World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Impact of Cigarette Smoking on Salivary Proteomic Alterations: A Comprehensive Literature Review

Aprilia Rahma Shafiya * and Dimas Bagus Rahmawan

Undergraduate Program, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.

World Journal of Advanced Research and Reviews, 2025, 28(03), 1723-1727

Publication history: Received 17 November 2025; revised on 23 December 2025; accepted on 25 December 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.28.3.4256

Abstract

Background: Cigarette smoking is a major risk factor for various oral diseases and is known to alter the biological environment of the oral cavity. Saliva plays an essential role in maintaining oral homeostasis, and changes in its protein composition may reflect early molecular disturbances caused by tobacco exposure. Alterations in salivary proteins may contribute to impaired oral defense mechanisms and increased susceptibility to smoking-related oral diseases.

Purpose: This literature review aims to evaluate the effects of cigarette smoking on the salivary proteome and to summarize the major categories of salivary protein alterations associated with smoking.

Methods: Relevant studies published between 2019 and 2024 were obtained from major electronic databases and analyzed narratively to identify salivary proteomic changes associated with smoking.

Result: The reviewed studies consistently demonstrated that cigarette smoking induces significant alterations in salivary proteins related to immune defense, oxidative stress regulation, inflammatory response, protease inhibition, and epithelial stress. Reduced levels of protective immune proteins and protease inhibitors, along with increased oxidative stress markers and inflammatory mediators, were commonly reported in smokers.

Conclusion: Cigarette smoking disrupts the salivary proteome and may contribute to increased susceptibility to smoking-related oral diseases. Salivary proteomic analysis has potential as a non-invasive approach for understanding the biological impact of smoking on oral health.

Keywords: Saliva; Proteomics; Smoking; Oxidative Stress; Biomarkers; Oral Health

1. Introduction

Cigarette smoking remains one of the most prevalent and preventable risk factors associated with a wide range of systemic and oral diseases. Tobacco use continues to contribute significantly to global morbidity and mortality, not only through respiratory and cardiovascular disorders but also through its adverse effects on oral health [1]. In the oral cavity, smoking has been strongly associated with periodontal disease, delayed wound healing, oral mucosal lesions, and an increased risk of oral potentially malignant disorders and oral squamous cell carcinoma [2].

Saliva plays a crucial role in maintaining oral homeostasis and serves as the first biological fluid exposed to cigarette smoke. It functions as a protective medium by providing lubrication, buffering capacity, antimicrobial activity, and facilitation of tissue repair. Saliva contains a wide range of proteins, enzymes, immunoglobulins, and glycoproteins that

* Corresponding author: Aprilia Rahma Shafiya

are essential for preserving oral tissue integrity and regulating the oral microbiome [3]. Any disruption in salivary composition may compromise these protective functions and increase susceptibility to oral disease.

Cigarette smoke contains thousands of chemical compounds, including nicotine, aldehydes, heavy metals, and reactive oxygen species, which directly interact with salivary components and oral epithelial cells. Chronic exposure to these toxic substances induces oxidative stress and inflammatory responses within the oral environment, leading to cellular damage and altered salivary gland function [4]. These mechanisms are believed to underlie the observed changes in salivary protein expression among smokers.

Advances in proteomic technologies over the past decade have enabled comprehensive profiling of salivary proteins. Techniques such as liquid chromatography–mass spectrometry, Fourier-transform infrared spectroscopy, and gel-based proteomics have allowed for the identification of subtle molecular alterations in saliva associated with pathological conditions [5]. Salivary proteomics has emerged as a promising approach for biomarker discovery due to its non-invasive nature, ease of collection, and ability to reflect both local and systemic physiological changes [6].

Several recent studies have demonstrated that smoking is associated with significant alterations in multiple categories of salivary proteins, including immune-related proteins, antioxidant enzymes, mucins, protease inhibitors, inflammatory mediators, and stress-response proteins [7]. These proteomic changes are thought to result from complex biological mechanisms involving oxidative damage, chronic inflammation, protein denaturation, and impaired secretory activity of salivary glands. However, reported findings vary between studies due to differences in analytical methods, smoking intensity, duration of exposure, and population characteristics.

Given these variations, a literature review is essential to synthesize existing evidence and identify consistent proteomic patterns associated with cigarette smoking. Such synthesis is crucial for identifying potential salivary biomarkers that may be useful for early detection, risk assessment, and monitoring of smoking-related oral diseases.

Therefore, this literature review aims to comprehensively analyze studies published between 2019 and 2024 that investigate the effects of cigarette smoking on the salivary proteome. The review focuses on identifying major categories of proteins affected by smoking, elucidating the underlying biological mechanisms of protein damage and dysregulation, and discussing the potential clinical implications of these findings.

2. Materials and methods

This study employed a literature review approach to synthesize recent evidence regarding the effects of cigarette smoking on salivary proteomic alterations. Scientific articles were retrieved from PubMed, Scopus, ScienceDirect, and Google Scholar, focusing on publications between 2019 and 2024. The search utilized keywords including “salivary proteome,” “salivary proteins,” “cigarette smoking,” “tobacco exposure,” and “salivary biomarkers.”

Articles were included if they were original human studies that evaluated salivary proteins or proteomic profiles and compared smokers with non-smokers or different levels of tobacco exposure. Animal studies, review articles, in vitro studies without salivary analysis, case reports, conference abstracts, and studies published before 2019 were excluded. Duplicate records were removed, and full-text screening was conducted to ensure relevance.

Data extracted from eligible studies included author, year, study design, sample characteristics, analytical methods, and key findings related to salivary protein alterations. The findings were analyzed descriptively and synthesized narratively to integrate heterogeneous study designs and proteomic methodologies commonly used in oral health research.

3. Results

Table 1 Summary of studies on salivary proteomic alterations associated with cigarette smoking

No	Title	Method	Results
1	Lee et al. (2020). Alterations in salivary immunoglobulin levels among cigarette smokers.	Cross-sectional study comparing salivary immunoglobulin profiles between smokers and non-smokers using immunoassay techniques.	Smokers showed significantly reduced salivary secretory IgA levels, indicating impaired mucosal immunity.

2	Baalbaki et al. (2021). Oxidative stress biomarkers in saliva of smokers and non-smokers.	Comparative study evaluating salivary oxidative stress markers and antioxidant enzyme activity.	Smokers exhibited increased oxidative stress biomarkers and reduced antioxidant capacity in saliva.
3	Rodrigues et al. (2020). Effect of smoking cessation on salivary compounds assessed by FTIR spectroscopy.	Observational study analyzing salivary protein and glycoprotein profiles using FTIR spectroscopy.	Smoking altered salivary protein and glycoprotein composition, which partially improved after smoking cessation.
4	Al-Maweri et al. (2022). The impact of cigarette smoking on salivary biomarkers: a case–control study.	Case–control study assessing various salivary biomarkers in smokers and non-smokers.	Salivary cystatin levels were significantly lower in smokers, suggesting reduced protease inhibition.
5	Sapkota et al. (2023). Proteomic profiling of saliva in cigarette smokers compared with non-smokers.	Proteomic analysis using LC–MS/MS to compare salivary protein expression profiles.	Upregulation of oxidative stress and stress-response proteins was observed in smokers.
6	Sharma et al. (2023). Salivary inflammatory biomarkers in cigarette and e-cigarette users.	Comparative analysis of inflammatory cytokines in saliva using ELISA.	Cigarette smokers showed higher levels of IL-6 and IL-8 compared to non-smokers and e-cigarette users.
7	Yap et al. (2021). Matrix metalloproteinase activity in the saliva of smokers and its association with periodontal destruction.	Cross-sectional study measuring salivary MMP activity.	Increased MMP-8 and MMP-9 activity was associated with tissue degradation in smokers.
8	Chen et al. (2022). Salivary proteomic biomarkers associated with oral epithelial dysplasia in smokers.	Proteomic analysis of saliva samples from smokers with epithelial dysplasia.	Elevated expression of stress-related proteins such as HSP70 and S100 was detected.
9	Rai et al. (2024). Comparative salivary proteomic analysis in cigarette smokers, e-cigarette users, and non-smokers.	Comparative proteomic study using mass spectrometry.	Distinct salivary proteomic signatures were identified according to type of tobacco exposure.
10	Zięba et al. (2024). Oxidative stress and protein oxidation in saliva of long-term smokers.	Cross-sectional study evaluating protein oxidation and antioxidant status in saliva.	Long-term smokers demonstrated increased protein oxidation and reduced antioxidant defenses.
11	Abbas et al. (2021). Salivary cytokine alterations in cigarette smokers: association with chronic inflammation.	Observational study assessing salivary cytokine levels.	Elevated TNF-α and IL-6 levels indicated chronic inflammatory conditions in smokers.
12	Omar et al. (2023). Salivary proteomic changes associated with smoking-related oral mucosal lesions.	Proteomic profiling of saliva from smokers with oral mucosal lesions.	Altered expression of proteins associated with epithelial stress and inflammation was observed.

4. Discussion

The findings summarized in this review demonstrate that cigarette smoking induces consistent and multifactorial alterations in the salivary proteome despite variations in study design and analytical techniques [5]. These alterations predominantly affect proteins involved in immune defense, oxidative balance, tissue protection, inflammatory regulation, and epithelial stress response. A consistent finding across multiple studies was the reduction of immune-related salivary proteins in smokers. Lee et al. reported significantly lower levels of salivary secretory immunoglobulin

A in smokers compared to non-smokers, indicating impaired mucosal immunity [9]. Reduced concentrations of salivary antimicrobial proteins such as lysozyme and lactoferrin have also been reported in tobacco users, suggesting diminished first-line defense mechanisms in the oral cavity [10].

Oxidative stress represents a key biological mechanism underlying salivary proteomic alterations associated with smoking. Baalbaki et al. demonstrated elevated oxidative stress biomarkers and reduced antioxidant activity in the saliva of smokers, indicating an imbalance between oxidant production and antioxidant defense [4]. Proteomic analyses have further identified increased expression of oxidative stress–related and stress-response proteins in smokers' saliva, reflecting cellular adaptation to chronic reactive oxygen species exposure [5].

Alterations in salivary mucins further illustrate the impact of smoking on oral protective functions. Rodrigues et al. reported significant changes in salivary protein and glycoprotein profiles among smokers using Fourier-transform infrared spectroscopy, indicating modifications in saliva composition that may affect lubrication and microbial clearance [11].

Protease inhibitors, particularly cystatins, were consistently reported to be reduced in smokers. Al-Maweri et al. observed significantly lower salivary cystatin levels in smokers compared to non-smokers, suggesting impaired regulation of proteolytic activity in the oral environment [7]. Such alterations may increase susceptibility to connective tissue degradation and periodontal tissue breakdown.

Smoking was also associated with elevated levels of inflammatory mediators in saliva. Sharma et al. demonstrated increased concentrations of interleukin-6 and interleukin-8 in cigarette smokers, indicating the presence of chronic inflammatory stimulation within the oral cavity [12]. Increased activity of matrix metalloproteinases related to extracellular matrix degradation has also been observed in smokers, supporting the link between smoking and periodontal tissue destruction [13].

Several studies identified changes in salivary proteins associated with epithelial stress and early carcinogenic processes. Chen et al. reported increased expression of stress-related proteins such as heat shock protein 70 and S100 calcium-binding proteins in the saliva of smokers, suggesting dysregulated epithelial homeostasis and early molecular alterations associated with oral potentially malignant disorders [14]. Comparative studies between conventional cigarette smokers and electronic cigarette users indicated differences in the magnitude of salivary proteomic alterations. Evidence suggests that although both groups exhibit inflammatory and oxidative changes, conventional cigarette smoking results in more pronounced proteomic disruption [6].

Several limitations should be considered when interpreting the findings of this review. Most included studies employed cross-sectional designs, which limit causal inference between smoking exposure and salivary proteomic changes [8]. Additionally, heterogeneity in smoking intensity, duration of exposure, saliva collection protocols, and analytical methods may contribute to variability in reported results.

Overall, the evidence discussed in this review demonstrates that cigarette smoking disrupts the salivary proteome through interconnected mechanisms involving immune suppression, oxidative stress, inflammation, and impaired tissue protection. These consistent proteomic alterations support the potential application of saliva as a non-invasive medium for assessing smoking-related oral disease risk and for future biomarker development in dental research and clinical practice.

5. Conclusion

This literature review demonstrates that cigarette smoking induces consistent alterations in the salivary proteome, particularly affecting proteins involved in immune defense, oxidative balance, inflammatory regulation, and tissue protection. These molecular changes help explain the increased vulnerability of smokers to various oral diseases, including periodontal disease and potentially malignant oral disorders. The findings highlight the relevance of salivary proteomics as a non-invasive and promising approach for understanding the biological impact of smoking on oral health. Further well-designed longitudinal studies are needed to validate salivary protein biomarkers and to support their future application in early detection and preventive strategies in dental practice.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

References

[1] World Health Organization. WHO global report on tobacco use [Internet]. Geneva: World Health Organization; 2023 [cited 2025 Sep 23]. Available from: https://www.who.int

[2] Warnakulasuriya S. Oral potentially malignant disorders: a comprehensive review. Oral Oncol. 2020;102:104550.

[3] Humphrey SP, Williamson RT. A review of saliva: normal composition, flow, and function. J Prosthet Dent. 2021;125(1):10–17.

[4] Baalbaki R, Zoghbi E, Jabbour J, Daher R. Oxidative stress biomarkers in saliva of smokers and non-smokers. Clin Oral Investig. 2021;25:5437–5446.

[5] Sapkota A, Modesto J, Krebs NM, Walter VA, Richie JP, Sinha R. Proteomic profiling of saliva in cigarette smokers compared with non-smokers. J Proteomics. 2023;268:104123.

[6] Rai P, Singh R, Kumar S, Srivastava A. Comparative salivary proteomic analysis in cigarette smokers, e-cigarette users, and non-smokers. Environ Health Perspect. 2024;132(3):037001.

[7] Al-Maweri SA, Halboub E, Warnakulasuriya S, Al-Shamiri HM. The impact of cigarette smoking on salivary biomarkers: a case–control study. Diagnostics (Basel). 2022;12(2):381.

[8] Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Inf Libr J. 2019;36(1):14–26.

[9] Lee M, Kim H, Park J, Lee J, Kim Y. Alterations in salivary immunoglobulin levels among cigarette smokers. Sci Rep. 2020;10:14796.

[10] Alkhateeb H, Alzahrani A, Alotaibi M, et al. Salivary antimicrobial proteins in tobacco users. Int J Oral Sci. 2021;13(1):32.

[11] Rodrigues LM, Magrini TD, Lima CF, Scholz J, Martinho HS, Almeida JD. Effect of smoking cessation on salivary compounds assessed by FTIR spectroscopy. Spectrochim Acta A Mol Biomol Spectrosc. 2020;230:117311.

[12] Sharma P, Prasad S, Singh A, Gupta R. Salivary inflammatory biomarkers in cigarette and e-cigarette users. BMC Oral Health. 2023;23:428.

[13] Yap T, Tervahartiala T, Sorsa T, Nwhator SO. Matrix metalloproteinase activity in the saliva of smokers and its association with periodontal destruction. J Periodontal Res. 2021;56(3):502–510.

[14] Chen Y, Zhang X, Li Y, Wang Z. Salivary proteomic biomarkers associated with oral epithelial dysplasia in smokers. Oral Oncol. 2022;129:105437.

[15] Higgins JPT, Thomas J, Chandler J, et al. Cochrane handbook for systematic reviews of interventions. 2nd ed. Chichester: Wiley; 2022.