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Salivary biomarkers and their diagnostic importance in oral diseases

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Highlights

- Salivary biomarkers enable non-invasive diagnosis and monitoring of oral diseases.
- Salivaomics and point-of-care tools improve sensitivity and clinical feasibility.
- Multi-omics and artificial intelligence drive future precision oral diagnostics.

Abstract

Objective

This review critically evaluates the diagnostic potential of salivary biomarkers in oral diseases, highlighting their role as non-invasive tools for early detection, disease monitoring, and precision oral healthcare.

Design

A narrative review was conducted using PubMed, Scopus, Web of Science, and Google Scholar for studies published between 2005 and 2026. Keywords included salivary biomarkers, salivaomics, oral diseases and diagnosis. Only English peer-reviewed articles focusing on salivary biomarkers and analytical methods in oral diseases were included, while studies lacking clinical relevance were excluded.

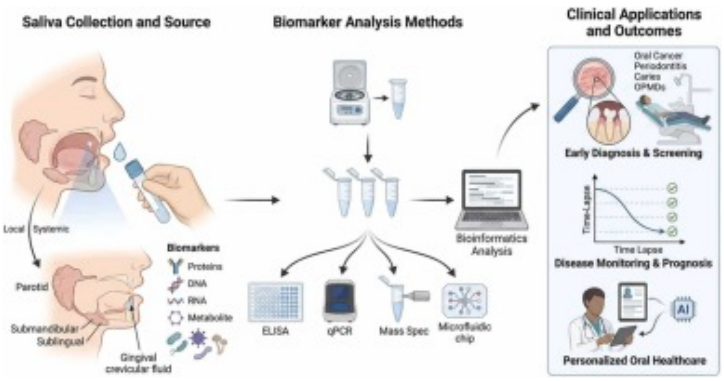
Results

Saliva harbors a variety of molecular biomarkers, such as proteins or nucleic acids, that mirror local and systemic pathological phenomena8. In oral squamous cell carcinoma, salivary biomarkers like Interleukin-6 (IL-6) and Interleukin-8 (IL-8) have a sensitivity of 70–90% and a specificity of 75–95%; however, salivary microRNAs display strong discriminatory power with AUC values ≥0.85.For periodontal diseases, MMP-8, among others, found in the biomarkers, shows high accuracy (AUC > 0.80). Recent progress in salivaomics, including proteomics, genomics, metabolomics, and microbiomics, has notably increased detection sensitivity, specificity, and clinical applicability. However, heterogeneity of biomarker expression, lack of a clinically validated standardized protocol for the collection and processing of saliva, and insufficient large-scale clinical validation are still significant limitations to everyday clinical utilization.

Conclusions

Salivary biomarkers are non-invasive and offer an opportunity to complement traditional diagnostic sources in oral health. Further standardization, clinical validation and adaptation of multi-omics and artificial intelligence-based technologies are necessary to facilitate their positive translation into precision oral medicine.

Graphical Abstract



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Introduction

Oral diseases are one of the most significant public health burdens in the world, as they impact almost half of the population worldwide. Dental caries, periodontal diseases, oral potentially malignant disorders (OPMDs), and oral squamous cell carcinoma (OSCC) are all frequent oral disorders that relate to pain, functional impairment, esthetic issues, and higher healthcare expenditure. Even with improved dental treatment, most oral conditions are diagnosed later because they are usually asymptomatic in their early stages and common diagnostic methods include clinical examination, radiographic imaging, and invasive tissue biopsy (Kalmar & McNamara, 2022). Such methods are frequently insensitive to early disease detection, time-consuming and can cause patient discomfort, thus limiting their usefulness in large-scale screening and longitudinal disease monitoring (Yarman & Rathore, 2025).

Recent global estimates demonstrate a substantial and escalating burden of oral diseases, affecting approximately 3.5–3.7 billion individuals worldwide and ranking among the most prevalent non-communicable diseases (World Health Organization, 2024). Untreated dental caries represents the most common health condition, while severe periodontal disease affects nearly 1 billion people, significantly contributing to tooth loss and reduced quality of life (GBD, 2019 Diseases and Injuries Collaborators,19 Diseases and Injuries Collaborators, 2020). Despite being largely preventable, the global burden of oral diseases has increased over recent decades, particularly in low- and middle-income countries, underscoring disparities in access to preventive and therapeutic care.

There is a growing need for non-invasive, reliable, and cost-effective diagnostic strategies in oral healthcare, driven by the focus on early diagnosis and precision medicine. Liquid biopsy is a non-invasive diagnostic technique that involves the detection of biomarkers in body fluids such as blood or saliva to monitor disease presence and progression. The field of diagnostics based on liquid biopsy has been proposed as a promising alternative to traditional approaches, enabling real-time measurement of molecular changes that correlate with disease (Armakolas et al., 2023). Saliva is one of several biofluids that have received significant focus owing to its readily collectable nature, non-invasive nature, and proximity, both anatomically and physiologically, to the oral cavity (Nagpal et al., 2024). Compared with blood-based diagnostics, saliva collection requires no trained staff, reduces the risk of infection and is readily accepted by patients, making it especially appropriate for recurrent sample collection and community-level screening programs (Laxton et al., 2023).

Saliva is a complex biological fluid composed of proteins, nucleic acids, metabolites, electrolytes, microorganisms, and host-derived inflammatory mediators, all of which contribute to local and systemic health (Alavi et al., 2025). With the development of high-throughput technologies, there has been a rise in the concept of salivaomics, which includes salivary proteomics, salivary genomics, salivary transcriptomics, salivary metabolomics and salivary microbiomics (Rosa, 2025). Salivaomics refers to the comprehensive analysis of all molecular constituents in saliva, including proteins, nucleic acids, metabolites, and microorganisms, using high-throughput technologies. These

molecular signatures have proven useful as diagnostic, prognostic and therapeutic-response biomarkers across a wide range of oral disorders particularly OSCC, periodontal diseases and dental caries. Novel salivary biomarkers have distinct benefits in early disease identification, aiding risk stratification and treatment planning. Hence, it is a revolution in contemporary oral health diagnostics (Papale et al., 2022, Alotaiby, 2024).

Periodontitis is a long-lasting disease caused by many factors that create lots of inflammation affecting all the things holding your teeth in your mouth, like your gums, ligaments, and the bone around your teeth (Ray, 2023). Not only is there evidence of the effect periodontitis has on the oral cavity, but it's also well established that periodontitis is associated with increased levels of inflammation in the body and is linked to increased risk factors for heart disease, including atherosclerosis, heart attack, and stroke (Dembowska et al., 2022). Recent research has shown that adding antimicrobials like chlorhexidine to sodium DNA may provide an effective way to lower oral bacteria (Rocco et al., 2025) and that a structured supportive protocol for dental hygiene improves periodontal conditions through the use of predictive analytics about patient success (Isola et al., 2025). This confirms the importance of using a combination of both antimicrobial and supportive techniques to manage periodontal disease and indicates that early intervention can prevent progression of dental disease.

Based on this evidence, non-invasive diagnostic techniques, such as using saliva to diagnose periodontal disease, are a promising area for early detection and tracking of how an individual is responding to periodontal treatment. Salivary biomarkers can demonstrate in real-time how the body is responding to inflammation, what type of bacteria are present in the mouth and at what quantities, and what inflammatory mediators are present and in what concentrations, which is essential for determining if the patient has periodontal disease or if it has a potential systemic impact (Hu et al., 2025). Incorporating salivary biomarker assessment into clinical practice will improve risk stratification, assist with developing patient-specific treatment plans, and ultimately improve oral health and systemic health.

This review will critically evaluate the significance of salivary biomarkers in the diagnosis and management of oral diseases. The review summarizes the nature and origin of salivary biomarkers, their applicability in significant oral pathologies and the methods used to detect them analytically. Moreover, the existing challenges, translational opportunities and future approaches to saliva-based diagnostics are outlined, with a particular focus on the latest developments in oral and dental research.

Section snippets

Composition and biological significance of saliva

Saliva is a multifaceted and dynamic biological fluid that is released mainly by the major (parotid, submandibular, and sublingual) and minor salivary glands. It consists mainly of water (99%), a great variety of organic and inorganic components, such as electrolytes, proteins, enzymes, immunoglobulins, hormones, nucleic acids, metabolites, and microorganisms. These components play crucial roles in maintaining oral homeostasis by enabling mastication, swallowing, digestion, lubrication, …

Salivary biomarker classification

Salivary biomarkers are quantifiable biological molecules that indicate physiological and pathological events associated with the oral cavity and in certain cases, the whole-body circulation. The multifaceted nature of saliva and its constant interaction with oral surfaces and microbes make salivary biomarkers provide a combined picture of host-microbe interactions, immune reactions, metabolic changes, and disease-related molecular modifications. The recent development of high-throughput …

Salivary biomarkers in oral diseases

Salivary biomarkers have become useful in early diagnosis, prognosis and follow-up of a broad range of oral diseases. Recent progress in salivaomics, an array of proteomics, genomics, metabolomics and microbiomics has enabled the identification of disease-specific molecular signatures that reflect both local and systemic pathologic alterations. The clinical significance of salivary biomarkers in severe oral diseases is discussed below. …

Salivary biomarker detection techniques

Detecting and quantifying salivary biomarkers accurately requires sensitive, specific and reproducible analytical methods due to the low concentrations and complexity of saliva. These are the crucial technological developments from the last two decades that made it possible to reliably assess proteins, nucleic acids, metabolites, and microbial constituents in saliva. The methods can be generally categorized as conventional laboratory techniques, omics-based technology, and new biosensors and …

Clinical applications of salivary biomarker

Salivary biomarkers have attracted growing interest as a platform to facilitate the non-invasive, rapid and cost effective diagnosis and treatment of oral diseases. Research on analytical technologies and biomarker validation has enabled the incorporation of saliva-based diagnostics into clinical decision-making especially for diagnosing mild diseases in the early stages, longitudinal care and individual oral health (Constantin et al., 2025). Salivary biomarkers have emerged as valuable tools …

Challenges and limitations

Although the field of salivary diagnostics has made significant progress, there are still obstacles that prevent its widespread adoption in clinical practice. Overcoming the limitations of research on salivary biomarkers to transfer findings into everyday practice in oral healthcare is essential. …

Future perspectives

Technology and data analysis promises will remove the existing constraints and, according to current predictions, boost the speed of clinical acceptance of salivary diagnostics. …

Conclusion

The growing body of evidence indicates the usefulness of saliva as a diagnostic biofluid in the diagnosis and management of oral diseases. The discovery of proteomic, genomic, metabolomic, and microbial biomarkers has demonstrated that saliva can be used for non-invasive disease measurement. A combination of omics and biosensing platforms has significantly increased the diagnostic capacity of salivary biomarkers. Saliva-based diagnostics offer several clinical benefits, including non-invasive …

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. …

Recommended articles

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