

Heat-not-burn tobacco products and periodontal

health: a review

(IQOS and periodontal health)

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Abstract

Tobacco use remains a leading preventable cause of morbidity and mortality worldwide, with profound effects on periodontal health. Traditional cigarette smoking exacerbates periodontal diseases by promoting inflammation, oxidative stress, and microbial dysbiosis. However, declining cigarette use due to stricter regulations, public health campaigns, and cultural shifts has driven tobacco companies to introduce alternative products, such as heat-not-burn devices. These products heat tobacco without combustion, producing a nicotine-containing aerosol marketed as a reduced-risk alternative to conventional smoking. Despite these claims, the impact of these devices on periodontal health are not well understood.

The current review examines the evidence on the effects of heated tobacco products on periodontal tissues. In vitro studies suggest that their aerosol may impact cell proliferation and the cell cycle. Furthermore, next-generation sequencing of 16S rRNA genes from the subgingival microbiome has shown that heated tobacco products alter the microbial composition, increasing the prevalence of certain key periodontopathogens. Clinical studies indicate that while users of heated tobacco products exhibit periodontal indices that are closer to those of non-smokers than traditional smokers, the nicotine and toxicants in their aerosol still pose risks to periodontal health.

Although heat-not-burn products may represent a less harmful alternative to traditional smoking, they are not without risks. The significant lack of independent, long-term studies complicates efforts to fully assess their safety and potential health impacts. Further research is critically needed to comprehensively evaluate the risks associated with their use.

Keywords: heated tobacco products, IQOS, heat-not-burn, smoking, periodontal health

Introduction

Tobacco use remains a leading preventable cause of morbidity and mortality worldwide, with its detrimental effects extending to numerous organ systems, including the oral cavity. Among these, periodontal health is particularly vulnerable, as tobacco use exacerbates periodontal diseases by promoting inflammation, oxidative stress, and microbial dysbiosis (1–3).

Over the past few decades, traditional cigarette smoking has been steadily declining in popularity due to a combination of factors. Increasingly stringent government regulations, such as public smoking bans and higher taxation on tobacco products, have made smoking less accessible and socially acceptable. Extensive public health campaigns, driven by the World Health Organization (WHO) and other health organizations, have successfully raised awareness of the long-term health risks associated with smoking, including cancer, cardiovascular disease, and respiratory illnesses.

The accumulation of robust longitudinal research has further solidified the connection between cigarette smoking and severe health consequences, leading many individuals to quit or avoid smoking altogether. In addition, cultural shifts and the rise of smoke-free norms have contributed to the growing stigma around traditional tobacco use.

Faced with a shrinking consumer base and mounting pressure from public health advocates, tobacco companies have been forced to adapt in order to remain competitive in the market. This has led to the development and aggressive marketing of alternative products, such as electronic cigarettes, vaping devices, and heat-not-burn (HNB) systems. These innovations are often positioned as "reduced-risk" alternatives to conventional smoking, appealing to both existing smokers seeking less harmful options and a younger demographic drawn to modern, high-tech solutions.

Heat-not-burn products, represent a distinct category of devices that use real tobacco, heated to a lower temperature (~300°-350°C) rather than burned. This process eliminates combustion, which is responsible for producing many of the harmful byproducts found in traditional cigarettes (4). This mechanism generates a nicotine-containing aerosol that aims to mimic the sensory experience of smoking while purportedly reducing harm. Nevertheless, HNB aerosol retains significant levels of toxicants such as nicotine, volatile organic compounds, and tobacco-specific nitrosamines, which may pose risks to periodontal health (5).

These products based on the concept of heating tobacco without combustion or smoke and referred to as "Heat-Not-Burn" tobacco devices, were initially introduced in the late 1980s but failed to achieve commercial success at the time (6). In recent years, however, major tobacco companies have revisited and rebranded these systems, incorporating advanced technology and updated designs. One of the latest examples is the I-Quit-Ordinary-Smoking (IQOS®) device, first launched in Japan and Italy. In 2016, the company sought approval from the U.S. Food and Drug Administration to market IQOS® under the Marlboro® brand as a modified-risk tobacco product (7). However, the IQOS® application, which included claims of reduced risk, was ultimately denied, and the product was allowed on the US market only as a traditional tobacco product (8).

The impact of IQOS® on periodontal structures and health has become a growing focus of scientific research. However, its long-term effects remain poorly understood due to the relatively recent introduction of these products, leaving insufficient time for comprehensive evaluation. This review aims to examine the current evidence on the effects of IQOS® on periodontal health and to offer an idea of the potential risks and implications associated with its use.

Review results

In an *in vitro* study by Pagano et al. (9), the biological effects of IQOS® smoke on human gingival fibroblasts and keratinocytes were explored through assessments of cell viability, morphology, migration, apoptosis, and cell cycle dynamics. Some gene expression levels were also analyzed using RT-PCR. The findings revealed that IQOS aerosol exposure did not significantly affect the survival or morphology of oral fibroblasts and keratinocytes. However, it did influence cell proliferation and the cell cycle, suggesting potential underlying

biological impacts. The study acknowledges limitations, especially the short exposure period (24 hours), which precluded insights into long-term or chronic effects.

Another research group investigated whether IQOS® exposure produces the same harmful effects on human airway epithelial and smooth muscle cells as traditional tobacco cigarettes and e-cigarettes in vitro. Their findings indicated that, similar to cigarette smoke and e-cigarettes, IQOS® has the potential to increase oxidative stress and inflammation, promote infections, contribute to airway remodeling, and trigger epithelial mesenchymal transition-related changes in the airways. However, they emphasized the need for prospective clinical studies to validate their in vitro, cell-based findings (10).

In a systematic review assessing the effects of traditional cigarettes, heat-not-burn tobacco products, and electronic cigarettes on periodontal and peri-implant health, D'Ambrosio et al. (11) highlighted several key findings. They reported a significant lack of clinical data on HNB tobacco systems, while the available data on electronic cigarettes were highly heterogeneous, making it impossible to conduct a meta-analysis. Despite these limitations, the review cautiously suggested that e-cigarettes may result in less severe clinical inflammatory signs of periodontitis - and potentially peri-implantitis - compared to conventional tobacco smoke. The authors emphasized that both electronic cigarettes and HNB tobacco products, as alternative nicotine-containing smoking devices, may negatively affect periodontal and peri-implant health. Furthermore, the researchers underscored the need for deeper investigation into the influence of e-cigarettes and HNB tobacco products on periodontitis progression rates. Such insights, similar to those already established for traditional tobacco use, could help guide the optimal scheduling of active periodontal treatment sessions and the maintenance phase recall intervals.

A research group from Croatia compared the prevalence and abundance of periodontopathogens in classic cigarette smokers, IQOS® consumers, and non-smokers, in relation to clinically diagnosed periodontitis (12). The study found that *E.nodatum* levels were significantly higher in individuals with periodontitis, particularly among IQOS® users, compared to traditional smokers, suggesting that IQOS® aerosol may have a greater impact on the abundance of *E.nodatum* than cigarette smoke, potentially increasing the risk of severe periodontal disease in IQOS® users. *P.gingivalis* and *P.intermedia* were specific for smokers suffering from periodontal disease, regardless of whether the tobacco was heated or burned. The highest levels of *A.actinomycetemcomitans* were observed in non-smokers without periodontal disease, contrary to most published research (13). Conversely, this bacterium was notably deficient in IQOS® users, regardless of their periodontal health status. This discrepancy might indicate an inhibitory effect of IQOS® aerosol on *A.actinomycetemcomitans*, although further studies are needed (12).

While the study did not find statistically significant differences in the overall quantities of subgingival microbiomes among the groups, smoking, including IQOS® use, appeared to favor the colonization of periodontal pathogens. IQOS® aerosol was associated with increased prevalence and abundance of key pathogens such as *P.gingivalis*, *F.nucleatum*, and *P.intermedia*, reinforcing its detrimental effects on periodontal health.

The same research group investigated the association between HNB consumption and periodontal parameters, focusing on differences compared to conventional cigarette smokers and non-smokers (14). The study demonstrated that IQOS® aerosol negatively affects periodontal tissues, though to a lesser extent than smoke from traditional cigarettes. The authors highlighted that one contributing factor to these differences was the shorter overall smoking experience of IQOS® users compared to cigarette smokers, which may have resulted in better periodontal health.

In terms of periodontal indices, IQOS® users were more similar to non-smokers than to traditional smokers. However, the nicotine-containing aerosol from heat-not-burn products is not entirely harmless to periodontal health. The longer smoking history in the cigarette group was again emphasized as a contributor to the more

severe periodontal damage observed, as the harmful effects of tobacco use are both time- and dose-dependent.

In the cited study, cigarette smokers had the highest values for probing depth (PD), gingival recession, plaque and bleeding scores, and clinical attachment loss (CAL), while tooth loss was comparable between the cigarette and IQOS® groups. Among these, PD and CAL exhibited statistically significant differences, indicating active periodontal disease in cigarette smokers. The frequency of gingival bleeding (FMBS) was highest in cigarette smokers and lowest in IQOS® users, despite the differences in smoking duration.

In 2020, the World Health Organization released an information sheet highlighting key concerns about heated tobacco products (15). It emphasized that HTPs contain tobacco and are classified as tobacco products, do not assist in quitting smoking, and emit toxic substances similar to those in cigarette smoke, many of which are carcinogenic. It is emphasized that HTPs expose users and bystanders to toxic emissions, including unique harmful substances not found in conventional tobacco smoke and while they may have lower levels of certain toxicants compared to traditional cigarettes, some are present at higher levels, and new substances may pose additional health risks. HTPs deliver nicotine, which is highly addictive and harmful, especially for children and adolescents.

Conclusion

Despite the growing popularity of heat-not-burn tobacco products, there is a significant lack of studies specifically investigating their effects on periodontal health. Moreover, much of the existing research has been conducted or funded by Philip Morris International (PMI), the manufacturer of IQOS®, raising concerns about potential conflicts of interest. Industry-sponsored studies may prioritize favorable outcomes while underreporting or overlooking potential adverse effects. To ensure the credibility of this review, studies funded by PMI or conducted by its employees have been intentionally excluded.

The long-term health impacts of HTP use and exposure remain largely unknown. Independent, comprehensive research is urgently needed to fully assess the risks associated with these products and their implications for periodontal health.

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Maynalovska Hr, Pashova-Tasseva Zdr, Kotsilkov K, Heat-not-burn tobacco products and periodontal health: a review(IQOS and periodontal health), *Medinform* 2025; 12(1):1964-1968.