**Journal of Medical and oral biosciences**
**ISSN (Online): 3007-9551**
**ISSN (Print): 3007-9543**

**JMOB**
**Open Access DOAJ**

IRAQI Academic Scientific Journals

**Type: Review article**
**Publish online: 30/ 05 /2026**

# The Impact of Heat-not-Burn Tobacco Products on Periodontal Diseases: A Review

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**OPEN ACCESS**

**ARTICLE INFO**
Received: 29 /04/2026
Revised: 19/ 05/ 2026
Accepted: 25 / 05 / 2026
Publish online: 30 / 05 / 2026
Plagiarism percentage at publication: 13 %

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**CITATION**

Zainab Ahmed Mahmoud, Ghasaq Asim Abdul-Wahab. (2026). The Impact of Heat-not-Burn Tobacco Products on Periodontal Diseases. JMOB. 3; (2):150-165.
https://doi.org/10.58564/jmob.179



## Abstract

***Periodontitis is a complex chronic multifactorial*** inflammatory disease, and among the various risk factors, the one of the most important modifiable risk factors is smoking. Smoking is a significant public health problem because it affects not only the mouth, but also the immune system, and increases the risk of cancer, respiratory diseases and cardiovascular diseases. Smokers have higher risk of developing periodontal disease at about five to six times compared with non-smokers. Heat-not-burn tobacco products do not burn directly but produce an aerosol, marketed as a potentially reduced-risk alternative to conventional cigarettes. However, their impact on periodontal health remains to be determined. This literature review aims to underscore the potential role of heat-not-burn tobacco products on the periodontium, with particular focus on oxidative stress and antioxidant homeostasis. Current evidence indicates that heat-not-burn products may still be harmful to periodontal tissues, although some studies report that they may be less harmful than conventional cigarettes. These effects may include changes in the inflammatory response, oral microbiome, and oxidative stress/antioxidant balance, which may contribute to the progression of periodontitis. Therefore, more longitudinal clinical studies are required to elucidate the long-term effects of heat-not-burn tobacco products on periodontal health.

**Keywords:** Periodontitis, Smoking, Heat-not-Burn tobacco products, Oxidative stress, Public health.

## Introduction

Periodontal diseases PDs include a broad variety of inflammatory conditions which affect the supporting structures of the teeth including (the gingiva, bone and periodontal ligament), and can lead to tooth loss and also systemic inflammation (4), the mildest type of periodontal disease, gingivitis, its induced by the bacterial biofilm (dental plaque) accumulation on teeth near the gingiva. Nevertheless, gingivitis is a reversible condition that has no effect on the underlying supporting structures of the teeth. Gingivitis is regarded as the preliminary condition to periodontitis (5). Periodontitis is a chronic inflammatory condition affects the supporting periodontal tissues, resulting in loss of periodontal attachment and resorption of alveolar bone, which if left untreated can lead

to tooth loss (6). Periodontal disease, especially periodontitis, is a chronic inflammatory disease characterized by a progressive destruction of the periodontal supporting tissue including connective tissue attachment and alveolar bone. The disease develops as a dynamic interaction between pathogenic microbial biofilms and the host immune response, whereas genetic and environmental factors influence individual susceptibility and disease progression. Periodontitis remains a major public health problem and one of the leading causes of tooth loss in adulthood due to its high worldwide prevalence and significant implications for oral health.(6, 7). The pathogenesis of periodontal disease is closely related to the changes of the composition of the oral microbiota, a phenomenon called microbial dysbiosis. The imbalance favors the proliferation of pathogenic microorganisms such as Porphyromonas gingivalis, Tannerella forsythia, Fusobacterium nucleatum and Aggregatibacter actinomycetemcomitans. The pathogens interact with host immune cells and trigger inflammatory responses that are protective initially but can be destructive if they are excessive or prolonged. Therefore, persistent inflammation causes connective tissue destruction and alveolar bone loss. Other factors that affect disease susceptibility and severity are aging, local oral conditions, lifestyle habits (smoking), stress, dietary patterns, systemic diseases (especially diabetes mellitus), and genetic predisposition (8) . Among the environmental factors associated with periodontal disease, tobacco smoking is recognized as one of the most important and well-established risk factors. Smokers have a significantly higher risk of developing destructive periodontal disease compared to non-smokers, with studies reporting a five to six fold increase in disease risk (9). The oral cavity is the first site of contact with tobacco smoke and its various chemical components. Many smoke-derived compounds are absorbed through contact with saliva and through the oral epithelium where they interact directly with oral tissues. Cigarette smoke contains thousands of chemicals. Many of these chemicals are poisonous and can damage cells. Oxidative stress is mainly induced by oxidizing agents, such as superoxide radicals, hydrogen peroxide, and nitrogen oxides, which also activate inflammatory pathways and participate in the destruction of periodontal tissue. (10, 11). In recent years, the tobacco industry has introduced a number of alternative nicotine delivery systems, bringing about significant changes in the global tobacco market. These innovations include heat-not-burn (HnB) tobacco products, which were cleared by the U.S. Food and Drug Administration (FDA) for commercial distribution. severalgulatory approval is not to be confused with safety confirmation, and the absence of health risks associated with their use (12). Heat-not-burn tobacco products produce an inhalable aerosol by heating processed tobacco to relatively low temperatures—typically in the range of 250°C to 350°C—rather than burning it. This method minimizes the production of a number of toxicants associated with combustion, such as tar and other toxic chemicals normally found in regular cigarette smoke. Further, the lack of side stream smoke may decrease passive exposure in the environment surrounding the product. These products are similar in appearance and pattern of use to conventional cigarettes (13) and are therefore popular among smokers who are looking for an alternative to combustible tobacco products. Consumer acceptance of heat-not-burn tobacco products is growing, but their impact on periodontal tissues remains unclear. Although several studies suggest reduced exposure to selected toxic compounds compared with conventional cigarettes, evidence regarding the long-term effect on periodontal health is still limited. Thus, further clinical and experimental studies are necessary to clarify their potential role in the pathogenesis and progression of periodontal

disease (14). This review aims to critically analyze the published studies on the effect of heat-not-burn tobacco products on the periodontium. The review will synthesize the available evidence to provide a comprehensive understanding of their effects on periodontal health and discuss potential implications and associated risks.

## Methodology

The literature review conducted by an electronic search of significant scientific databases, Scopus, Google Scholar, PubMed and ResearchGate. The initial assessment included 69 articles published between 2015 and 2026 based on the keywords smoking, heat-not-burn, periodontitis, and oxidative stress.

## Inclusion Criteria

This review used recent published in English articles, reviews, case-control studies, cross sectional, randomized control trial, in-vitro and animals studies.

## Exclusion Criteria

Studies published before 2015, Old articles, and Philip Morris International (PMI) funded studies were excluded (Figure.1).

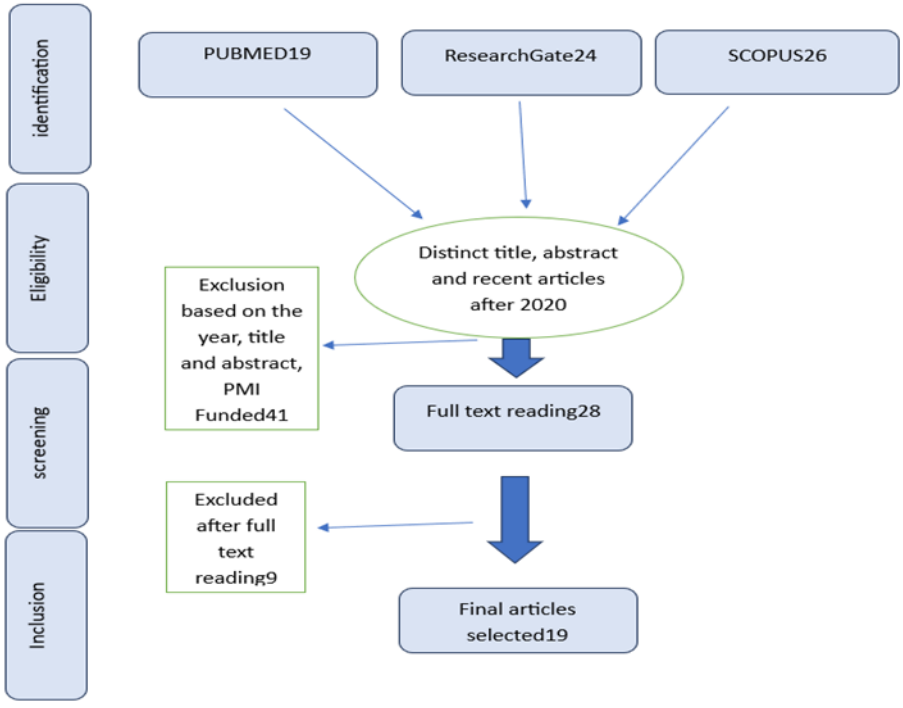


**Figure. 1:** Flowchart of Research and Selection Process

## Pathogenesis of Periodontal Diseases

Periodontal health is defined by the lack of clinically detectable inflammation and the establishment of a stable balance between the host immune system and the resident oral microbiota. Under health conditions, mechanisms of immune surveillance regulate microbial communities and preserve the structural integrity of periodontal tissues, while maintaining tissue homeostasis (15). Periodontal disease development is a multifactorial process involving a complex interplay between pathogenic microorganisms, host immune responses, genetic susceptibility and environmental influences. Periodontitis is not merely a consequence of bacterial accumulation but rather a dysregulated host response to a dysbiotic microbial community in the dental biofilm (7, 16). Microbial dysbiosis is a qualitative and quantitative imbalance in the oral microbiota composition, which favors the overgrowth of pathogenic species. These microbes and their virulence factors stimulate epithelial and immune cells to begin inflammatory responses that are meant to control microbial challenge. However, persistence of bacterial stimulation can lead to exaggerated and prolonged inflammation, resulting in collateral tissue damage (16). The gingival epithelium represents the first line of defense against microbial invasion, acting as a physical barrier and as an active player in immune regulation. Langerhans cells are antigen-presenting cells that capture microbial antigens and interact with lymphocytes to initiate adaptive immune responses. At the same time, neutrophils migrate continuously into the gingival sulcus to limit bacterial proliferation. These defense mechanisms are vital for the maintenance of periodontal health, but an extended microbial challenge can overcome host protective responses and promote inflammation(4). Chronic inflammatory activity is associated with the release of cytokines, reactive oxygen species and matrix metalloproteinases (MMPs) which contribute to degradation of connective tissue components and destruction of periodontal ligament fibers. Furthermore, inflammatory mediators stimulate osteoclast differentiation and activation, leading to progressive alveolar bone loss. The net effect of these processes is periodontal pocket formation, clinical attachment loss and eventual destruction of the tissues supporting the tooth (4). The “red complex,” which is strongly associated with advanced periodontitis, comprises Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia. These bacterial species have virulence factors that allow them to invade tissue and evade the immune system while maintaining an inflammatory response, making them important contributors to the progression of periodontal disease (17).

## Smoking

Smoking is a well-known and important modifiable risk factor for oral diseases, especially periodontitis and oral cancer. Epidemiological evidence indicates that tobacco users have a significantly higher risk of developing destructive periodontal disease, estimated to be five to six times greater than that of non-smokers (9). There is a large body of evidence linking smoking to chronic inflammation. Cigarette smoke contains a number of oxidizing compounds including superoxide radicals, hydrogen peroxide and nitrogen oxides which promote oxidative stress and contribute to the initiation and maintenance of inflammatory responses within periodontal tissues(11) After inhalation, components of the smoke are taken up by the alveolar epithelium and are transported to

the tissues of the body by the systemic circulation. Cigarette smoke in direct contact with periodontal tissues also leads to vasoconstriction of the gingival microvasculature and fibrotic changes in the gingiva. Therefore, smokers often have decreased clinical signs of gingival inflammation in the presence of increased plaque accumulation and accelerated periodontal destruction. This masking effect can mask the presence of underlying gingivitis and complicate clinical assessment (18). Recent clinical findings also have demonstrated that people who smoke conventional cigarettes or use heat-not-burn tobacco products have worse periodontal health than people who do not smoke. Increased probing pocket depth, gingival bleeding, plaque accumulation and clinical attachment loss were observed in both groups. Although the periodontal parameters are less severe in heat-not-burn users than in conventional cigarette smokers, these products seem to adversely affect the periodontal tissues and cannot be considered biologically safe (19).

## Heat-not-Burn Tobacco Products

Heat-not-burn tobacco products (HTPs) (also called heated tobacco products) are electronic nicotine delivery devices that produce an inhalable aerosol by heating, not burning, processed tobacco. Conventional cigarettes work by burning tobacco. HTPs work at lower temperatures, generally less than 350°C , and thus produce fewer combustion - derived toxicants . Commercial devices generally comprise a rechargeable power source, a heating element and specially designed tobacco sticks, capsules or plugs containing reconstituted tobacco. Depending on the device design, the tobacco is heated either internally by a blade type heating element or externally by a heated chamber (20, 21) (Figure 2). The resulting aerosol delivers nicotine and tobacco flavor, without combustion. The growing popularity of HTPs is due in large part to claims that these products deliver lower levels of harmful chemicals to users than do traditional cigarettes. In July 2020, the U.S. Food and Drug Administration authorized the THS system and its corresponding tobacco sticks as a Modified Risk Tobacco Product (MRTP) based on evidence that complete switching from combustible cigarettes to the THS product could reduce exposure to certain harmful substances. However, this authorization is not a statement that the product is safe or is without health risks. The health effects of HTPs remain an area of great scientific interest. Manufacturers usually market these products as a lower-risk alternative to traditional smoking, but independent evidence of their long-term biological effects is limited. More research is needed to confirm if lower exposure to toxicants results in significant reductions in disease risk and adverse health outcomes.(19) . There is still comparatively little known regarding the association between periodontal diseases and HTP use. The lack of available studies and the recent advent of these products make it difficult to draw definite conclusions regarding their effects on the gingival and periodontal tissues. Thus, more clinical and epidemiological studies are required to clarify their role in oral health (19). HTP aerosols have considerably lower levels of several harmful constituents than conventional cigarette smoke because tobacco is heated, not burned. Heating temperatures of approximately 350°C are considerably lower than the temperatures attained in the combustion of cigarettes which can often exceed 600°C. This reduction in thermal degradation reduces the formation of many toxic compounds, which has contributed to the rapid growth of HTPs in the global tobacco market. However, tobacco is still the main ingredient for these

products, and the generation of aerosols still requires complex chemical reactions that can lead to biologically active substances (22). Studies comparing HTP emissions to conventional cigarette emissions have consistently shown quantitative differences in aerosol composition. While exposure to many toxic compounds is reduced, nicotine delivery is similar to that of combustible cigarettes. HTP aerosols are said to contain approximately 50% less tar and up to 99% less carbon monoxide than cigarette smoke. However, these reductions do not eliminate the potentially harmful chemicals completely, highlighting the need for further investigation of their long-term health effects (23-25).

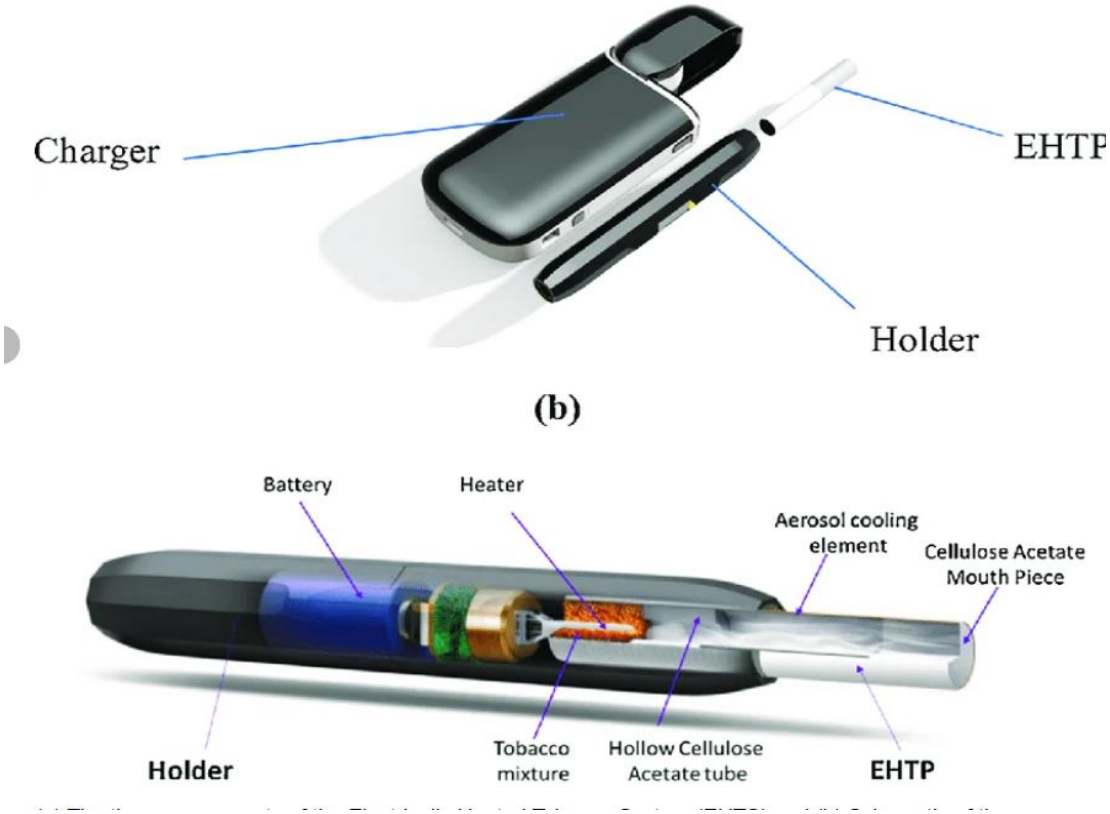


**Figure.2:** Components of Electrically heated tobacco products (EHTP) (1)

## Smoking and Periodontal Diseases

The association between periodontitis and smoking has been well established for several decades. Numerous studies have consistently demonstrated that cigarette smoke has a harmful impact on periodontal tissues with odds ratio 85% of periodontal disease (26) the actual mechanisms by which smoking are less well identified, an explain its effects on the periodontal tissues locally by its effect on all components of the inflammatory response and on the innate and adaptive immune responses, (27). Because of its well-known negative impact on the development, progression and therapeutic outcome of periodontal disease it is a grade modifier in the 2017 classification system for periodontitis (28).

## Heat-not-Burn tobacco Products and Periodontal Diseases

Several studies evaluated the effect of Heat-not-Burn tobacco products HnBtp on general health and others on periodontium. Some studies have demonstrated the adverse effect of this type of cigarettes on general health and environment, according to study by Auer et al. reveals that smoke produced by HnB products contains substances from pyrolysis and thermogenic degradation that are the same harmful components of conventional tobacco cigarette smoke(29). In contrast to the company's claims, the presence of polycyclic aromatic hydrocarbons PAHs in Heat-not-Burn tobacco products aerosol can be a sign of burning tobacco. However, it is also toxic chemicals are still present in HnB tobacco products smoke, and the product could lead to people taking up smoking cigarettes and current evidence remain insufficient for definitive safety conclusion (30, 31). With regard to periodontal health ,available evidence suggest that HnB products may be less harmful than Conventional cigarette, And the authors reveal by using measurable periodontal indices (PPD and CAL) the Exposure to nicotine-containing aerosol of HnB products in adults has a less harmful effect on periodontal tissues (26). A study assessing a wide range of immune markers in unstimulated saliva of smokers provided insight into the early immunological changes associated with tobacco use in young and otherwise healthy individuals. The results suggest that regular cigarette smoking and heat-not-burn tobacco products have the ability to alter local immune responses in saliva, indicating the onset of immune dysregulation. These findings run counter to the widespread belief that heat-not-burn products are significantly safer than traditional cigarettes and suggest that their use might also negatively impact oral immune homeostasis (32). Experimental data of the biological effects of heated tobacco products are limited but suggest that their impact might be different from that of conventional cigarette smoke. Pagano et al. [19] observed that in vitro exposure of oral keratinocytes to IQOS aerosol was associated with increased cellular proliferation, migration and viability of oral keratinocytes without significant morphological damage or apoptosis. Similarly, oral fibroblasts and keratinocytes demonstrated normal survival characteristics after exposure. Although these results suggest lower cytotoxicity compared with conventional cigarette smoke, the observed changes in cell-cycle regulation and proliferative activity suggest that heated tobacco aerosols may still affect cellular behavior, which warrants further investigation into the responsible aerosol constituents (10). Although promoted as a lower-risk alternative to cigarettes, heat-not-burn tobacco products still exert deleterious biological effects. Laboratory and experimental studies have demonstrated that exposure to heated tobacco aerosols may have adverse effects on periodontal and peri-implant tissues, through mechanisms such as cellular toxicity, impaired tissue repair and altered healing process. However, the interpretation of current results is limited by the relatively small number of available studies and the methodological heterogeneity among investigations, which has hindered a quantitative synthesis in previous systematic reviews (33, 34). Recent epidemiological evidence has raised additional concerns about the periodontal consequences of heated tobacco use. A longitudinal analysis of the data from the Japan COVID-19 and Society Internet Survey showed that those who switched from exclusive use of conventional cigarettes to concurrent use of conventional cigarettes and heated tobacco products were at increased risk of severe periodontitis. These results suggest that the concurrent use of both products

does not confer any significant advantage in reducing periodontal harm and should not be considered as a viable strategy for preventing progression of periodontal disease (35).

## Oxidative Stress / Antioxidants Homeostasis

An imbalance between excessive oxidant radicals and low antioxidant defense mechanisms within an organism is called Oxidative stress OS (36).
Reactive oxygen species (ROS) include oxygen-centered free radicals and non-radical oxygen-containing molecules. The free radical group includes species like superoxide anion ($O_2^{\bullet -}$), hydroxyl radical (•OH) and nitric oxide (NO•), while non-radical ROS include hydrogen peroxide ($H_2O_2$) and hypochlorous acid (HOCl). The hydroxyl radical is one of the most damaging and reactive oxidants among these molecules because of the unpaired electrons in its outer orbital structure, allowing it to interact and damage cellular macromolecules with ease (37). Reactive oxygen species (ROS) play a role in several biological processes under physiological conditions, such as antimicrobial activity, regulation of immune responses and intracellular signaling pathways in periodontal tissues. Excessive production of ROS by chronic pathogenic stimulation or dysregulated immune responses may overwhelm antioxidant capacity, even though ROS are essential for maintaining tissue homeostasis. Oxidative stress can lead to structural and functional damage of DNA, proteins, and lipid membranes, which can promote periodontal tissue injury and disease progression(38) (Figure 3).

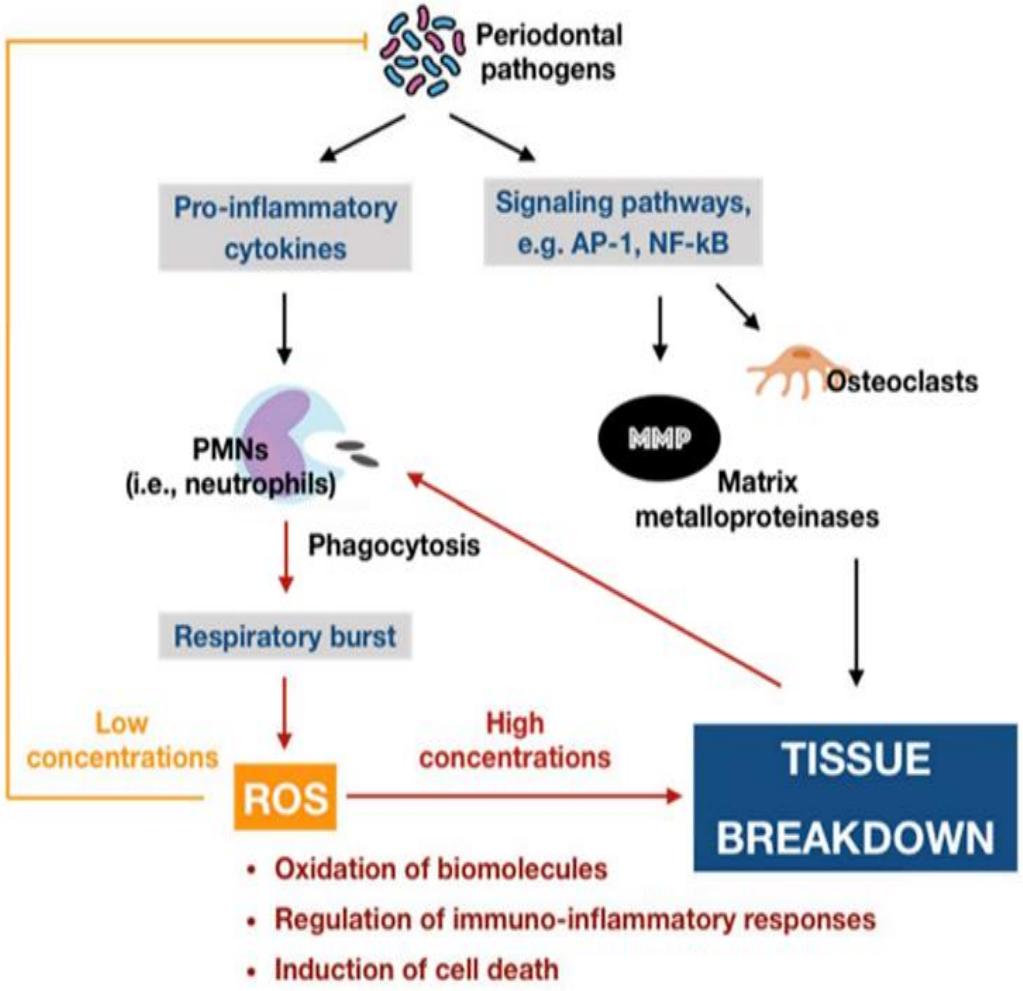


**Figure 3:** Diagram illustrate the double-edged effects of ROS in periodontal disease(2)

Antioxidants are protective molecules that neutralize reactive oxidant species and limit oxidation reactions to combat oxidative damage. They can effectively inhibit or delay oxidation processes even in relatively small quantities, thereby helping preserve cellular integrity and maintain redox balance(39). In healthy physiological conditions, the periodontium exhibits a redox homeostasis, where low concentrations of reactive oxygen species (ROS) are continuously detoxified by the endogenous antioxidant defense mechanisms, preventing oxidative damage of the periodontal tissues. However, periodontal inflammation induces the activation of innate immune cells including neutrophils and macrophages, leading to the overproduction of ROS due to the respiratory burst associated with phagocytic activity. This overproduction of redox species perturbs redox homeostasis and overwhelms the antioxidant defense system. As a result, the accumulation of ROS exceeds the antioxidant capacity of the tissue, leading to oxidative stress and consequently cellular and tissue damage (3). Oxidative stress plays an important role in the injury of periodontal tissues. High levels of reactive oxygen species may directly degrade components of the extracellular matrix such as collagen, elastin, proteoglycans and hyaluronic acid. Moreover, oxidative stress promotes inflammatory responses through an enhanced generation of cytokines, such as IL-6, IL-8, TNF-α, and

NF-κB signaling activation. The increase in the activity of NADPH oxidase (NOX) leads to increased generation of free radicals, while the release of lysosomal enzymes promotes local tissue destruction, which together accelerate the progression of periodontitis(3, 40-43) (Figure 4).

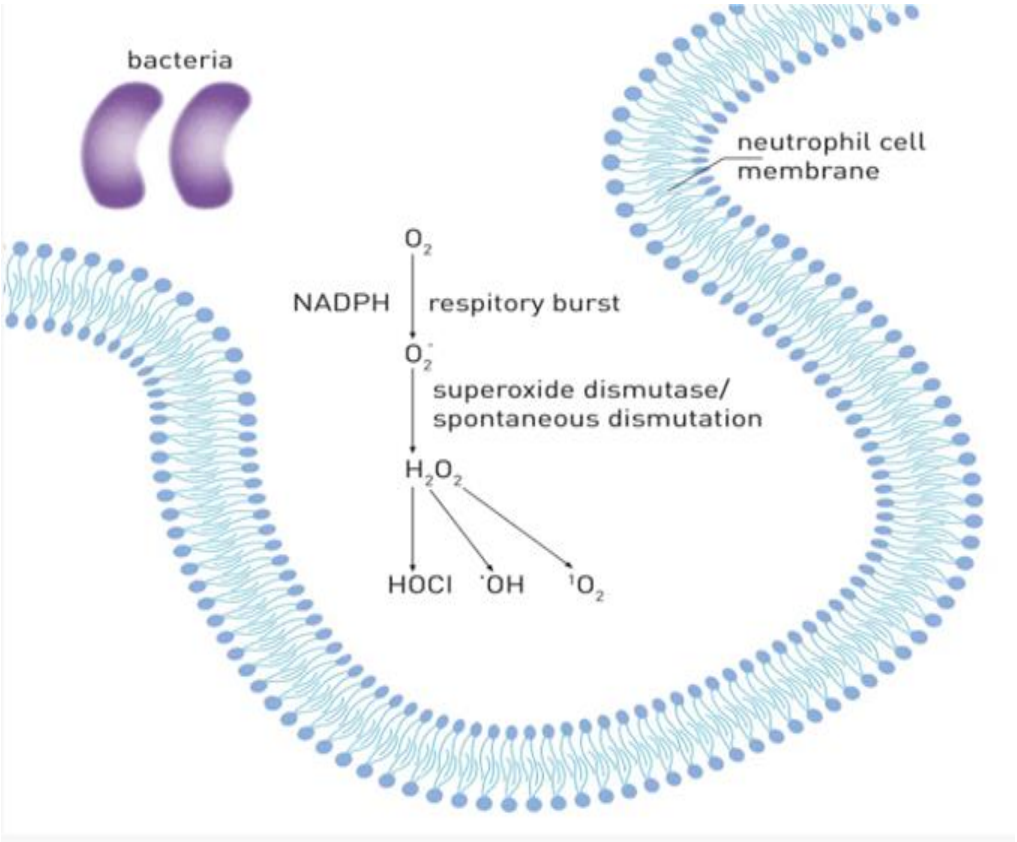


**Figure. 4 :** Production of ROS in periodontal disease(3)

Tobacco smoke is comprised of a complex mixture of chemicals, including ROS with extended half-life which can directly affect macromolecules such as lipids, proteins and nucleic acids, causing harm(36) Periodontal tissue can also be indirectly damaged by changes in intracellular signaling pathways and transcription factors that control inflammatory and immune responses.(38),which lead to generation of more ROS. As a result, oxidative stress biomarkers may help as early indicators of exposure-related biological effects(36). Smoking decreases the activity and expression of antioxidants, thus impairing the antioxidant defense system. (Figure 5). This diminishes the ability of periodontal tissues to combat reactive oxygen species, resulting in oxidative and nitrosative damage to cellular macromolecules and contributing to the destruction of periodontal tissue (40, 44). Several studies have described that exposure to heated tobacco products (HTPs) induces oxidative stress and cellular alterations similar to those observed after exposure to conventional cigarette smoke, suggesting the involvement of similar pathogenic mechanisms (21, 45). The level of oxidative damage associated with HTPs,

however, appears to be considerably lower than that associated with conventional cigarettes. Experimental studies have demonstrated that the adverse effects of HTP aerosols are typically only observed at very high concentrations, above physiological exposures, suggesting a potentially reduced toxicological impact under normal use patterns (24). The transition from conventional cigarettes to heat-not-burn tobacco products has been linked to significant reductions in exposure to formaldehyde, acetaldehyde, and reactive oxygen species (ROS). Nevertheless, experimental data from animal models show that aerosol constituents produced by these devices can still trigger pro-inflammatory responses (46).

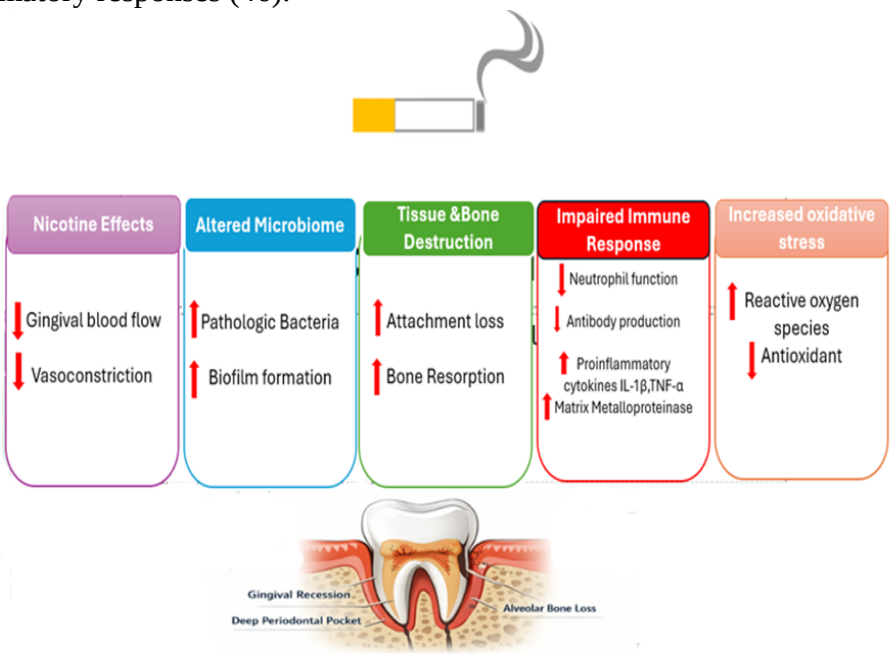


**Figure. 1:** Effect of smoking on periodontium and oxidative stress/antioxidant homeostasis periodontium compiled from finding reported in previous studies (44, 47-49)

## Conclusion

Heat-not-Burn tobacco products or Heated tobacco products are becoming very prevalent among the population, especially as many people think they have less detrimental effect than traditional classical tobacco cigarettes. Heat-not-burn (HnB) tobacco products are gaining popularity and becoming more widely used. However, data on the effects of HnB tobacco products on periodontal health are limited. Furthermore, many of the existing studies have been funded, sponsored or conducted by Philip Morris International (PMI), the manufacturer of IQOS®, which raises concerns about potential conflicts of interest and the possibility of biased findings. For the purpose of ensuring objectivity and credibility of the present review, literature selected did not include studies funded by PMI or with PMI-affiliated researchers. Despite that HnB products are often perceived as a safer alternative to conventional cigarettes, some studies find that they still have detrimental effects on health and periodontium and current evidence remains insufficient for ultimate safety conclusion. The inconsistencies among studies due to differences in study design, duration of exposure and sample characteristics make

comprehensive research necessary to completely evaluate the hazards associated with exposure to these products and their effects for periodontal\ health because the long-term health influences of HnB tobacco products usage remain largely unknown.

## Declarations

**Acknowledgment**
None

**Ethics statement**
The author confirms that this research follows the journal's attached Ethics Approval guidelines, as appearing on the journal's author guidelines page.

**Funding**
None

**Competing interest's statement**
The authors declare no conflicts of interest.

**Author contributions**
**ZAM** designed the conception of the study, methodology, manuscript writing, coordinated the research activities, and handled the submission and revision process; **GAA** contributed to the literature search, data collection and interpretation, critical review of the manuscript, editing of the content, and approval of the final version for publication.

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