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Review Article

Intraoral biomarkers: Unlocking the future of oral health diagnostics - A narrative review

Albi Infanta Thayananthamn[1], Divya Vinayachandran[1]*, Ganesh Chakkarai[1], Shanthi Mathialagan[1]

[1]Dept. of Oral Medicine and Radiology, SRM Kattankulathur Dental College and Hospital, SRM Institute of Science and Technology, Chengalpattu, Tamilnadu, India.

Abstract

Oral health is crucial for overall well-being, with the oral microbiome playing a significant role in preventing diseases. Biomarkers, measurable indicators of biological or pathogenic processes, have become essential tools in modern diagnostics. Saliva, a readily accessible and non-invasive fluid rich in proteins, DNA, RNA, and microorganisms, has emerged as a promising medium for detecting oral and systemic diseases—a field known as salivaomics. Salivary biomarkers can effectively indicate dental caries, oral cancers, periodontal diseases, and systemic conditions such as stress and viral infections. Proteins like histatin and proline-rich proteins correlate with dental caries, while markers such as tissue polypeptide antigen and microRNAs assist in early cancer detection. Saliva also enables monitoring of systemic immunity and stress-related hormones, offering advantages over blood testing in cost, safety, and ease of collection. Intraoral biosensors, devices converting biological reactions into electrical signals, are advancing diagnostic capabilities, though their commercialization remains limited in regions like India. Continued innovations in molecular techniques and biosensor technology hold promise for enhancing early diagnosis and health surveillance, reinforcing saliva's potential as a versatile diagnostic fluid in dental and systemic medicine.

Keywords: Saliva, Diagnostics, Biomarkers, Oral health

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1. Introduction

Preventing oral illnesses and maintaining oral health are the fundamental objectives of dental medicine. Opportunistic infections can cause disease outbreaks and progressions when the overall structure of the oral micro biome changes.[1] The process of determining a sickness, ailment, or issue by looking at someone or something is called diagnosis. It can also be a statement or conclusion that explains the cause of a disease, illness, or problem.[2] Diagnostic instruments have evolved over time, becoming more sensitive and accurate as a result of novel advances in dental research and technological breakthroughs. This is where Health markers come into play.[1] These are referred to as 'Biomarkers' in modern medicine. Below is a detailed discussion of intraoral biomarkers in both health and illness.

2. What is a Biomarker?

The word "biomarker," a contraction of "biological marker," describes a broad spectrum of objective manifestations of a patient's health that can be measured and perceived from outside the patient precisely and consistently.[1] In accordance with National Institute of Health,2001, Biomarker is 'A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention or other health care intervention.

3. Saliva-the Miracle Fluid

Saliva is an exceptional bodily fluid that indicates a profound yet innate component of our well-being.[3] Similar to serum, saliva is rich in different proteins, microorganisms, metabolites, DNA, mRNA, and miRNA, among other biomolecules. To highlight its use in the creation of biomarkers and the prediction of disease, the term

Corresponding author: Divya VC
Email: divyav@srmist.edu.in

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"salivaomics" was created. Saliva's lower analyte level is no longer a constraint owing to new, extremely sensitive methodologies.[3] It is possible to measure nearly every parameter in saliva that can be measured in blood. Viral hepatitis A, B, and C as well as HIV can be accurately detected in saliva. Alcohol, cocaine, marijuana, and other drugs can all be monitored with it.

There are strong arguments in favour of using saliva as a diagnostic fluid to track illnesses and health.[3] It satisfies the need for low-cost, non-invasive, and user-friendly diagnostic techniques. Saliva is inexpensive to get in large enough amounts for analysis and relatively easy to gather, preserve, and transport. Non-invasive collection methods significantly lessen patients' discomfort and anxiety while making it easier to get repeated samples for long-term longitudinal monitoring. Saliva collection is safer for professionals than blood testing, which could expose medical personnel to the hepatitis virus or HIV. As a result, saliva-based diagnostics are less hazardous for patients than existing techniques and are more affordable, accurate, and accessible.

4. Role of saliva in Oral Diseases

4.1. Dental caries

Dental health is maintained by the cleansing action, antibacterial activity, buffering capacity, and remineralisation characteristic of saliva.[3] A significant fraction of the global population suffers from dental caries, a highly prevalent multifactorial illness. There is some evidence that dental caries and an array of salivary factors are interrelated. Saliva's levels of statin and histatin S are helpful indicators of tooth decay.[4] Proline-containing proteins (PRP1 and PRP3), histatin1, and statin levels are high in those without cavities, but they fall in people with high caries. Dental caries has been closely linked in reports to an increase in salivary microbes such as Lactobacillus and Streptococcus mutans. Additionally, they have been found to be useful in identifying proteomic and microbial biomarkers in early childhood caries.

4.2. Oral oncology

Saliva is a highly valuable tool for the identification of oral cancer and other precancerous lesions and diseases, making it a potential strategy for health surveillance and disease diagnostics1. Saliva collection is also relatively simple and non-invasive. People with oral cancer have been found to have common indicators in their saliva, including tissue polypeptide antigen, cytokeratin, and cancer antigen-125 (CA-125).

MicroRNAs (miRNAs) are small, noncoding RNAs that repress translation or break down target genes.[1] They are very important for controlling many biological processes. Saliva contains miRNAs, which indicate possibility as potential biomarkers for dental disorders based on recent study findings.A high concentration of a tumor marker is thought to indicate benign and malignant disorders, as well as malignancies associated with the teeth.[4] These biomarkers, which have recently been effectively identified, are useful in determining the genesis of the condition at a prodromal phase, namely that keratocystic odontogenic tumors may result from aberrant activity of the tumor suppressor gene PTCH. Therefore, novel molecular techniques (such as proteomics, transcriptomics, and genomics) and metagenomic studies have been driving recent advancements in oral fluid biomarker diagnostics, expanding the identification of microbial pathogens linked to systemic and oral disorders.

Salivary indicators are crucial for assessing orthodontic tooth mobility and identifying periodontal illnesses early on, when the prognosis is favorable, as recent research has demonstrated.[1]

Table 1: Types and principles

Type of biosensor	Transduction method
Electrochemical	Amperometric
	Potentiometric
Electric	Conductometric
	Ion-sensitive
Optical	Fluorescence
	Chemiluminescence
Piezoelectric	Bulk wave
	Surface acoustic wave

5. Saliva- Systemic Biomarker

5.1. Psychiatric disorders

Saliva testing is a valuable tool for examining psychiatric conditions like anxiety, sadness, and PTSD1. Testing alpha amylase and cortisol levels, which are indicators of stress levels, is its primary objective. Cortisol levels are linked to long-term stress because they increase gradually over time and take a while to return to baseline levels. Since alpha amylase spikes fast and goes back to baseline shortly after tension has subsided, measuring salivary amylase could be a useful tool for researching acute stress reactions.

5.2. Infectious diseases

The use of saliva as a diagnostic tool for seasonal respiratory viruses has been hotly debated since the COVID-19 pandemic, when saliva-based diagnostic assays were first implemented.[5] There is a correlation between serum IgG levels and salivary sand serum HCV antibodies, CMV, EBV, HIV, and Rubella virus.[1] Following vaccination, salivary antibodies against the rotavirus and poliovirus have been reported. Thus, salivary testing for particular antibodies is a valid way to assess systemic immunity in vaccination, illness, and health. Salivary samples from bite marks, skin surfaces, envelopes, and other objects are a useful tool for deciphering DNA and establishing the link with the suspect.

5.3. Diabetes mellitus

According to Barnes et al., diabetic individuals had significantly higher levels of glucose and α-hydroxybutyrate, along with significant changes in their levels of oxidative stress, lipids, and carbohydrates.[6] The diagnosis, treatment, and prognosis of diabetes may therefore be influenced by the metabolites.

According to Aitken-Saavedra et al., in people with type 2 diabetes mellitus, HbA1 was inversely correlated with saliva pH and strongly correlated with total protein quantity.[7] Analyzing the qualitative and quantitative changes in saliva may be a cost-effective and practical way to monitor individuals with diabetes, a common chronic illness with many associated problems.

5.4. Cardiac disorders

Assessing the risk of acute myocardial infarction in individuals with insulin resistance is a significant use of salivary diagnostics in cardiology.88. Cardiovascular disease patients also showed decreased salivary levels of α-2-HS-glycoprotein, indicating that the peptidome could be a valuable tool for cardiovascular disease early detection.

6. Intra oral Biosensors

An analytical tool that transforms a biological reaction into an electrical signal is referred to as a "biosensor".[9] A biosensor consists of the biological element that are sensitive and produced by biological engineering: cells, nucleic acids, enzyme antibodies, tissue, the material element and the electrical component. The types and principles of biosensors are emphasized as **Table 1.** The biosensors are made of a biological element, Physical element, Transducer/Detector and Amplifier/Display Unit.[10] Biological engineering-produced sensitive bio-elements include enzyme antibodies, nucleic acids, cells, tissue, etc.[11] Serum, saliva, urine, feces, etc. are examples of analytes. When the analyte and biological element interact, the signal is transformed into a different signal that is easily measurable and subsequently quantified with the aid of a transducer or detector.[12] The electrical component or signal processor in charge of presenting the results in a usable manner is called an amplifier or display unit.

7. Commercialization of Biosensors

In India, intraoral biosensors are not yet widely accessible for sale. Newer advancements will, nevertheless, take place in due course.[9] Blood-glucose biosensors have achieved significant success, accounting for approximately 85% of the global market.
Optical biosensing, which is based on the fluorescent phenomenon and detects the analytes' fluorescent characteristics, is another popular biosensor.[13] Another widely used biosensor makes use of optical biosensing, which is based on the fluorescent phenomena and detects the analytes' fluorescent characteristics.[14] Biacore, Bio-Rad, Graffinity Pharmaceuticals, and Research International are a few biosensor producers.

8. Discussion

Saliva has advantages over serum as a diagnostic fluid since it is non-invasive, accessible to all people with basic training, and provides an economical method for screening huge populations.[15] Saliva collection poses little danger of infection, and it can be utilized in clinically difficult conditions, like taking samples from toddlers or patients who are apprehensive or disabled, when taking blood samples could be a laborious task. With the combination of biomolecules having clinical relevance and the development of detection technology, saliva has the potential to become the preferred first-line diagnostic sample. Biosensor development and invention have changed lives and will continue to advance over time.[16] The compactness, low power consumption, and possibility for personal health care with oral point-of-care testing—thus rapid health monitoring—are the foundations of technological advancement. Biosensors will become more sought-after due to their high specificity, sensitivity, and environmentally benign methodology.[17] Life-altering and revolutionary possibilities could result from the creation of dynamic nanosensors with multivariate properties that can simultaneously detect many pathogens or diseases.[17] The use of oral fluids for medication development and the detection of systemic and oral disorders is presently being studied by biotechnology and medical researchers.[19,20] Biomarkers are being actively produced in the pharmaceutical sector for use in drug metabolism and customized dosing studies. The spectrum of applications is expanding along with the technological developments in the biosensors sector. These days, biosensors are employed in diagnostic and treatment planning since they are non-invasive, easy to use, and take less time.

9. Conclusion

Health care depends on a precise diagnosis since it clarifies a patient's condition and directs future treatment decisions. Data collection and clinical reasoning are two components of the complex, team-based process of identifying a patient's health problem. Therefore, oral markers are a remarkable discovery in the ongoing efforts of contemporary medicine to develop innovative methods for the provision of health services with the ultimate outcomes achievable. Researchers in the fields of biotechnology and medicine are currently investigating the use of oral fluids for drug development and the identification of oral and systemic illnesses. The pharmaceutical industry is actively producing biomarkers for use in tailored dosage studies and drug metabolism. The spectrum of applications is expanding along with the technological breakthroughs in the biosensors sector. These days, because biosensors are quick, simple, and non-invasive, they are used in diagnostic and treatment planning. As a result, oral markers represent a noteworthy advancement in modern medicine's continuous endeavours to create novel approaches for delivering healthcare services with the best possible results.

10. Source of Funding

None.

11. Conflict of Interest

None.

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