Keywords
salivary biomarkers, oral diagnosis, preventive dentistry, prosthodontics, precision dentistry

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Received: 11.04.2026
Revised: 16.05.2026
Accepted: 25.05.2026

Doi: 10.1922/ejprd.v34i3s.1422

A Comprehensive Study on Salivary Biomarkers in Oral and Systemic Diseases: Biochemical Insights and Diagnostic Applications in Dental Practice

Abstract
Salivary biomarkers have become an exciting non-invasive diagnostic method of monitoring and risk evaluation of oral diseases in modern dentistry. This review examines the biological basis of saliva, the major classes of salivary biomarkers, and their clinical relevance in caries, periodontal disease, peri-implant disorders, and oral potentially malignant and malignant lesions. The review also discusses the growing role of salivary analysis in restorative and prosthodontic treatment planning, where salivary composition influences material performance, tissue response, and long-term treatment outcomes. Recent advances in chairside diagnostic technologies, particularly biosensors and microfluidic platforms, have strengthened the clinical feasibility of saliva-based testing and supported its integration into precision dentistry. Despite these developments, significant barriers remain, including biological variability, lack of standardized collection and analytical protocols, and inconsistent diagnostic validation across studies. Current evidence suggests that salivary diagnostics is most effective when used as an adjunct to conventional clinical assessment rather than as a standalone diagnostic tool. With continued methodological refinement, multi-biomarker validation, and improved translational frameworks, salivary biomarkers may contribute substantially to earlier diagnosis, individualized prevention, and more biologically informed dental care. This review highlights the current scope, clinical relevance, and future direction of salivary biomarker research within restorative, prosthodontic, and broader oral healthcare practice.

1. Introduction

Saliva has now become an extensively studied biofluid that has been used for diagnosis in dental medicine and has clinical relevance. Due to easy accessibility, minimal expertise needed for manipulation of specialized equipment and friendly interaction with the patient, it makes a possible alternative to established methods of diagnosis, including blood tests and tissue biopsies [1]. It offers a useful matrix that is capable of providing information about dynamic processes in the oral cavity that are important for the proper evaluation of patients' conditions, where quick diagnosis and cooperation from the patient are required. Increasing interest in diagnosing diseases at the early stages and minimizing risks for the patient due to less invasive approaches of analysis has resulted in the popularity of the salivary approach to diagnosis [2].

The reason for the diagnostic capacity of saliva is its complicated biochemical composition of saliva. It contains many organic and inorganic compounds, such as enzymes, immunoglobulins, antimicrobial peptides, nucleic acids and metabolites that provide information about healthy and diseased conditions [3]. The compounds of saliva can be acquired from several different sources, including salivary glands, gingival crevicular fluid, oral epithelial cells and oral microbiota. This etiology that is multifactorial

enables saliva to be a single diagnostic platform, to both local oral change and a systemic effect.

When applied to dental diseases, these biochemical components indicate the processes of demineralization, inflammation, microbial activity, and tissue breakdown, which play a key role in the formation and development of diseases [4].

The development of new diagnostic tools has also enhanced the use of saliva in the modern dental practice. The sensitivity and specificity of salivary biomarkers have been enhanced with high-throughput analytical methods such as molecular assays and biosensor-based platforms. Such developments help in detecting the small biochemical alterations that can be detected before the clinical symptoms, and as such, it helps to intervene early and better control of diseases. New modalities of imaging and diagnostics in the field of dentistry are being more and more complemented with biomarker-based modalities, with the shift towards more integrative and data-driven clinical decision-making [5].

The idea of precision dentistry has also highlighted the applicability of salivary biomarkers in clinical practice. The unique differences in susceptibility to diseases, disease progression, and response to treatment require tailored approaches to diagnostics. Salivary biomarkers can be used to stratify patients according to biological risk profiles to facilitate preventive and therapeutic actions. The method is also quite useful in the field of restorative and prosthodontic dentistry, where the outcome of treatment is closely associated with the oral environment of a patient, such as the level of salivary flow, buffering capacity, and inflammatory conditions [6].

Another promising area where the role of salivary diagnostics can be highly valuable for improving patients' conditions is related to the identification of molecular and cellular biomarkers that can be involved in the development of potentially malignant diseases and even oral cancers. The early identification of these conditions will help enhance the effectiveness of treatment, and salivary diagnostics can help avoid the need for invasive measures [7,8]. Timely prevention of these diseases is important in regard to better health outcomes and survival rates, so salivary diagnostics can turn into an effective tool for regular screenings that can be performed at the dental check-up.

Furthermore, there are also various salivary biomarkers useful for the examination of other oral diseases, especially dental caries and periodontal disease. Not only do they help identify these diseases and track their development, but they can also give information about the degree of activity, severity of a disease, and the treatment's success. Using salivary diagnostics to complement the traditional techniques used in dentistry may help ensure better accuracy of the procedures through the unbiased biochemical data.

2. Review Methodology

The purpose of this literature review is to provide a thorough literature review that will be based on salivary biomarkers and their usage in relation to oral diseases, preventive dentistry, periodontal and peri-implant diseases, prosthodontics, and diagnostic dentistry. In order to identify relevant articles, a combination of words such as saliva, biomarkers, oral disease, diagnosis, restorative dentistry, prosthodontics, and dental practice-related words was used. Literature articles that were more relevant, novel and clinically important, and fit the scope of the review were included. The highest priority for inclusion was peer-reviewed articles, systematic reviews, and the most recent evidence that explained biological principles, diagnostic uses, and clinical applications of salivary biomarkers. The identified literature was then categorized based on the subject matter.

3. Biological Characteristics of Saliva and Their Clinical Significance

Saliva is considered to be a biologically active liquid, which is highly useful for both diagnosis and treatment of dental diseases. It comes from big and small salivary glands and is composed of different biomolecules such as proteins, metabolites, nucleic acids and microbial components that indicate the physiological status of the mouth environment. The development of techniques allowed scientists to study in detail these components and increased the significance of saliva as one of the high-quality means to detect and trace diseases [9]. Thanks to the emergence of metabolomics in the study of saliva, its use has extended further by linking biochemical profiles to specific physiological processes connected with oral health and disease [10]. The main functional characteristics of saliva can be described by physicochemical parameters, including secretion rate, buffer effect and pH. These factors play an essential role in maintaining homeostasis of the oral cavity through regulating acid-base balance and cleaning food remnants, as well as microorganisms. This balance can be disturbed by the change in flow or composition and hence cause such oral diseases as caries and erosion. Buffer activity plays an important role in neutralizing acid generated as a result of bacterial metabolism that aids in maintaining the mineral organization of enamel and dentine [11].

Saliva helps in maintaining the structural integrity of tooth enamel and dentin through its interaction with their surfaces. The saliva facilitates the development of acquired pellicle as the protective layer against enamel and dentin erosion and mechanical polishing due to chemicals and abrasion. Saliva, erosion, and attrition interactions are quite complex and rely on the saliva composition, saliva flow and exposure to either dietary or intrinsic acid. The described process is particularly useful when dealing with restorative dentistry, where materials' performance and durability are linked to the patient's oral environment [12]. Besides the protective purpose of saliva, the diagnostic purpose of saliva concerning oral health cannot be ignored. The use of saliva for monitoring purposes is connected with the presence of saliva biomarkers, which reflect the progression of inflammation and destruction of tissues, as well as microbial activities. Recent research is dedicated to the creation of clinically useful diagnostic tools on the basis of saliva analysis and the usage of saliva markers in order to monitor disease progression

and the effectiveness of the treatment. The saliva collection procedures must be standardized owing to the influence of methodology on the levels of the biomarkers [13,14]. The relationship between oral microbiota and saliva makes its importance in clinical settings evident. As a reservoir of microorganisms, saliva is where microorganisms can come in contact with host tissues. Contacts not only the state of the mouth, but also more global biological processes, such as the well-being of the system and aging. The significance of the salivary bacterial community can be explained in terms of its application in predicting the risk and occurrence of diseases by taking into consideration the variations of the community [15]. In Figure 1, the biological functions of saliva that involve oral homeostasis and diagnostics are indicated.

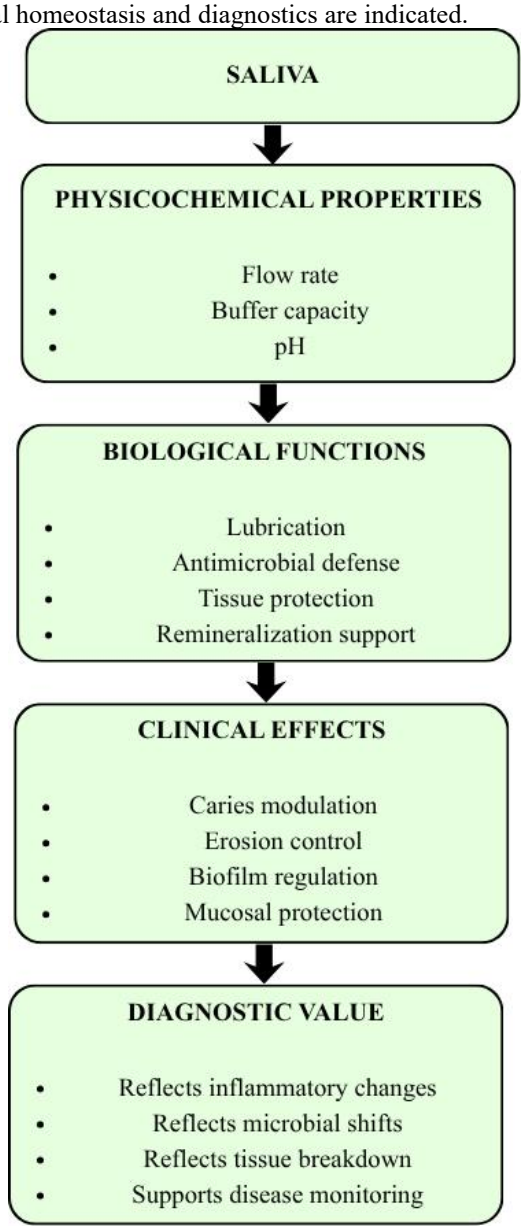

Figure 1. Biological basis of saliva in oral homeostasis and diagnostics

Its biological and diagnostic qualities, coupled with its accessibility, make saliva a fundamental aspect of contemporary dental practice. Its effect on the integrity of the oral tissue, its interplay with restorative materials, and its ability to indicate changes associated with diseases justify its use in clinical examination and management of the patient over the long term.

4. Classification of Salivary Biomarkers Relevant to Dental Practice

Salivary biomarkers denote the number of biological indicators that point towards the physiological and pathophysiological processes which are occurring in the oral cavity at present. Depending on their biochemical character and clinical applications, they can be roughly divided into proteomic biomarkers, enzymatic biomarkers, microbial biomarkers and nucleic acid biomarkers. This type of classification offers a conceptual framework of how these biomarkers can be used in diagnosing diseases and predicting and assessing risks in the field of dental care. Proteomic biomarkers consist of various types of proteins and other biopolymers like enzymes, immunoglobulins, mucin and antimicrobial peptides that have significant roles in the health protection of the mouth, lubrication and homeostasis. The alterations of salivary protein composition have been established as a significant factor in the caries development in the mouth, particularly due to its effects on bacterial adhesion and demineralization of the teeth [16]. Moreover, salivary proteins cannot only be used as a disease surveillance tool, but also as a risk predictor, and can be used in preventive and conservative dentistry.

Another important type of biomarkers includes enzyme biomarkers, which are related to metabolism and cell breakdown within the oral cavity. Breakdown of extracellular matrix and regulation of microorganism activity involves such enzymes as matrix metalloproteinases, amylase and other proteases. Increased levels of some enzymes are often related to pathological conditions like periodontal disease and active carious lesion development. Enzymatic tests were extensively analyzed for their ability to provide sensitive and flexible detection in clinical settings; however, the problem of achieving optimal specificity and reproducibility remains challenging [17]. Microbial biomarkers derived from the composition of the oral microbiome can be useful for the analysis of processes occurring within the oral cavity ecosystem. Initiation and development of diseases are associated with the presence of certain bacteria in particular numbers and with their metabolites. Experiments conducted both clinically and biochemically indicated that using both microbial profile data and salivary markers improved caries risk assessment and monitoring [18]. This biomarker type is especially suitable for the analysis of biofilms and their application for the restoration of tooth structure.

Such biomarkers as DNA, RNA, and microRNA are referred to as nucleic acid-based and have become particularly prominent because these biomarkers are highly sensitive to changes in the molecules. Of these, microRNA-bearing salivary exosomes have gained particular prominence in their role in intercellular communication and in gene expression regulation. Periodontal diseases have been shown to have a unique microRNA profile, suggesting that they can be used to diagnose the disease at an early stage, as well as

predict it [19]. Biomarkers that are based on nucleic acids have tremendous potential for identifying subclinical changes, which can be treated at an early stage. Another aspect that is essential for clinical applications of salivary biomarkers is their stability. Enzymatic reactions and environmental factors may destabilize salivary biomarkers, thus compromising the accuracy of the test results. Strategies have been adopted to ensure the stability of salivary biomarkers while they are in storage and in testing phases [20]. In addition to categorizations of individual groups of biomarkers, a composite approach to evaluate the state of oral health using salivary biomarkers and the burden of oral microorganisms will be more accurate. Scientific studies have shown that there are differences in the amounts of biomarkers that can be distinguished by grouping of microorganism profiles in relation to various dental diseases and their severity in different patient groups [21]. This would lead to enhanced precision in diagnosing oral diseases and better decisions based on those diagnoses. Table 1 provides a summary of the different groups of salivary biomarkers and dental uses of the biomarkers. Figure 2 shows the classification scheme of salivary biomarkers.

Table 1. Major categories of salivary biomarkers and their dental relevance

Biomarker category	Representative examples	Dental relevance
Proteomic biomarkers	Immunoglobulins, mucins, antimicrobial peptides	Reflect host defense, lubrication, and caries susceptibility
Enzymatic biomarkers	Amylase, matrix metalloproteinases, proteases	Indicate tissue breakdown, inflammatory activity, and lesion progression
Microbial biomarkers	Cariogenic and periodontopathogenic microorganisms, microbial metabolites	Reflect biofilm activity and disease-associated ecological shifts
Nucleic acid-based biomarkers	DNA, RNA, microRNA, exosomal RNA	Support early molecular detection and disease monitoring

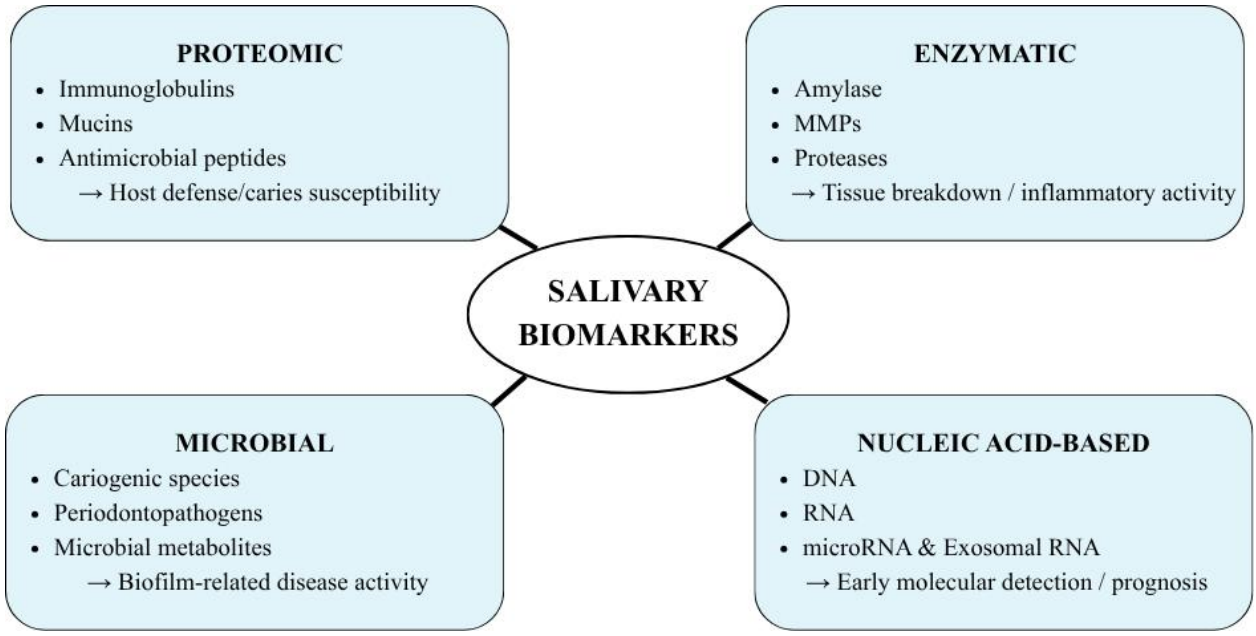

Figure 2. Classification framework of salivary biomarkers in dentistry

These unique but intertwined categories highlight the multiple uses of salivary biomarkers in diagnosis. Their combined use offers a multidimensional view of oral diseases, which justifies their applicability in the current dental practice, particularly in the domain of preventative and restorative treatment.

5. Salivary Biomarkers in Caries Risk Assessment and Preventive Strategies

Present-day approaches towards the risk assessment of caries are based on the detection of biological changes occurring prior to the appearance of carious lesions. Caries experience models, historically driven, and models driven by behavior, have traditionally been gradually substituted with biomarker-driven models, which are indicative of continuously progressing pathogenesis processes. This is in line with the provisions of predictive and preventive measures, which can predetermine at-risk subjects [22]. The biomarkers of the saliva give an understanding of the dynamic balance between the processes of demineralization and remineralization in the mouth. They are proteins, enzymes, and microbial activity products which suggest acidogenicity, host reactions and mineral deficiency. They discovered that there are certain salivary profiles that are associated with caries

susceptibility, thereby making them effective disease risk predictors. These findings substantiate the suitability of saliva in assessing disease risk in adolescents who have an anatomy that is predisposed to caries but shows no clinical signs [23].

The theory of precision-based healthcare solutions is consistent with biomarkers in the use of saliva in preventive dentistry. Although the concept of biomarker-based diagnostic processes in periodontology is not new and is actively studied, the concept of biomarkers in the context of caries prevention can also imply an individual assessment of the risks, which can be used to develop a beneficial approach to preventive measures. It incorporates the individualized fluoride therapy, the diet therapy and the recall time in terms of the biochemical parameters of the patient, thus enhancing the preventive outcomes [24]. In practice, saliva-based diagnostics can prove to be extremely useful in community and clinic care due to their noninvasiveness and due to the ease of collection, therefore making them an ideal source of material utilized in mass screening, particularly in children. The importance of saliva biomarkers was proven by school-based saliva studies to be a relevant predictor of caries risk and to be able to measure the effectiveness of preventive interventions. These applications indicate the potential of these tests in the sense that they can be used in public health intervention programs to help in reducing the rate of caries by detecting and treating it at an early stage [25, 26]. Nevertheless, even though it possesses a number of strengths, there are some methodological issues that need to be discussed so that they can be successfully implemented into clinical practice. The salivary biomarker concentration can depend on some patient-related factors, such as age, nutritional habits, circadian fluctuations, and systemic disorders. These variables might affect the obtained results, therefore making it difficult to understand them. Hence, there is a need to standardize such processes. Salivary biomarkers are also an interesting addition to the caries risk assessment instrument, which offers objective biological data that can be used to supplement the current diagnostic devices. These help in providing a paradigm shift in early treatment, personal care and improved dental health because they are used in preventive dentistry.

6. Salivary Biomarkers in Periodontal and Peri-Implant Health

The etiology of periodontal and peri-implant diseases is an inflammatory disease that is marked by progressive degeneration of supporting tissues, and which must be well diagnosed and regularly monitored to ensure that there is no progression. The conventional diagnostic tools, such as probing and radiographic techniques, mainly point out tissue damage in the past and not the disease process itself. This makes salivary biomarkers a more reliable technique for evaluating the disease activity and prognosis for periodontal and implant therapies [27]. There are numerous studies that demonstrate the existence of different inflammatory markers, which trigger periodontal and peri-implant diseases. They are interleukins 16 (IL-16), 10 (IL-10) and 12 (IL-12), and TNF- cytokines, bone remodeling factors such as the receptor activator of nuclear factor kappa-B (RANK) and osteoprotegerin (OPG). Studies have shown that changes in these biomarkers affect the progression of disease and the responses of patients to different treatments [28].

Salivary biomarker profile has also been analyzed in terms of its diagnostic capability in the identification of salivary biomarkers to differentiate between healthy conditions, gingivitis, periodontitis and peri-implant disease. It has been noted that the multiple use of biomarkers as opposed to a single biomarker implies increased sensitivity and specificity rate in the detection of the present state of the disease and future developments [29]. This method takes into consideration the multifactoriality of the disease and gives more information about the biological factors. Procalcitonin is one of the biomarkers that have been tested in saliva and peri-implant crevicular fluid in peri-implant health. High concentrations of these markers show inflammation and infection of peri-implant regions, which is why they are appropriate to diagnose peri-implantitis. The results can be applied clinically due to the importance of detecting inflammatory activities around the implants to avoid bone loss and implant failure [30].

Salivary biomarkers find significant applications in the prosthodontic treatment procedures, especially where the salivary gland functionality has been affected or where the saliva makeup has been affected. Salivary flow and biochemical components of saliva will differ and this change will affect the development of periodontal diseases and stability of peri-implant tissues. This association plays a vital role in treatment, such as in patients with systemic diseases or xerostomia, where the inability to produce saliva normally may affect their natural teeth and also dental implants [31]. Salivary diagnostics and periodontal or peri-implant treatment are evidence of the transition to bio-inspired and minimally invasive treatment processes. More sophisticated methods of salivary diagnostics have been advanced to offer the capability of designing fast and effective diagnostic tools that can be applied in the clinical environment. These methods contribute to constant observation of the disease activity and the timely response of practitioners to achieve improved treatment results [32]. Table 2 highlights some of the oral diseases analyzed using salivary biomarkers and their impacts on patients' clinical health. Applications of salivary biomarkers in the treatment of oral diseases are shown in Figure 3.

Table 2. Salivary biomarkers in major oral conditions

Condition	Key salivary biomarkers	Clinical significance
Dental caries	Salivary proteins, enzymes, microbial byproducts	Risk assessment, early lesion prediction, and preventive planning

Periodontal disease	IL-1β, TNF-α, IL-10, MMPs, RANK/OPG-related markers	Detection of inflammation, tissue destruction, and treatment monitoring
Peri-implant disease	Procalcitonin, inflammatory cytokines, and crevicular inflammatory markers	Early detection of peri-implant inflammation and risk of implant failure
Oral cancer and precancer	Molecular and inflammatory salivary markers	Non-invasive screening, prognostic evaluation, follow-up

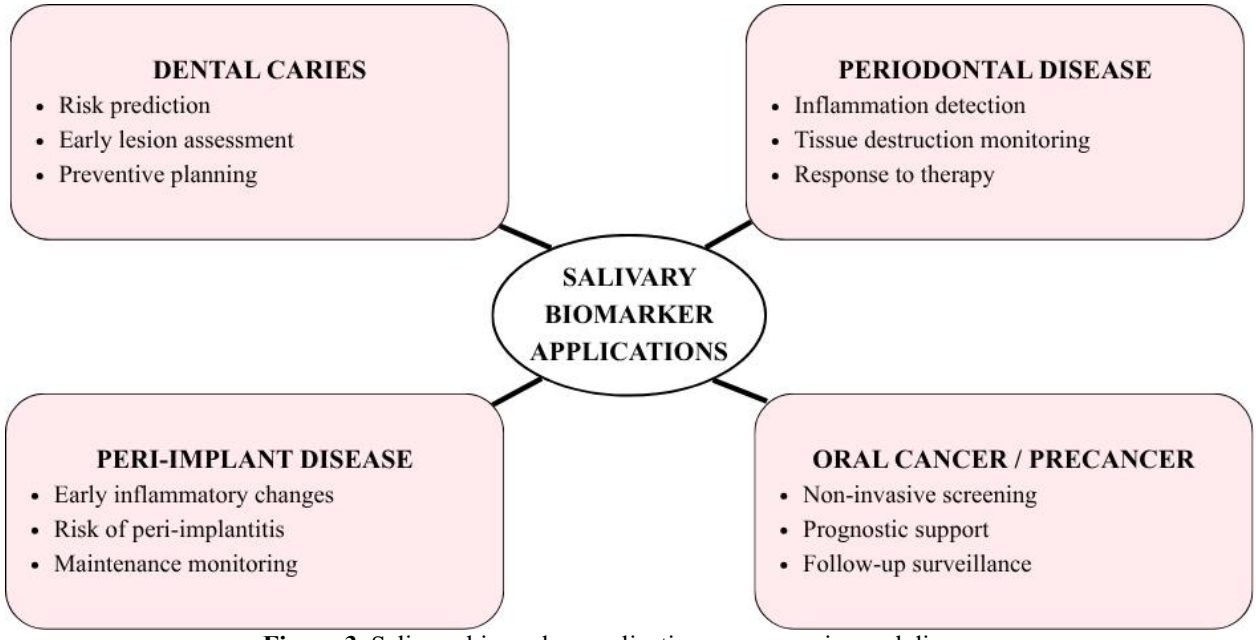

Figure 3. Salivary biomarker applications across major oral diseases

Salivary biomarkers, therefore, provide a valuable adjunct to conventional diagnostic methods by offering insight into current disease status and future risk. Their application in periodontal and peri-implant health enhances clinical decision-making, supports personalized treatment strategies, and contributes to improved maintenance of both natural teeth and implant-supported prostheses.

7. Salivary Diagnostics in Prosthodontic and Restorative Treatment Planning

Salivary biomarkers are acquiring great significance in the treatment planning of prosthodontic and restorative therapies, as they provide biologically derived information, surpassing the standard clinical and radiological investigation. Salivary biomarkers are useful in providing information regarding inflammatory burden, tissue response, material changes, and patient-related risk factors that might influence the treatment planning, prognosis, and maintenance. It can be important to prosthodontics where the outcome of the prosthodontic treatment not only depends on the design and choice of appropriate materials, but also on the biological state of the mouth cavity [33].

One of the uses of salivary biomarkers is associated with the durability and longevity of the bonding process and the material. The oral cavity is a highly dynamic environment in which saliva is in constant contact with dental tissues, adhesive interfaces, and prosthodontic materials. The study of artificial saliva aging models found that the release of ions from the ion-releasing restorative materials has an effect on the long-term stability of the adhesive restorations that are used in conjunction with universal adhesives [34]. The effects are consequently directly connected with the restoration of the bonding interface stability throughout time, which must be considered when addressing the impact of salivary fluid on the restoration treatment planning.

Salivary biomarkers can also be applicable in analyzing biological changes in caries and dental restorations. It is important to understand that dental caries are not merely defects within hard tissues but represent diseases that include the presence of inflammatory and oxidative processes within the mouth. Based on the results of several longitudinal short-term studies, it has been shown that caries and their restorative management are capable of altering periodontal inflammatory and oxidative conditions, indicating that the planning of restoration treatments must not be viewed as purely mechanical actions, but must rather be seen in the context of global biology [35]. This suggests that saliva testing might serve as a tool for determining whether the patient needs special attention after the procedure due to increased inflammation or oxidation in the mouth.

It is especially crucial in prosthodontic cases of patients with medical issues and the aged population. Poor retention, comfort level, oral mucosa health, caries resistance, and tolerance of prosthesis are associated with salivary flow, composition changes, and drug-induced xerostomia in removable or fixed prosthodontics. Xerogenic drugs are common for frail elderly patients, as well as those with poor oral health. Therefore, the conditions of prosthodontic treatment for elderly patients, in which saliva is a crucial element

in prosthodontics [36], can be analyzed with salivary assessment, and preventive actions can be taken both pre and post-prosthetically.

Also, saliva is a very good medium for monitoring the course of the treatment in the case of any discomfort in prosthetic treatment. Specifically, local and systemic markers have been researched in TMJ disorders in order to be used as diagnostic tools or indicators of effectiveness in the treatment of such cases. Therefore, the field of salivary monitoring expands into more complicated cases and makes it possible to apply salivary diagnostic procedures not only in tooth or implantology but in oral rehabilitation in general [33].

These recent advances in the area of analytics technology contribute further to increasing the importance of diagnostic tests based on saliva in restoration and prosthodontic procedures. The new biosensor and molecular systems can now identify small fluctuations in biomarkers alongside traditional laboratory procedures by increasing sensitivity. These technologies could contribute to making saliva a more practical and effective tool for diagnosis, risk assessment, and monitoring treatment [37]. The third table presents the analysis of the salivary test in terms of the major implications for prosthodontics and restorative dentistry.

Table 3. Prosthodontic and restorative implications of salivary assessment

Clinical domain	Salivary factor or marker	Implication for treatment planning
Adhesive restorations	Salivary chemistry and aging environment	Influences bond durability and restorative longevity
Caries-related restorative care	Inflammatory and oxidative salivary changes	Supports follow-up intensity and preventive reinforcement
Geriatric prosthodontics	Reduced salivary flow, xerostomia-related changes	Affects comfort, retention, mucosal tolerance, and caries risk
Complex oral rehabilitation	Local or systemic biomarker changes	Supports risk stratification and individualized maintenance planning

Salivary diagnostics, therefore, offers a clinically meaningful adjunct in prosthodontics and restorative dentistry. By linking treatment planning to the biological status of the oral environment, salivary biomarkers can support more individualized, preventive, and prognosis-oriented care.

8. Chairside Diagnostic Technologies for Salivary Biomarker Assessment

Salivary biomarkers' use in clinical practice cannot simply depend on the importance they have biologically; it is also contingent upon the tools that could assist in translating experimental findings into actual instruments for clinical use in the chairside setting. That is why point-of-care diagnostic equipment is so appealing to dental medicine, enabling quick decision making, reducing the number of medical operations required and being easily integrated into clinical practice. In fact, salivary fluid can be used most appropriately in such a setting because saliva collection does not involve any invasive procedure, is rather simple and can be analyzed with miniaturized devices. The most promising development in salivary biomarker analysis at the chairside is probably the microfluidic point-of-care systems. Such systems can work with small sample volumes, but with an exceptionally high analytical sensitivity and a potential to integrate a variety of steps, including sample preparation, isolation of biomarkers, and their analysis into small sizes. In addition, the applications of these devices in saliva analysis have become significantly more common since they can be analyzed quickly and need minimum involvement on the part of the operator. The strategies listed above are particularly applicable to the dental field, in which a fast diagnosis of any inflammatory, infectious, or metabolic alterations can prove useful in the initial diagnosis and prompt treatment planning [38]. Chairside saliva testing technology has also been improved with the use of biosensor technology to improve its usefulness. Dental biosensors are under development with the aim of detecting a broad spectrum of targets, such as proteins, enzymes, nucleic acids, and bacteria. The sensitivity, specificity, and the possibility to perform the test in real-time in the clinic are some of the highest benefits of these devices. It is possible to make such devices useful in terms of screening and monitoring, particularly when it is necessary to perform repetitive tests to evaluate caries, periodontal diseases, or peri-implant diseases [39].

The recent developments in the area of salivary biomarker technologies have further increased the pace of transformations that take place in the diagnostic process in the field of dentistry. The saliva tests have been made more precise and even clinically applicable due to the improved molecular detection, miniaturization and signal amplification. This implies that the era of salivary diagnostic tests is at hand, as its implementation will enable quick, dependable, and versatile biomarker identification as per the needs of the dentist. Besides the change of concept, there is a technological change, i.e. it has become more common to regard salivary biomarker tests as a means of incorporating biological data in decision making [40]. The introduction of chairside salivary diagnostic tests may be seen as part of the overall trend of precision medicine in dentistry. Precision medicine implies that patients' biological characteristics should be used in developing personalized plans for disease prevention and treatment. Such a shift can be achieved through the incorporation of salivary diagnostic technologies into the dental practice to diagnose disease susceptibility, the effect of treatment, and tailor the maintenance

schedule based on a particular biomarker profile as opposed to the traditional clinical indicators [41].

On the other hand, the implementation of the chairside paradigm promises great success; still, the issues associated with analytical validity, cost-effectiveness, user-friendliness, and standardization need to be considered as well. To ensure that these diagnostic tools are incorporated as a routine part of dentistry, they need to prove to be reliable in a clinical practice as well as be user-friendly by the dental practitioners who, in most cases, do not have much laboratory training. The technologies will be more and more applicable in the sphere of restoration, periodontics and prosthodontics, where they help to prevent the disease and to create their own treatment plan. The introduction of the chairside diagnostic technologies can thus be considered to be the most significant interface between the salivary biomarker's knowledge and its clinical use. The latter tools can help transform the salivary diagnostics into a component of traditional tooth treatments because they will offer immediate outcomes and reduce the invasiveness of the sampling process.

9. Current Challenges, Standardization Needs, and Future Directions

The potential of salivary biomarkers in clinical settings is great, but the overall implementation of these tools in dentistry remains hindered by many scientific and translational issues. To begin with, saliva is a highly intricate and dynamic biofluid that is subject to multiple factors like inflammation, overall health, diurnal change, dietary patterns, medication, and sampling and saliva hydration. All this could alter the level of biomarker expression and affect their interpretation, making them even more difficult to differentiate physiological changes related to pathology. That is still a serious problem in the development of a robust diagnostic framework for chronic inflammatory diseases [42]. The next issue is related to the poor consistency of diagnostic properties across different research studies. Host-derived salivary biomarkers show great sensitivity and specificity in relation to a specific definition of a disease, sample collection method, technology used for analysis, and demographic parameters of patients. Based on the systematic review in periodontology, it can be said that even though many biomarkers are potentially diagnostic, their performance is far from being consistent [43]. There is an analogous situation regarding the diagnosis of oral cancers, whereby there have been many proposals for salivary biomarkers, but reproducibility, threshold setting, and comparative testing still present challenges [44].

What is necessary is the standardization of the salivary diagnostics if salivary diagnostics is to evolve from being merely experimental to becoming a reliable clinical process. There are various factors that influence the stability of biomarkers and the results of any assay conducted, and these include variability in methods of collecting saliva, stimulating saliva flow, storing samples, and processing samples. In addition, differences in the type of sample that is analyzed (whole saliva, gland-specific saliva, or combinations of oral fluids) can affect results. It has been found that even in relation to periodontitis where comparative studies were carried out, the diagnostic ability is greatly influenced by methodological variations. What this means is that there is a need for standardized methodologies and verified reference standards [45]. However, the issue of methodological consistency and standardization is only one side of the problem, because there is a need for the clinical application of biomarkers in restorative, periodontal, and prosthodontic treatments. In some cases, even though a device has the capability for analysis, it may still remain infeasible because it lacks the ability to define the thresholds, reproduce the results under field conditions, or fit into chairside procedures. This is not uncommon in other dental devices as well. It is important to note that no matter how promising the technology appears, the device should always be validated to confirm whether it can actually be used. For instance, the utilization of intra-oral scanners during the preparation of subgingival crowns is an example of a scenario where technological advancements alone were not sufficient [46].

There are several simultaneous improvements that will drive forward the development of salivary diagnostics in the future. Biomarker cutoffs, multi-marker panels, and disease-specific models require large-scale longitudinal investigations for their establishment. To enhance the comparability of studies and regulatory approval, standardized methods of sample collection, preprocessing and data analysis should be used. By combining digital diagnostics with biosensors and artificial intelligence interpretation with salivary biomarkers, they will be even more valuable as they will allow them to assess risks promptly and individually [42]. In the diagnosis of multifactorial diseases, including periodontitis and oral squamous cell carcinoma, multi-biomarkers will probably be more informative than individual analyses [44]. The latest development in the analysis of salivary biomarkers is that they are now not just showing the proof-of-concept, but instead are creating standardizable systems and clinical systems. This will require the improvement of methodological reliability, analysis of diagnostic tests and the disjuncture between biomarker discovery and clinical dentistry. As soon as these obstacles are surmounted, salivary diagnostics may be a part of the precision-based oral health care.

10. Conclusion

Salivary biomarkers are a clinically useful tool, and this is an opportunity to examine the oral disease activity and diagnose it. Their worth is that they can reflect biochemical, microbial, and inflammatory alterations and be utilized to evaluate carious lesions, periodontal disease and peri-implant states. The reason why this topic is important is due to the role of salivary markers in the field of restorative dentistry and prosthodontics, since the properties of saliva will influence how the restorative material will work and the biological response and result of the procedure. The technique has also been applied to everyday dental

practice, although this is now through the application of chairside devices to sample and analyze saliva (biosensors and microfluidic systems). These devices aid decision-making and match the concept of precision dentistry. Nonetheless, questions of variability, standardization and diagnostics need to be tackled before the implementation of salivary biomarkers into clinical use. Standardized approaches and multi-biomarker diagnostics should be used in order to resolve these issues.

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