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(REVIEW ARTICLE)

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Recent advances in digital saliva biosensors for point-of-care testing and periodontitis monitoring: A Narrative Review

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Abstract

Background: Periodontitis is a chronic inflammatory disease of periodontal tissues with an age-standardized prevalence rate (ASPR) of 12,498.3 per 100,000 population (GBD 2021), and 74.1% of Indonesians suffer from periodontal problems (Riskesdas 2018). Conventional diagnostic methods are invasive, subjective, and tend to detect disease at an advanced stage. Saliva has the potential as a non-invasive diagnostic alternative through portable biosensors and digital integration.

Objective: This review aims to analyze the potential integration of saliva-based biosensors with digital systems in enhancing the effectiveness of diagnosis and monitoring of periodontitis.

Methods: A literature search was conducted on PubMed, ScienceDirect, Research Gate and Google Scholar using predetermined keywords and the results were limited to articles published in 2020-2025

Discussion: Biosensors are used as Point-of-Care Testing (POCT) by detecting saliva inflammatory biomarkers, then integrated with digital technology for biomonitoring, such as smartphones, artificial intelligence, or Internet of Things (IoT) in the form of mouth guards and intraoral patches. Surface Plasmon Resonance-based Plasmonic Fiber-Optic Biosensors work by utilizing specific antigen-antibody bonds detected by spectrophotometry, while Electrochemical Impedance Spectroscopy (EIS) works by measuring changes in resistance or impedance at the electrode. Molecularly Imprinted Polymer (MIP) detects biomarkers by electric current changes and then converts them into concentrations. Biomarker signals detected by biosensors are transmitted wirelessly to external devices, where noise is filtered using deep learning, thereby improving accuracy and also enabling real-time personalized monitoring.

Conclusion: Saliva biosensors as POCT and digital biomonitoring offer earlier, minimally invasive, rapid, and personalized disease detection.

Keywords: Salivary Biosensors; Biomonitoring; Periodontitis; POCT; Artificial Intelligence

1. Introduction

Periodontitis is a chronic inflammatory disease of the tooth-supporting tissues and remains one of the most prevalent oral conditions worldwide[1]. With an incidence of 12,498.3 per 100,000 population globally and 74.1% of Indonesians exhibiting periodontal problems, the disease represents a major public health concern[2,3]. Its multifactorial nature, involving bacterial biofilms, host immune responses, and environmental factors such as smoking, often leads to progressive tissue destruction when not detected early[1,4].

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Conventional diagnostic methods including probing depth, clinical attachment level, and radiographic assessment are invasive, subjective, and unable to detect biochemical changes during the early stages of disease progression[3,5]. Consequently, diagnosis frequently occurs only after irreversible periodontal breakdown has taken place, underscoring the need for early, accurate, and minimally invasive diagnostic approaches[1].

Saliva has emerged as a promising diagnostic medium because it reflects the biochemical status of periodontal tissues and contains key biomarkers involved in inflammation and tissue degradation[6,7]. Among these, matrix metalloproteinase-8 (MMP-8), human odontogenic ameloblast-associated protein (ODAM), and the chemokine MIP-1α are of particular interest due to their strong associations with periodontal inflammation and collagen breakdown[6,8,9,10].

Advances in biosensing technologies have facilitated the development of saliva-based biosensors capable of rapid, sensitive, and real-time detection of these biomarkers[11,5]. Multiple platforms have been explored, including Electrochemical Impedance Spectroscopy (EIS) integrated with Molecularly Imprinted Polymer (MIP) technology, which enhances selectivity through engineered molecular recognition sites[12,13,14]. Surface Plasmon Resonance (SPR) systems coupled with Plasmonic-Fiber Optic (PFO) structures, which improve sensitivity through refractive index modulation[1,15,16,17].

Recent developments integrating biosensors with digital systems including IoT connectivity and machine-learning based signal processing further support the possibility of real-time, personalized monitoring of periodontal conditions[18,19,20]. This technological shift aligns with the emerging concept of digital dentistry and precision oral healthcare, enabling continuous assessment of disease progression beyond traditional clinic-based evaluation[5,15,18].

Therefore, this article aims to examine recent advancements in saliva-based biosensor technologies for detecting and monitoring periodontitis, emphasizing their potential to overcome the limitations of conventional diagnostic methods and support the future development of personalized periodontal care.

2. Methods

This article aims to explore recent advancements related to saliva biosensors in detecting and monitoring periodontitis. Comprehensive research was performed using PubMed, ScienceDirect, Research Gate databases by applying a Boolean operator–based strategy to identify relevant publications. The literature search was carried out between September and November 2025, focusing on English-language articles published within the last five years. The search keywords included the following combinations ("periodontitis" OR "periodontal inflammation") AND ("biosensor" OR "wearable biosensor") AND ("point-of-care testing" OR "point-of-care diagnosis" OR "digital integration" OR "deep learning").

The inclusion criteria fortapi this literature review were: (a) studies related to the topic, (b) original research articles, and (c) publications released between 2020 and 2025. Exclusion criteria were: (a) articles published outside the 2020–2025 period, (b) case reports and review papers, (c) articles not written in English.

3. Results

The initial selection of search strategy in digital databases were 497 articles. Review articles were excluded, resulting in 67 articles. These articles were reviewed by their introductions to verify whether they addressed the focus of this review, those that did not were excluded. Based on the predetermined inclusion criteria, a total of eleven articles were ultimately included to gather the relevant data.

Table 1 List of Articles

Biosensor Types	Title	Author	Target	Outcome
Enzymatic biosensor (Electrochemical)	Washing and Separation- Free Electrochemical Detection of Porphyromonas gingivalis in Saliva for Initial Diagnosis of Periodontitis	Park et al., 202121	Arg-gingipain	GPR–AP released by Arg-gingipain activity generates electrochemical signals, enabling highly specific detection of P. gingivalis.
Nonenzymatic biosensor (Electrochemical)	Non-enzymatic electrochemical detection of H2O2 by assembly of CuO nanoparticles and black	Wang K et al., 202222	H2O2	High sensitivity and selectivity, enables detection of periodontitis patients through saliva and GCF,

	phosphorous nanosheets for early diagnosis of periodontitis			capable of real-time H_2O_2 monitoring in live cells.
Nonenzymatic biosensor (Optical)	Highly-sensitive ultra-thin dental patches assisted with artificial-intelligence recognition for mapping hidden periodontitis lesions	Liu et al., 202523	H2S	High sensitivity (LOD 25 pmol/L), maps hidden periodontal lesions within 15 minutes using AI-assisted fluorescence image analysis, user-friendly and suitable for routine screening.
Nonenzymatic biosensor (Electrochemical)	A Wearable Electrochemical Biosensor for Salivary Detection of Periodontal Inflammation Biomarkers: Molecularly Imprinted Polymer Sensor with Deep Learning Integration	Jeon Y et al., 20251	MMP-8	Real-time and non-invasive salivary detection, high specificity, AI integration enhances diagnostic accuracy, suitable for use as a wearable mouthguard device.
Immunosensor (Electrochemical)	Integrated dual-channel electrochemical immunosensor for early diagnosis by detecting multiple biomarkers in saliva	Zhang et al., 202315	IL-1β, MMP-8	Simultaneous detection of two salivary biomarkers, detection range of 0.1–100 ng/mL (IL-1β) and 1–200 ng/mL (MMP-8);, high accuracy in determining periodontitis severity levels.
Immunosensor (Optical)	A disposable immunosensor for the detection of salivary MMP-8 as biomarker of periodontitis	Tortolini et al., 20248	MMP-8	Rapid and sensitive salivary detection comparable to ELISA, SAM improves antibody orientation and reduces signal noise.
Immunosensor (Optical)	Plasmon resonance biosensor for interleukin-1β point-of- care determination: A tool for early periodontitis diagnosis	Cennamo et al., 20246	IL-1β	Picomolar-level LOD, rapid incubation (3 minutes), high accuracy in saliva, ideal for label-free detection.
Immunosensor (Electrochemical)	Performance Validation of Fabricated Nanomaterial- Based Biosensor for Matrix Metalloproteinase- 8 Protein Detection	Lowpradit et al., 20257	MMP-8	High sensitivity, efficient and excellent reproducibility, low-cost fabrication process
Immunosensor (Optical)	Plasmonic Optical Fibre-Based Point-of-Care Test for Periodontal MIP-1α Detection: A Validation Study of a Multiplexed Biosensor Prototype	Annunziata et al., 202511	MIP-1α	Detection and quantification of MIP-1α comparable to ELISA, a multiplexed three-arm design provides faster analytical response.
Aptasensor (Electrochemical)	Aptamer duo-based portab;e e;ectrochemical biosensors for early diagnosis of periodontal disease	Joe et al., 20229	ODAM	Portable system connected to a mini-potentiostat and smartphone, more sensitive than SPR/LFA, suitable for early saliva-based periodontitis diagnosis.
Aptasensor (Optical)	An IoT-based aptasensor biochip for the diagnosis of periodontal disease	Nguyen et al., 20245	ODAM	Integrated POC and IoT system detects ODAM within 30 minutes with a LOD of 0.011 nM, differentiates healthy and periodontitis individuals with 100% specificity, results can be transmitted to clinicians via email.

4. Discussion

4.1. Biosensors Classification and Detection Mechanism

Biosensors generally consist of three essential components: a bioreceptor, a transducer, and a signal-transduction mechanism. Based on the type of bioreceptor, salivary biosensors can be categorized into enzymatic biosensors, non-enzymatic biosensors, immunosensors, and aptasensors. Each category offers distinct advantages and challenges in detecting biomarkers relevant to periodontal disease.

Enzymatic biosensors utilize enzymes as both recognition elements and catalysts for specific biochemical reactions. One example is the work by Park et al[21] who developed an enzymatic biosensor for detecting Arg-gingipain. In their system, the peptide substrate Cly-Pro-Arg-AP functions as the bioreceptor; upon interaction with Arg-gingipain in saliva, the substrate is cleaved, producing measurable changes in resistance or impedance on the electrode, which are then translated into electrochemical signals. By contrast, non-enzymatic biosensors detect analytes without relying on enzymatic activity, typically through direct electrochemical reactions between the analyte and the electrode transducer. Wang et al[22] demonstrated this approach using a CuO nanoparticle black phosphorus nanosheet (CuO-NPs/BP-NSs) composite to detect hydrogen peroxide (H_2O_2), a reactive oxygen species implicated in periodontal pathogenesis, through redox reactions. Similarly, Jeon et al[1] employed Molecularly Imprinted Polymers (MIPs) synthetic polymers engineered with molecular recognition cavities to detect MMP-8. MIPs offer excellent chemical stability and are suitable for long-term monitoring. Other examples include the work by Liu et al[23] who measured hydrogen sulfide (H_2S) through the formation of ZnS from its reaction with ZnO quantum dots, resulting in fluorescence quenching that can be quantitatively assessed. Compared with enzymatic biosensors, non-enzymatic platforms offer higher stability because they are not affected by enzyme denaturation; however, they tend to have lower specificity.

In addition to enzymatic and non-enzymatic systems, immunosensors and aptasensors represent another major class of biosensors that rely on highly specific molecular interactions. Immunosensors detect biomarkers based on antigen antibody binding and have been widely applied to measure inflammatory mediators in periodontitis, including MMP-8, IL-1β, and MIP-1α[6,7,8,15]. Aptasensors operate through an analogous mechanism but use aptamers synthetic nucleic acid sequences capable of folding into selective two or three dimensional structures to bind target molecules with high affinity[9]. Current literature demonstrates a distinction in target analytes between these two types: immunosensors primarily detect inflammatory biomarkers, whereas aptasensors are increasingly utilized to detect ODAM, a protein released during early junctional epithelium degradation. Notably, recent advancements show a shift toward multiplex detection, where immunosensors and aptasensors can now measure two biomarkers simultaneously, improving diagnostic utility[5,9]. After binding to their respective targets, these biosensors convert molecular interactions into measurable electrochemical or optical signals via their transducers.

The biosensor mechanism begins with a redox reaction or specific bioreceptor–biomarker interaction occurring at the transducer interface. The transducer detects antigen–antibody complexes or redox changes and converts them into electrical or optical signals. Electrochemical transducers commonly include screen-printed electrodes[1,9,21], nanoparticle-modified electrodes[8,15,22], or combinations of both[7]. Optical transducers may incorporate surface plasmon resonance–plasmonic optical fiber systems[6,11] or CMOS-based platforms coupled with LED illumination[5]. These diverse transducer designs allow biosensors to achieve high sensitivity and selectivity depending on the biomarker and detection method required.

4.2. Digital Integration and Intelligent Biosensing System

With the advancement of digital technologies, modern biosensor systems no longer function solely as standalone detection devices but are increasingly integrated with intelligent platforms based on the Internet of Things (IoT) and deep learning algorithms. Joe et al[9] developed a portable electrochemical aptasensor connected to a wireless mini-potentiostat for detecting biomarkers. Through a sandwich-type binding mechanism, the biosensor demonstrated high sensitivity and enabled direct analysis via mobile devices, thereby strengthening the concept of portable point-of-care testing (POCT) for the early diagnosis of periodontitis.

Further development of the POCT concept was demonstrated by Nguyen et al[5] who integrated IoT technology into a fluorescence-based microfluidic aptasensor biochip. This device is controlled through a smartphone application, allowing automated detection processes and wireless transmission of diagnostic results between patients and clinicians. The incorporation of IoT enables real-time oral health monitoring and supports the implementation of teledentistry. Similarly, Liu et al[23] applied an AI model based on U-Net architecture to identify fluorescence-quenching patterns and rapidly visualize the distribution of hidden periodontal lesions with greater accuracy.

At a more advanced stage, Jeon et al[1] combined deep learning technology with a wearable electrochemical biosensor using molecularly imprinted polymer (MIP) for detecting MMP-8 in saliva. This system utilizes deep learning for signal filtering, identifying progression trends of periodontal inflammation, and adaptively enhancing diagnostic accuracy. The platform, designed as a wearable mouthguard, enables continuous and non-invasive monitoring of inflammation within the context of AI-assisted personalized care.

The integration of these digital technologies allows biosensors to acquire biomarker data in real time, upload them to cloud servers for deep learning–based analysis, and present interpretive results through smartphone applications. As a result, biosensors evolve beyond laboratory detection tools into portable, automated, and individualized systems for monitoring periodontitis. Despite these advancements, several limitations remain, including variability in reproducibility, limited dataset sizes for deep learning training, and the need for broader validation across diverse clinical cohorts to improve model generalizability and reduce data-driven bias.

5. Conclusion

Saliva-based biosensors hold substantial potential as non-invasive diagnostic tools for detecting and monitoring periodontitis. Inflammatory biomarkers such as MMP-8, IL-1β, IL-6, and MIP-1α reflect the underlying periodontal inflammatory processes, offering clinically relevant targets for salivary detection. The integration of biosensors with digital technologies including IoT connectivity, wireless data transmission, and artificial intelligence enables precise, real-time, and personalized monitoring of periodontal status. Therefore, digital saliva biosensors present a promising approach for Point-of-Care Testing (POCT) and support the implementation of precision oral healthcare within the era of digital dentistry.

Compliance with ethical standards

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Disclosure of conflict of interest

No Conflict of interest to be disclosed

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