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Review Article

Effect of Vaping on the Development and Progression of Periodontitis

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Abstract

Introduction: The use of Electronic Nicotine Delivery Systems (ENDS), commonly known as e-cigarettes or vapes, has increased exponentially in recent years, particularly among adolescents and young adults. Although these devices are often promoted as a safer alternative to conventional tobacco, emerging evidence indicates that the aerosols they generate, containing nicotine, aldehydes and metallic nanoparticles, may exert detrimental effects on oral tissues.

Objective: To analyze the available scientific evidence on the impact of vaping on periodontal health, with particular emphasis on its effects on the oral microbiota, inflammatory response, oxidative stress and tissue healing mechanisms.

Methods: A literature review was conducted in the PubMed/MEDLINE database using the keywords ("vaping" OR "e-cigarettes") AND ("periodontitis" OR "periodontal disease"). Articles published in English or Spanish between 2010 and 2025 were considered. The selection included *in-vitro* experimental studies, clinical trials, systematic reviews and meta-analyses that evaluated the relationship between the use of ENDS and periodontal or peri-implant health. A total of 28 studies that met the inclusion criteria were analyzed. These studies were qualitatively assessed according to their methodology, study population and main findings.

Results: Evidence suggests that aerosols generated by ENDS induce oxidative stress, stimulate the release of pro-inflammatory cytokines (IL-6, IL-8, TNF-α) and activate the NF-κB signaling pathway. These mechanisms contribute to neutrophil dysfunction and increased levels of MMP-8 in the gingival crevicular fluid. Collectively, these alterations promote a state of persistent inflammation, reduce fibroblast function and delay the healing of periodontal tissues. Additionally, ENDS use disrupts the balance of the oral microbiota, favoring the proliferation of periodontopathogenic species such as Porphyromonas, Prevotella and Fusobacterium, which contributes to the loss of periodontal hard tissue support. Clinically, ENDS users present higher biofilm indices, increased probing depths and greater clinical attachment loss, while paradoxically showing reduced bleeding on probing-an effect attributed to nicotine-induced vasoconstriction. Although periodontal alterations associated with ENDS use appear less severe than those observed in conventional smokers, the available evidence indicates that their biological and clinical impact remains significant.

Conclusion: Vaping does not represent a biologically safe alternative to conventional smoking. Exposure to aerosols generated by ENDS induces oxidative, inflammatory and microbiological alterations that compromise the stability and healing capacity of periodontal tissues. Current evidence highlights the urgent need for long-term, controlled studies to define the cumulative effects of these devices and to support the development of effective prevention and public health strategies.

Keywords: Electronic Nicotine Delivery System; E-Cigarettes; Vaping; Periodontitis; Oxidative Stress; Inflammation; Microbiota Oral; Peri-Implantitis; Nicotine

Introduction

Periodontitis is defined as an inflammation associated with the presence of microorganisms and mediated by the host, leading to periodontal attachment loss and bone resorption, ultimately causing tooth loss [1,2]. It has a multifactorial etiology involving microorganisms and host susceptibility is a determining factor. Microorganisms initiate the infection and modulate the immune response, while environmental, systemic and genetic factors influence susceptibility. Smoking is the main modifiable risk factor, affecting the prevalence and progression of the disease in a dose-dependent manner and interfering with healing. It can also contribute to the transition from gingivitis to periodontitis [3]. All forms of tobacco use are associated with periodontal disease. In recent years, the use of Electronic Nicotine Delivery Systems (ENDS) has increased, especially among adolescents and young adults. However, the marketing, warnings and presentation of these products are not sufficiently clear to inform consumers of their potentially harmful effects, given that these devices contain nicotine and other chemical compounds that can affect both oral and general health.

Due to the exponential growth of electronic cigarettes in the last decade, these devices have become a popular alternative to traditional tobacco. Their marketing as a safer, smoke-free, less expensive option with fewer health impacts has driven their adoption, especially among young people and smokers seeking to reduce or quit conventional cigarettes. In this context, the term "vaping" will be used to refer to the use of electronic cigarettes or devices that produce vapor from a liquid, with or without nicotine.

However, despite its growing popularity, the impact of vaping on oral health remains a topic of concern and debate within the scientific community. This habit has been shown to alter the oral microbiota, induce inflammation and affect the immune response, thereby increasing the risk of periodontal disease. Some of its components, such as propylene glycol and vegetable glycerin, may promote bacterial adhesion and contribute to periodontal tissue damage. *In-vitro* studies have demonstrated that flavored e-cigarette vapor can cause DNA damage, generate oxidative stress and increase inflammatory responses in oral cells. Additionally, increased gingival inflammation has been reported in vapers, although many of these individuals were former traditional cigarette smokers [4]. Hang, et al., highlight the need to improve communication about the risks of vaping to oral health and emphasize the crucial role of dentists in disseminating accurate information regarding these devices [5].

The risk that vaping poses to periodontal tissues remains uncertain; therefore, the objective of this literature review is to determine its effects on periodontal health by exploring its impact on the oral microbiota, gingival inflammation and the progression of periodontitis.

Methodology

The search was conducted in the PubMed/MEDLINE database using the keywords ("Vapers" OR "Vaping") AND ("periodontal disease" OR "Periodontitis"). The strategy was limited to indexed articles in English and Spanish published between 2010 and 2025 with full-text availability. *In-vitro* experimental studies, cross-sectional and longitudinal clinical studies, systematic reviews and meta-analyses investigating the association between vaping and periodontal or peri-implant health were included. Of the 120 initial articles, a preliminary review of titles and abstracts was conducted to eliminate duplicates and studies outside the scope of the review. Subsequently, the preselected texts were read in full. In the end, 28 articles were deemed eligible, critically evaluated and grouped according to their methodological design, study population and main findings. The information was synthesized qualitatively, with emphasis on the biological mechanisms involved (oxidative stress, inflammation, dysbiosis and impaired wound healing) and the clinical consequences for periodontal tissues associated with the use of ENDS (Fig. 1).

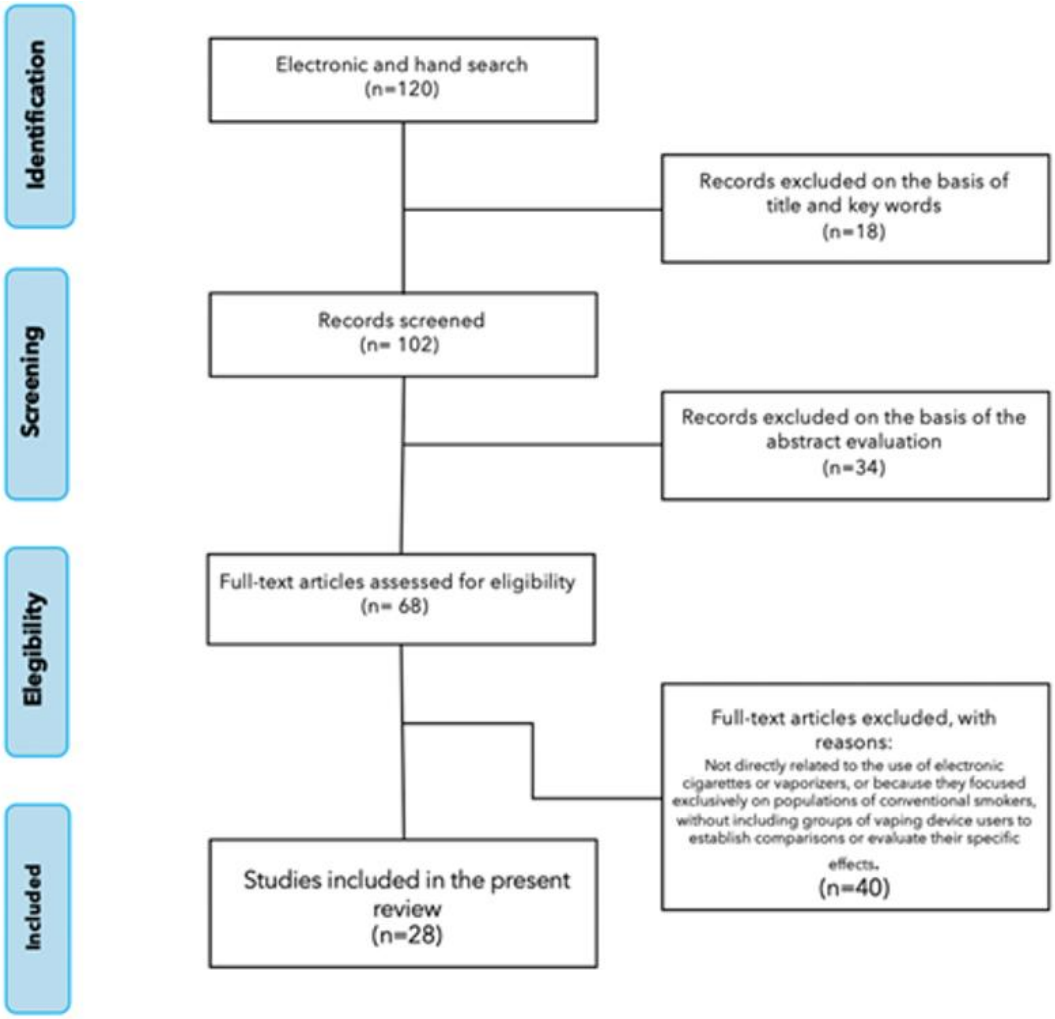

Figure 1: Flowchart of identified, excluded and included literature.

Background

Vaping is defined as the inhalation of vapor produced by heating liquids that typically contain nicotine and flavorings. These devices have been promoted as a safer and cheaper alternative to tobacco, as well as a tool for smoking cessation. Their marketing has been particularly effective among young people, with the FDA reporting a 78% increase in use among high school students in 2018 [6]. The desire to consume nicotine without the harmful effects of tobacco has driven multiple attempts at innovation over time. In 1927, Joseph Robinson designed the first electric vaporizer; later, in 1963, Herbert Gilbert created a "smokeless cigarette," although it did not achieve commercial success. In the 1980s, Jed Rose further developed vaporized nicotine. Finally, in 2003, Hon Lik created the first functional electronic cigarette as an alternative to traditional tobacco and by 2006, vaping had become popular in Europe and the United States [7].

The operation of vaporizers is based on a battery that activates a heating element capable of warming a liquid composed primarily of propylene glycol, vegetable glycerin, nicotine and flavorings (e.g., tobacco, mint, fruit, bubblegum). This process generates an inhalable aerosol that contains not only nicotine but also carbonyl compounds (formaldehyde, acetaldehyde, acrolein), volatile organic compounds, metals released from the heating element (such as nickel and chromium) and nanoparticles (Fig. 2) [6].

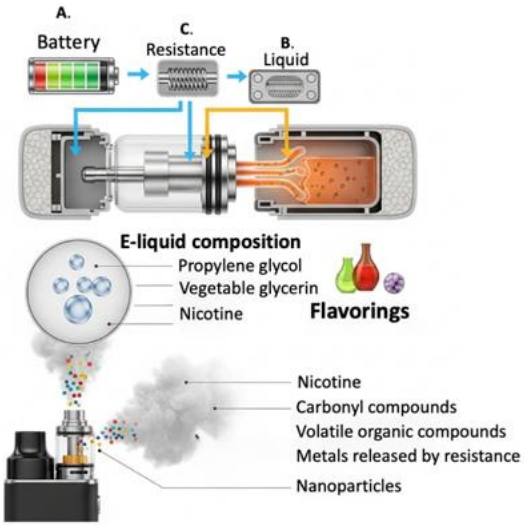

Figure 2: A typical ENDS integrates. A: A rechargeable battery; B: A wick/cotton soaked in e-liquid; C: A heating coil; they also have a tank or capsule and control sensors. When the device is activated the coil evaporates solvents (propylene gycol and/or vegetable glycerin), nicotine (free base or salts) and flavoring, forming an aerosol that may contain carbonyl compounds volatile organic compounds, metals and ultrafine particles from the coil and the liquid.

The chemical variations of the inhaled aerosols largely depend on the type of device, whose technological evolution has led to the development of different generations of vaporizers. The first generation, known as "cigalikes," included disposable devices or models with sealed cartridges and low power. The second generation consisted of "pens" or "tanks," which introduced refillable cartridges and moderate power. The third generation, called "mods," incorporated variable voltage and higher power, resulting in increased aerosol production. Finally, the fourth generation, represented by pods and modern disposables, uses nicotine salts in ultra-compact formats with sealed capsules that improve the efficiency of nicotine delivery. The type of device, the applied power and the user's consumption pattern largely determine the chemical profile of the aerosol and, consequently, its biological effects [6]. According to Dinardo, et al., e-cigarettes were introduced to the U.S. market in 2007 as purported smoking cessation aids; however, their popularity soon skyrocketed among teenagers and young adults due to the availability of appealing flavors and the perception that vaping is "less harmful" than smoking conventional cigarettes. The authors warn that this practice is not without risks, as the resulting aerosol can contain heavy metals, carbonyl compounds and carcinogenic nitrosamines, all of which pose toxic potential to the respiratory and cardiovascular systems. Moreover, it has been observed that nicotine in high concentrations, such as those found in Juul-type devices, can induce dependence more rapidly than traditional tobacco, particularly in developing brains. Early nicotine exposure has been associated with impairments in attention, memory and emotional regulation, prompting the U.S. Department of Health to declare e-cigarette use among youth a "major public health problem" [8].

Multiple studies have shown that prolonged exposure to ENDS aerosols triggers complex cellular and molecular mechanisms, including oxidative stress, activation of inflammatory responses, alterations in the oral microbiome and impaired healing of periodontal and peri-implant tissues [9].

1. Cellular and Molecular Mechanisms of Electronic Nicotine Delivery Systems (ENDS)

Oxidative Stress

One of the most important mechanisms by which ENDS exert adverse biological effects is oxidative stress. The aerosol generated during their use contains aldehydes (formaldehyde, acetaldehyde, acrolein), carbonyl compounds, heavy metals (nickel, chromium, lead) and nanoparticles released from the heating elements. These substances promote the excessive production of Reactive Oxygen Species (ROS), which exceed the physiological antioxidant capacity of tissues and saliva. Consequently, oxidative damage occurs in lipids, proteins and DNA, along with mitochondrial dysfunction, leading to altered energy metabolism and promoting cell apoptosis. In the oral cavity, this redox imbalance manifests as a reduction in salivary antioxidant capacity, a condition that increases the host's susceptibility to inflammatory and degenerative processes (Fig. 3) [6].

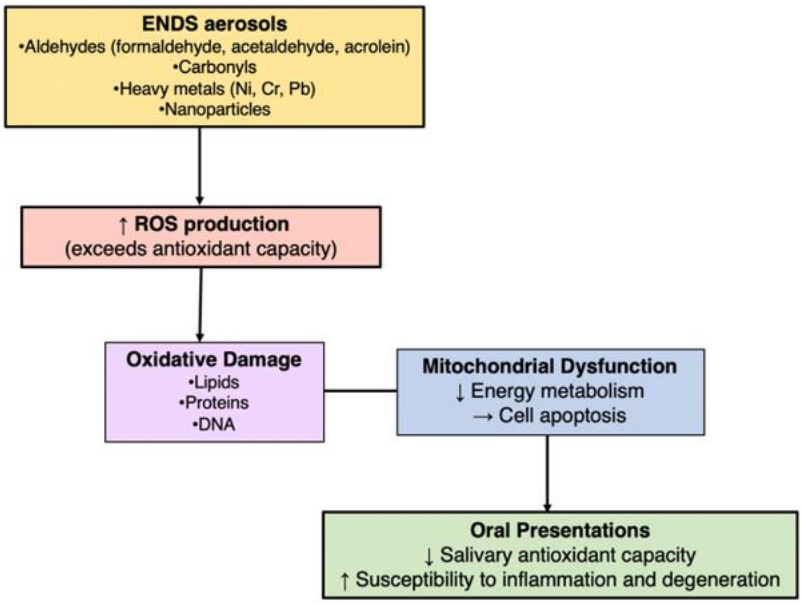

Figure 3: Oxidative stress induced by ENDS.

According to Cichońska, et al., e-cigarette use significantly reduces total salivary antioxidant capacity (TAOS and TEAC) in a manner comparable to that observed in conventional smokers and alters uric acid and purine nucleotide levels, which are indicators of redox imbalance. This reduction in salivary antioxidant capacity is associated with increased ROS production and diminished defense mechanisms against oxidative damage, contributing to deterioration of the oral mucosa and the development of chronic inflammatory processes [10].

At the immunological level, exposure to e-cigarette aerosol has been linked to the release of inflammatory mediators and growth factors, as well as to increased oxidative stress and the activation of apoptotic and necrotic pathways in lung and oral cells. This inflammatory cascade fosters a chronic, pro-inflammatory microenvironment, which has been associated with the development of periodontal and peri-implant diseases, as well as increased susceptibility to oral infections and neoplasms [11].

Inflammatory Response

In parallel with oxidative stress, aerosol emissions from ENDS trigger a robust inflammatory response. Experimental studies have shown an increased release of pro-inflammatory cytokines-particularly IL-6, IL-8 and TNF-α-which activates intracellular signaling pathways such as NF-κB. This cascade promotes chemotaxis and activation of immune cells, mainly neutrophils and macrophages, contributing to both local and systemic inflammation. Additionally, functional alterations have been reported in gingival fibroblasts and epithelial cells, which display greater susceptibility to apoptosis and a reduced regenerative capacity. These changes impair tissue healing and repair, thereby increasing the vulnerability of oral tissues to bacterial aggression [9].

Similar to what is seen in smokers, exposure to ENDS aerosols disrupts the balance between pro- and anti-inflammatory responses, resulting in increased leukocyte infiltration, neutrophil dysfunction and elevated MMP-8 levels in gingival crevicular fluid. In the 2023 study by Do, et al., involving patients with periodontitis, smokers exhibited an altered immune response, characterized by fewer Oral Neutrophils (ONN) and a smaller reduction in MMP-8 following nonsurgical periodontal therapy compared with nonsmokers. This pattern suggests a dysregulated and prolonged inflammatory response, leading to delayed tissue repair and greater collagen degradation. Although these findings come from long-term cigarette smokers, current evidence indicates that ENDS users may experience similar pathophysiological mechanisms due to comparable exposure to nicotine and oxidative by-products [12].

On the other hand, interaction with aerosols emitted by ENDS alters the function of gingival fibroblasts and epithelial cells, inducing a pro-inflammatory phenotype with increased susceptibility to apoptosis and cellular senescence. According to Kastratovic, et al., exposure of Periodontal Ligament Mesenchymal Stem Cells (PDL-MSCs) to ENDS aerosol reduces their immunomodulatory capacity, modifies their secretory profile and decreases the release of anti-inflammatory factors such as

TGF-β1. These changes impair tissue regeneration and sustain local inflammation. As a result, a persistently activated tissue microenvironment develops, characterized by the continuous release of inflammatory and oxidative mediators. Clinically, these mechanisms are associated with increased gingival crevicular fluid, bleeding on probing, elevated MMP-8 and neutrophil elastase levels and delayed resolution of inflammation following periodontal therapy. Consequently, ENDS users may experience a chronic inflammatory response with progressive loss of clinical attachment, even in the absence of substantial biofilm accumulation [13].

Alterations in the Microbiome

The biological environment altered by oxidative stress and inflammation has a direct impact on the oral microbiome. Changes in bacterial composition have been identified in ENDS users, with a proliferation of species associated with inflammatory and periodontopathogenic conditions. Furthermore, the reduction in salivary antioxidant capacity and the xerostomia induced by e-liquid solvents (propylene glycol and vegetable glycerin) create an acidic and less protective environment, facilitating the colonization of pathogenic microorganisms. Recent studies have demonstrated that vaping generates a unique and dysbiotic periodontal microbiome, characterized by an increase in *Porphyromonas, Treponema, Fusobacterium, Veillonella* and *Rothia*, as well as a greater abundance of *Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans*, all linked to chronic inflammatory processes and destruction of dental support tissue. These alterations in the microbial ecology reinforce local inflammatory processes and increase the risk of developing periodontitis and peri-implantitis [9,14].

Recent clinical studies have shown that ENDS users exhibit significant alterations in salivary pH and cotinine levels-the main metabolite of nicotine-compared to non-smokers. Hasan, et al., reported that both conventional smokers and e-cigarette users presented more acidic saliva (reduced pH) and higher cotinine concentrations, indicating continuous nicotine exposure and a disruption of the physiological balance of the oral cavity. The decrease in salivary pH creates an acidic microenvironment that negatively affects the composition of the oral microbiota and reduces the buffering capacity of saliva. This acidification favors the proliferation of aciduric pathogenic microorganisms such as *Porphyromonas gingivalis*, *Veillonella spp.*, *Streptococcus mutans* and *Fusobacterium nucleatum*, all implicated in the development and progression of periodontal disease and carious lesions. Furthermore, the acidic environment promotes enamel demineralization and alters the stability of the gingival extracellular matrix, increasing epithelial permeability and facilitating the penetration of bacterial endotoxins and pro-inflammatory compounds. Additionally, chronic exposure to ENDS aerosols with different flavors and nicotine concentrations has been shown to increase the gingival index and clinical signs of inflammation, even in the absence of advanced attachment loss. This suggests that the inflammatory and irritative effects of vapor are independent of the mechanical damage caused by conventional cigarettes and can manifest early as oxidant-induced gingivitis [15].

On the other hand, studies by La Rosa, et al., indicate that exclusive users of ENDS have significantly less biofilm (R30) and mature calculus (R120) than conventional cigarette smokers, but levels comparable to ex-smokers and non-smokers. In this cross-sectional study, using Quantitative Light-Induced Fluorescence (QLF), traditional smokers exhibited high R30 and R120 values ($p < 0.001$), reflecting a greater area and thickness of mature biofilm, whereas ENDS users showed values similar to those of non-smokers ($p > 0.05$). These results suggest that exclusive ENDS use may be associated with reduced visible dental biofilm accumulation, possibly due to the absence of combustion by-products such as tar and soot, which enhance bacterial adhesion and promote biofilm pigmentation. However, the authors caution that this apparent improvement in biofilm indices does not equate to a healthy periodontal environment, as ENDS aerosols contain carbonyl compounds (formaldehyde, acrolein and acetaldehyde), heavy metals (nickel, chromium, lead), aromatic aldehydes and metallic nanoparticles released from the device's heating elements-all of which can alter cellular oxidative metabolism and local immune responses [16].

Impact On Healing and Periodontal Tissues

The combination of oxidative stress, persistent inflammation and microbiome dysbiosis results in clinically relevant consequences for periodontal and peri-implant tissues. Evidence shows that ENDS users exhibit increased biofilm indices, bleeding on probing, greater probing depths and clinical attachment loss, although generally to a lesser extent than conventional cigarette smokers [17]. While traditional cigarette smoke induces vasoconstriction, impaired angiogenesis and more pronounced tissue destruction, ENDS generate a different pattern of damage characterized mainly by redox imbalance and inflammatory dysregulation. Nevertheless, these alterations can significantly compromise post-surgical healing and may negatively affect implant osseointegration [18].

Nicotine, present in both conventional cigarettes and e-cigarette liquids, produces microvascular alterations that reduce tissue oxygenation and perfusion, thereby affecting angiogenesis and the migration of fibroblasts essential for repair. Histological studies by Birlabose, et al., have shown that chronic nicotine exposure increases epithelial thickness through hyperkeratinization and alters the structure of the basal lamina and cell adhesion, ultimately compromising the barrier function of the gingival epithelium. Importantly, this epithelial thickening does not confer greater resistance; rather, it results in a more rigid and less vascularized tissue with a diminished capacity to respond adequately to inflammatory stimuli or surgical procedures [19].

Furthermore, the systematic review by Olsson, et al., demonstrated that smoking and nicotine exposure-even in alternative forms such as ENDS are associated with delayed postoperative healing and an increased risk of infection and wound dehiscence, attributable to impaired tissue oxygenation and a compromised local immune response. Although evidence regarding vaping cessation before oral procedures remains limited, findings from conventional smoking literature indicate that cessation significantly improves periodontal tissue repair and implant osseointegration [20]. In line with these findings, Nakayama, et al. and Hurrell, et al., as cited in the review by Olsson, et al., report that persistent nicotine use-regardless of the source-compromises implant healing and stability, increasing susceptibility to peri-implantitis and osseointegration failure. Therefore, chronic exposure to ENDS aerosols may induce a similar pattern of inflammatory and vascular alterations, potentially affecting long-term therapeutic outcomes and reinforcing that vaping is not a biologically safe alternative for periodontal or peri-implant tissues [20.21].

2. Association Between Vaping and Periodontitis

The use of electronic cigarettes or vapes has been proposed as a lower-risk alternative to conventional smoking. However, emerging scientific evidence suggests that these devices may have adverse effects on the oral cavity, particularly on periodontal tissues. Several studies, including systematic reviews and meta-analyses, have shown that vape users exhibit altered periodontal clinical parameters-such as increased probing depth, clinical attachment loss and marginal bone loss-when compared to non-smokers [17]. Thiem, et al., concluded that, although conventional tobacco smokers generally exhibited the most severe periodontal deterioration, e-cigarette users also demonstrated adverse clinical changes relative to non-smokers, including higher biofilm indices, deeper periodontal pockets and greater clinical attachment loss, along with a consistent reduction in bleeding on probing when compared to smokers [17].

Zhang and Wen, summarized that, although the oral risk profile of ENDS is lower than that of combustible tobacco, it is not negligible; their use is associated with an increased risk of oral diseases, including caries, mucosal alterations and periodontitis. Epidemiological studies also show a higher likelihood of reported periodontal disease among ENDS users compared with non-users [9]. Similar findings were reported by Holliday, et al., who noted that, while the periodontal damage linked to vaping appears less severe than that caused by combustible tobacco, its adverse effects in chronic users are clear and clinically relevant. They additionally cautioned that the perception of e-cigarettes as “safe” lacks solid scientific support [9].

Moreover, in a 2024 systematic review focused on peri-implant health, Guney, et al., observed comparable detrimental effects around dental implants. A recent meta-analysis on peri-implantitis identified increased probing depth, bone loss and elevated IL-1β levels in ENDS users, along with decreased bleeding on probing suggesting simultaneous tissue damage and clinical masking of inflammation [22,23]. These findings align with evidence in healthy periodontal tissues and reinforce the hypothesis that vaping may alter inflammatory pathways and bone remodeling mechanisms.

One of the most striking clinical observations is the reduced bleeding on probing reported in ENDS users compared with tobacco smokers and in some analyses, even with non-smokers. This finding should not be interpreted as an improved periodontal health; rather, it reflects the vasoconstrictive action of nicotine and certain local anti-inflammatory effects that mask gingival inflammation. Consequently, diminished bleeding may coexist with greater clinical attachment loss and periodontal destruction, potentially hindering the early detection of disease [9].

Recently, Kumar and Shlossman analyzed the impact of e-cigarette use on the response to Non-Surgical Periodontal Therapy (NSPT). In their retrospective study of 220 patients-non-smokers, ex-smokers, smokers and vapers-the authors reported that e-cigarette users demonstrated a poorer clinical response than non-smokers. Specifically, vapers exhibited a higher number of sextants requiring periodontal surgery after NSPT and a lower rate of periodontal pocket closure (66.6%) compared with non-

smokers (77.1%) and ex-smokers (74.9%). Notably, the clinical behavior of vapers closely resembled that of active smokers, indicating that ENDS use may impair periodontal and inflammatory resolution. This finding is clinically relevant, as it suggests that vaping could interfere with healing processes and reduce the effectiveness of periodontal therapy, ultimately compromising disease control even after professional intervention [24].

At a biological level, ENDS aerosols contain nicotine, propylene glycol, vegetable glycerin, heavy metals, aldehydes and flavoring agents-compounds that have demonstrated cytotoxic effects on gingival fibroblasts and the oral epithelium. Evidence from cellular and tissue models indicates that exposure to these aerosols induces oxidative stress, mitochondrial dysfunction and impaired cellular proliferation and tissue repair, thereby creating a microenvironment conducive to inflammation and periodontal breakdown [25,26]. Another key mechanism involves alterations in the oral and subgingival microbiome. Bagale, et al., reported that vapers exhibit a distinct microbial profile compared with non-smokers, characterized by an increased relative abundance of genera such as *Veillonella, Rothia* and *Haemophilus*, as well as a higher prevalence of *Candida* [25]. This dysbiotic profile favors colonization by periodontopathogenic microorganisms and modifies bacterial metabolic pathways associated with virulence and tissue degradation. In addition, greater biofilm accumulation has been observed in ENDS users. Proposed explanations include the effects of vegetable glycerin and propylene glycol on the oral cavity, which increase viscosity and enhance bacterial adhesion to the enamel surface. Collectively, these findings contribute to evidence indicating that individuals who vape harbor a distinct oral microbiome, which may predispose them to periodontal disease [13].

Clinically, these biological and microbial alterations translate into a periodontal profile characterized by higher biofilm accumulation, increased probing depths, greater clinical attachment loss, and, in some cases, marginal bone loss often accompanied by reduced bleeding on probing. Altogether, this evidence indicates that although the periodontal impact of ENDS is generally less severe than that of conventional smoking, these devices cannot be regarded as harmless. Instead, they represent a meaningful risk factor for the development and progression of periodontitis [17].

3. Histological and Molecular Changes in the Periodontium Associated with Vaping

The impact of ENDS on periodontal tissues is not limited to alterations in clinical parameters; it also encompasses histological and molecular disturbances that help explain the increased susceptibility to periodontitis observed in users. Exposure of gingival fibroblasts and epithelial cells to ENDS constituents has been shown to induce marked oxidative stress and accumulation of ROS, leading to mitochondrial dysfunction, cell-cycle disruption, apoptosis and premature cellular senescence [25]. Ganesan, et al., reported that exposure to ENDS aerosol components, including aldehydes, carbonyl compounds, heavy metals and metallic nanoparticles originating from heating coils, significantly increases oxidative stress biomarkers in gingival crevicular fluid. In particular, elevated levels of the oxidative DNA damage marker 8-OHdG and alterations in antioxidant enzyme activity, such as GSH-Px, were consistently observed. These findings, documented both in clinical comparisons of smokers, vapers and ex-smokers as well as in controlled *in-vitro* models, demonstrate that the oxidative microenvironment induced by ENDS compromises tissue regenerative capacity, promotes mitochondrial injury and contributes directly to periodontal breakdown [26].

Recent findings have expanded the understanding of ENDS-related damage to periodontal tissues, revealing effects that extend beyond clinical and inflammatory alterations. Kastratovic, et al., demonstrated that ENDS aerosols significantly reduce the viability, proliferation and regenerative capacity of PDL-MSCs. These cells play a critical role in maintaining and repairing periodontal structures. Yet, exposure to e-cigarette vapor components disrupts their metabolic activity, diminishes their osteogenic and cementogenic potential and impairs their immunomodulatory functions. Although these detrimental effects are generally less severe than those induced by conventional cigarette smoke, both exposures promote oxidative stress and a pro-inflammatory microenvironment that interferes with tissue regeneration and favors chronic periodontal breakdown [13].

At the tissue level, these alterations reflect a disruption in the balance of cytokines and inflammatory mediators. AlJasser, et al., reported that e-cigarette users exhibit significantly elevated salivary levels of IL-1β, IL-6, TNF-α and MMP-8, along with a reduction in the TIMP-1 inhibitor following peri-implantitis treatment. This biomarker profile is indicative of increased catabolic activity within peri-implant soft and hard tissues, suggesting that vaping may perpetuate a chronic inflammatory state and compromise bone repair after periodontal therapy or implant procedures [27]. In addition to oxidative stress, inflammatory dysregulation is another key pathogenic mechanism. Studies by Ganesan, et al. and Rouabhina, et al., conducted in ENDS users

demonstrate that vaping leads to significant alterations in the cytokine profiles of gingival crevicular fluid and saliva. These investigations report elevated levels of pro-inflammatory mediators implicated in periodontal tissue destruction, including IL-1β, IL-6, IL-8 and TNF-α, as well as activation of classical inflammatory pathways associated with collagen degradation and bone resorption [25,26]. Clinically, these molecular changes correspond to increased volumes of gingival crevicular fluid, deeper periodontal pockets and greater clinical attachment loss. Overall, the evidence confirms that cytokine-mediated inflammation contributes directly to extracellular matrix breakdown and progressive alveolar bone loss [26].

Another mechanism contributing to bone loss is the disruption of the RANKL/OPG system within the periodontal microenvironment. Comparative studies by Karaaslan, et al., reported elevated levels of RANKL an essential mediator of osteoclast differentiation-and OPG in the gingival crevicular fluid of ENDS users, water pipe users and conventional smokers compared with non-smokers. These findings point to an active and imbalanced bone remodeling process. Although further research is needed, current evidence indicates that ENDS use is associated with pro-resorptive biochemical signals that can promote osteoclastic activation and marginal alveolar bone loss (Fig. 4) [28].

Figure 4: Alteration of RANKL/OPG axis in users ENDS, waterpipes and cigarettes.

Furthermore, nicotine inhaled via ENDS induces hypoxic responses in periodontal tissues. Local hypoxia and the activation of Hypoxia-Inducible Factors (HIFs) have emerged as important mechanisms related to nicotine exposure from any source [28]. Sakellari, et al., measured HIF-1α, HIF-2α, HIF-3α and VEGF in gingival crevicular fluid and observed that both smoking and periodontal inflammation increase these biomarkers. The authors propose that nicotine-induced vasoconstriction and altered blood flow reduce tissue oxygenation, activate HIF/VEGF pathways and modulate angiogenesis and cellular metabolism. These conditions contribute to a chronic inflammatory microenvironment that compromises tissue repair [28]. Although direct research on HIF activation in ENDS users is still limited, the known effects of nicotine and the similarity of biological responses suggest that vaping may trigger comparable hypoxic mechanisms, thereby contributing to periodontal disease progression.

Discussion

The evidence available to date indicates that the use of ENDS produces significant biological and clinical alterations in oral tissues. These effects are primarily mediated by mechanisms involving oxidative stress, inflammatory dysregulation and microbial dysbiosis. Although ENDS were initially designed and promoted as a safer alternative to conventional cigarettes, growing scientific scrutiny challenges this perception and shows that their impact on oral health is far from harmless. It is important to emphasize, however, that current evidence remains limited: most available studies are *in-vitro*, short-term or involve small sample sizes, which restricts the ability to establish a definitive causal relationship.

The findings reported by Cichońska, et al., indicate that aerosols generated by ENDS contain potentially toxic compounds including aldehydes, heavy metals and nanoparticles that can trigger excessive production of ROS. This overproduction overwhelms the physiological antioxidant capacity of saliva and oral tissues, leading to reductions in antioxidant markers such as TAOS and TEAC and to increased oxidative damage to lipids, proteins and DNA. The resulting redox imbalance contributes to mitochondrial dysfunction and promotes apoptotic pathways, compromising tissue homeostasis and increasing susceptibility to inflammatory and degenerative processes. Although these mechanisms resemble those observed in conventional smokers, the

magnitude and timing of these effects in ENDS users have not yet been fully elucidated.
According to Zhang Q, et al., the inflammatory response triggered by exposure to e-cigarette aerosols is characterized by an increased release of pro-inflammatory cytokines such as IL-6, IL-8 and TNF-α, along with the activation of intracellular signaling pathways, particularly NF-κB. These responses promote the chemotaxis and activation of neutrophils and macrophages, creating a chronic inflammatory microenvironment. Such an environment contributes to the destruction of periodontal supporting tissues. Persistent inflammation has also been associated with functional alterations in gingival fibroblasts and epithelial cells, which present reduced regenerative capacity and an increased susceptibility to apoptosis. Together, these conditions compromise healing and tissue repair.

Clinical studies by Hasan, et al., indicate that ENDS users exhibit a more acidic salivary pH and elevated levels of cotinine, the primary metabolite of nicotine. These findings suggest continuous nicotine exposure and the presence of an oral environment conducive to inflammation and oxidative stress. The reduction in salivary pH alters the composition of the oral microbiota, favoring the proliferation of pathogenic bacterial species such as *Porphyromonas gingivalis, Veillonella spp. and Fusobacterium nucleatum*, all of which are associated with the initiation and progression of periodontal disease. Additionally, nicotine and the solvents present in e-liquids modify salivary viscosity and buffering capacity, contributing to xerostomia and creating a microenvironment that facilitates microbial colonization and chronic inflammation.

Most studies agree that the effects of ENDS on the periodontium are less severe than those of combustible tobacco; however, these effects should not be considered insignificant. Chronic users consistently exhibit increased biofilm indices, greater probing depths and clinical attachment loss. Additionally, a reduction in bleeding on probing is frequently observed, an effect attributed to nicotine-induced vasoconstriction, which may mask ongoing inflammation and hinder early diagnosis. Emerging evidence also indicates that prolonged exposure to ENDS aerosols may negatively affect postoperative healing and implant osseointegration, potentially compromising long-term therapeutic outcomes.

However, the scientific literature on the effects of ENDS still presents significant methodological limitations. The predominance of cross-sectional or *in-vitro* experimental studies limits the ability to extrapolate the results to clinical practice. Robust longitudinal studies with larger sample sizes and appropriate control groups are needed. Future research should distinguish the specific effects of nicotine from those derived from other aerosol constituents and should also evaluate variables such as dose, frequency and duration of exposure. Additionally, it is crucial to assess outcomes according to the type and generation of the device, as aerosol potency and composition vary substantially among different vaping models.

Conclusion

A thorough analysis of the existing literature indicates that the use of ENDS is neither a safe nor a risk-free alternative for oral health, despite being widely promoted as a safer option compared with conventional smoking. Current evidence shows that continuous exposure to ENDS-generated aerosols induces oxidative stress, inflammatory responses and microbial dysbiosis. These alterations directly disrupt the homeostasis of oral tissues, particularly affecting the periodontium. The effects reported in users of ENDS appear to be less pronounced than those associated with combustible tobacco; however, their clinical and biological impact remains significant. The reduction in bleeding on probing, attributed to the vasoconstrictive action of nicotine, may mask active inflammation and hinder the early diagnosis of periodontitis. Additionally, the impairment of tissue repair mechanisms may compromise long-term therapeutic outcomes. Nevertheless, it is important to recognize that the available evidence remains limited and methodologically heterogeneous. Most studies are cross-sectional, involve small sample sizes or rely on *in-vitro* models, which restricts the ability to establish definitive causal relationships. It is essential to conduct longitudinal, controlled and multicenter studies to evaluate the long-term effects of ENDS use and to distinguish the specific contributions of nicotine, solvents and other aerosol additives to periodontal pathophysiology.

In summary, vaping represents an emerging source of harmful exposure to the oral cavity, with clinical, biological and public health implications that warrant rigorous attention. Prolonged use can significantly disrupt the defensive, inflammatory and antioxidant mechanisms of the oral mucosa and periodontal tissues. From a dental and public health standpoint, a critical reassessment of the perceived safety of ENDS is necessary. Additionally, it is essential to promote education and preventive strategies, as well as to strengthen scientific research that supports effective interventions aimed at mitigating the impact of these devices on oral and systemic health.

Conflict of Interest Statement
All authors declare that there are no conflicts of interest.

Informed Consent Statement
Informed consent was obtained from the participant involved in this study.

Authors' Contributions
All authors have contributed equally to this work and have reviewed and approved the final manuscript for publication.

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Ethical Statement
Not applicable.

References
1. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: framework and proposal of a new classification and case definition. J Periodontol. 2018;89(S1).
2. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol. 1999;4(1):1-6.
3. Alvear FS, Vélez ME, Botero L. Factores de riesgo para las enfermedades periodontales. 2010;22.
4. Javed F, Abduljabbar T, Vohra F, Malmstrom H, Rahman I, Romanos GE. Comparison of periodontal parameters and self-perceived oral symptoms among cigarette smokers, individuals vaping electronic cigarettes and never-smokers. J Periodontol. 2017;88(10):1059-65.
5. Iacob AM, Escobedo Martínez MF, Barbeito Castro E, Junquera Olay S, Olay García S, Junquera Gutiérrez LM. Effects of vape use on oral health: A review of the literature. Medicina (Mex). 2024;60(3):365.
6. Wasfi RA, Bang F, De Groh M, Champagne A, Han A, Lang JJ, et al. Chronic health effects associated with electronic cigarette use: A systematic review. Front Public Health. 2022;10:959622.
7. Sharma K, Jha RK. Impact of vaping on lungs: An Indian prospect. Cureus. 2023.
8. Dinardo P, Rome ES. Vaping: The new wave of nicotine addiction. Cleve Clin J Med. 2019;86(12):789-98.
9. Zhang Q, Wen C. The risk profile of electronic nicotine delivery systems compared to traditional cigarettes on oral disease: A review. Front Public Health. 2023;11:1146949.
10. Cichońska D, Król O, Słomińska EM, Kochańska B, Świetlik D, Ochocińska J, et al. Influence of electronic cigarettes on antioxidant capacity and nucleotide metabolites in saliva. Toxics. 2021;9(10):263.
11. Abbott AJ, Reibel YG, Arnett MC, Marka N, Drake MA. Oral and systemic health implications of electronic cigarette usage as compared to conventional tobacco cigarettes: a review of the literature.
12. Do HT, Nguyen TT, Vo TL, Huynh NCN, Nguyen ATK. The influence of smoking on oral neutrophils and matrix metalloproteinase-8 in periodontitis patients before and after nonsurgical treatment. J Oral Biol Craniofac Res. 2023;13(3):442-7.
13. Kastratovic N, Milosevic-Djordjevic O, Harrell CR, Djonov V, Volarevic V. Effects of combustible cigarettes and electronic nicotine delivery systems on the regenerative properties of mesenchymal stem cells derived from periodontal ligament. Histol Histopathol. 2024;40(7):1041-9.
14. Xu F, Pushalkar S, Lin Z, Thomas SC, Persaud JK, Sierra MA, et al. Electronic cigarette use enriches periodontal pathogens. Mol Oral Microbiol. 2022;37(2):63-76.
15. Hasan NWM, Baharin B, Mohd N, Rahman MA, Hassan N. Comparative effects of e-cigarette smoking on periodontal status, salivary pH and cotinine levels. BMC Oral Health. 2024;24(1):861.
16. La Rosa GRM, Di Stefano A, Gangi D, Emma R, Fala V, Amaliya A, et al. Dental plaque quantitation by light induced fluorescence technology in exclusive electronic nicotine delivery systems users. J Dent. 2024;147:105223.
17. Thiem DGE, Donkiewicz P, Rejaey R, Wiesmann-Imilowski N, Deschner J, Al-Nawas B, et al. The impact of electronic and

conventional cigarettes on periodontal health: A systematic review and meta-analysis. Clin Oral Investig. 2023;27(9):4911-28.
18. Apatzidou DA. The role of cigarette smoking in periodontal disease and treatment outcomes of dental implant therapy. Periodontol 2000. 2022;90(1):45-61.
19. Birlabose B, Jebaraj J, Kannan A, Shelvan S, Kuduruthullah S, Challagulla A, et al. Effect of nicotine on the thickness of gingiva: A pilot study. J Pharm Bioallied Sci. 2020;12(5):168.
20. Olsson M, Nordendahl E, Klinge B, Ekbom A, Edlund C, Fored M, et al. Does smoking cessation affect postoperative healing following oral surgery among smokers? A systematic review. BMC Oral Health. 2024;24(1):242.
21. Nakayama Y, Mizutani K, Tsumanuma Y, Yoshino H, Aoyama N, Inagaki K, et al. A multicenter prospective cohort study on the effect of smoking cessation on periodontal therapies in Japan. J Oral Sci. 2021;63(1):114-8.
22. Guney Z, Altingoz S, Has H, Serdar MA, Kurgan S. The impact of electronic cigarettes on peri-implant health: a systematic review and meta-analysis. J Dent. 2024;143:104883.
23. AlQahtani MA, Alayad AS, Alshihri A, Correa FOB, Akram Z. Clinical peri-implant parameters and inflammatory cytokine profile among smokers of cigarette, e-cigarette and waterpipe. Clin Implant Dent Relat Res. 2018;20(6):1016-21.
24. Kumar S, Shlossman M. Does e-cigarette use affect response to non-surgical periodontal therapy? Evid Based Dent. 2023;24(4):179-80.
25. Holliday R, Chaffee BW, Jakubovics NS, Kist R, Preshaw PM. Electronic cigarettes and oral health. J Dent Res. 2021;100(9):906-13.
26. Karaaslan F, Dikilitaş A, Yiğit U. The effects of vaping electronic cigarettes on periodontitis. Aust Dent J. 2020;65(2):143-9.
27. AlJasser R, Zahid M, AlSarhan M, AlOtaibi D, AlOraini S. The effect of conventional versus electronic cigarette use on treatment outcomes of peri-implant disease. BMC Oral Health. 2021;21(1):480.
28. Bozyel B, Doğan Ö, Elgün S, Özdemir B. Hypoxic responses in periodontal tissues: Influence of smoking and periodontitis. J Clin Periodontol. 2025;52(2):249-57.