.
9	Free Radical Production in the Smoking of E-Cigarettes and their Possible Effects in Human Health	Menicagli; Marotta; Serra, 2020.	Understand the impact of electronic cigarettes on human health, linked to the formation of free radicals.	Cross-sectional comparative study.
10	Predictors of oxidative stress and vascular function in an experimental study of tobacco versus electronic cigarettes: A post hoc analysis of the SUR-VAPES 1 Study	Mastrangeli <i>et al.</i> , 2018.	To explore the effects of conventional cigarettes and electronic cigarettes on oxidative stress and endothelial dysfunction.	Experimental study.

11	Reviewing the oral carcinogenic potential of E-cigarettes using the Bradford Hill criteria of causation	Raj <i>et al.</i> , 2020.	To determine the carcinogenic potential of electronic cigarettes according to the Bradford Hill causality criteria.	Integrative literature review.
12	E-liquid alters oral epithelial cell function to promote epithelial to mesenchymal transition and invasiveness in preclinical oral squamous cell carcinoma	Lima <i>et al.</i> , 2023.	To evaluate, in vitro, the effects of e-cigarette liquid on the oral epithelium.	In vitro study

**SOURCE:** Authors' data, (2023).

The main results of the studies included in this literature review are shown in Table 3.

**TABLE 03:** Main results of the publications included in this review that present the relationship between electronic cigarettes and potentially malignant lesions in the oral cavity.

N°	Title	Main results
1	<i>Electronic cigarette aerosols alter the expression of cisplatin transporters and increase drug resistance in oral cancer cells</i>	In vitro, exposure to e-cigarettes during treatment with cisplatin has been shown to reduce cancer cell death and increase the dose of cisplatin needed to induce a 50% reduction in growth in head and neck cancer cells.
2	<i>Increasing Popularity of Waterpipe Tobacco Smoking and Electronic Cigarette Use: Implications for Oral Health Care</i>	Although the number of studies is still limited, it is confirmed that these nicotine-releasing devices can cause susceptibility to infections, periodontal diseases, modified inflammatory responses, alveolitis, potentially malignant lesions and cancer in the oral cavity. In addition, the adverse effects of e-cigarette aerosols are decreased cell viability, increased apoptosis rate, changes in cell morphology and others.
3	<i>Nicotine induces oral dysplastic keratinocyte migration via Fatty Acid Synthase-dependent Epidermal Growth Factor Receptor activation</i>	It has been reported that nicotine can function as a strong inducer of cell migration in oral dysplastic keratinocytes. Therefore, although nicotine is not a carcinogenic product, it can function as an inducer

		of proliferative and migratory responses in neoplastic cells.
4	<i>Vaping the Venom: Oral Cavity Cancer in a Young Adult With Extensive Electronic Cigarette Use</i>	There is substantial evidence that the chemicals present in the aerosols of nicotine-releasing electronic devices are capable of inducing DNA damage and mutagenesis, supporting the hypothesis that they can increase the risk of cancer. In addition, the aerosols from these devices have been found to decrease the transcription of proteins essential for repairing DNA damage in human oral cells, which further increases the risk of cancer. Therefore, it can be concluded that these aerosols are carcinogenic and contribute to direct DNA damage and the failure of DNA repair mechanisms.
5	<i>Electronic nicotine delivery systems: Oral health implications and oral cancer risk</i>	Currently, there is no strong evidence suggesting a direct role for electronic cigarettes in the pathogenesis of potentially malignant oral disorders. However, xerostomia is the most common chief complaint, and actinic stomatitis, hairy tongue and angular cheilitis have also been reported when related to the use of electronic nicotine delivery systems. In vitro, studies have found that the vapor from these devices induces alterations in the DNA of normal cells and head and neck squamous cell carcinoma cells.
6	<i>Association between E-cigarette use and oral HPV-16 infection</i>	After analyzing data from the National Health and Nutrition Examination Survey (NHANES), it was found that e-cigarette use is significantly related to oral HPV-16 infection.
7	<i>Use of electronic cigarettes and the risk of developing potentially malignant disorders: What are we really supposed to know?</i>	According to Tellrz et al. (2021), the aerosols generated by electronic cigarettes can induce stress and genotoxicity, i.e., they can cause DNA damage. E-cigarettes share some of the same toxic compounds as traditional tobacco and, in this sense, their mutagenic role cannot be ruled out, as well as their participation in the development of potentially malignant lesions.
8	<i>E-cigarettes and head and neck cancers: A</i>	It has been reported that there is some evidence

	<i>systematic review of the current literature</i>	suggesting a potentially carcinogenic role for e-cigarettes in the pathogenesis of head and neck cancer, but this literature is still scarce.
9	<i>Free Radical Production in the Smoking of E-Cigarettes and their Possible Effects in Human Health</i>	There have been sufficient findings that highlight how e-cigarette aerosols can promote and form many reactive oxygen species/oxidative stress. There is real evidence that some chemicals present in e-cigarette aerosols can cause DNA damage, which supports the possibility that this could increase the risk of cancer.
10	<i>Predictors of oxidative stress and vascular function in an experimental study of tobacco versus electronic cigarettes: A post hoc analysis of the SUR-VAPES I Study</i>	Absolute changes in oxidative stress and vascular characteristics after smoking a conventional cigarette or vaporizing an electronic cigarette were significantly correlated.
11	<i>Reviewing the oral carcinogenic potential of E-cigarettes using the Bradford Hill criteria of causation</i>	Evidence of the presence of carcinogens in e-cigarettes and their DNA breaks is convincing, but not sufficient to infer a causal relationship. The comparative analysis suggests that e-cigarettes may be less toxic than conventional cigarettes, however, this does not negate the fact that e-cigarettes are not risk-free.
12	<i>E-liquid alters oral epithelial cell function to promote epithelial to mesenchymal transition and invasiveness in preclinical oral squamous cell carcinoma</i>	It has been reported that e-cigarette liquid induces morphological changes associated with increased motility and invasive phenotypes. In addition, cells exposed to the liquid expressed significantly reduced cell viability. It has also been shown to induce changes in gene expression consistent with the epithelial to mesenchymal transition.

**SOURCE:** Authors' data, (2023).

One of the main points supporting the idea that electronic cigarettes may be related to potentially malignant oral lesions is the fact that this device can influence mutagenic reactions. It has been observed that the substances present in electronic cigarettes can induce alterations in the DNA of oral cells, which can contribute to the appearance of lesions that could become malignant (Klawinski *et al.*, 2021; Santana *et al.*, 2022).

Important carcinogenic substances have been found in e-cigarette aerosols, such as volatile organic compounds like acrolein, acetaldehyde, formaldehyde, benzaldehyde, acetone and toluene. These compounds can have carcinogenic actions when in contact with human cells and, in this sense, it is important to be concerned about the possible actions of these substances released by electronic nicotine delivery devices in contact with oral cells. However, these propositions have not yet been consolidated with major research. Therefore, it is essential that there is greater attention to this issue, as well as greater investment in research in the area (Manyanga *et al.*, 2021; Raj *et al.*, 2020).

According to Menicagli; Marotta; Serra (2020), the aerosols released by electronic cigarettes promote reactive oxygen species that can cause oxidative stress. This, again, is another potential carcinogen that can induce transformations in oral cells. It is important to note that e-cigarettes are harmful to oral cells, as the products released by these electronic devices can compromise treatments against cancer itself.

*In vitro*, exposure to e-cigarettes during treatment with cisplatin reduces cancer cell death and increases the dose of cisplatin needed to induce a 50% reduction in growth in head and neck cancer cells. Therefore, realizing the need to increase the dose of cisplatin after using the device, it is noted that the electronic cigarette was the protagonist in the need to increase the dose of cisplatin (Manyanga *et al.* 2021).

It has also been reported that absolute changes in oxidative stress and vascular characteristics after smoking a conventional cigarette or vaporizing an electronic cigarette were significantly correlated (Mastrangeli *et al.*, 2018).

As with some of the studies listed here, it is important to note that this literature review has some limitations. These limitations were due to the scarcity of literature on the subject, as well as the lack of consistent research linking potentially malignant lesions and electronic cigarettes. It is therefore essential that further research is conducted on this subject, given that electronic cigarettes can be a predisposing factor for oral cancer.

## **CONCLUSIONS**

Although the evidence is still developing and there are significant gaps in the research, the studies analyzed in this review indicate that e-cigarettes may pose a risk for the development of potentially malignant lesions in the oral cavity. It is important to note that many of the conclusions are based on *in vitro* studies and emerging evidence, and more research is needed to fully understand the relationship between e-cigarette use and potentially malignant lesions in the oral cavity.

However, these findings underscore the importance of raising public awareness of the potential health risks associated with e-cigarette use and highlight the need for regulation and continued research in this area.

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