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REVIEW A R T I C L E

Saliva's Biochemical Analysis for The Diagnosis of Systemic and Oral Diseases: A Review

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Abstract

Background The diagnostic use of saliva for systemic and oral disorders is reviewed in this article. Saliva has unique advantages over serum as a diagnostic fluid because it is non-invasive and can be obtained by anyone with a little training. Saliva may also provide a financially reasonable way to screen large populations. Saliva from a single large salivary gland can be used to diagnose diseases unique to that gland. However, because whole saliva is easy to obtain and contains serum components, it is commonly used to diagnose oral and systemic disorders. However, saliva contains a more diverse microbial habitat and a lower concentration of biomolecules compared to blood, which may have an unexpected impact on the detection results.

Purpose These issues will eventually be solved by creating and developing a highly sensitive detection platform, and saliva testing will likely open new horizons for saliva detection. Identify the disease . Researchers use a variety of techniques and techniques in an attempt to identify salivary biomarkers for systemic and oral disorders inLast few years. The review aspires to provide a comprehensive perspective on salivary biomarkers in relation to oral and systemic diseases. Saliva analysis may be useful in diagnosing genetic disorders, autoimmune diseases, malignant and infectious diseases, and endocrine disorders, as well as in assessing therapeutic levels of drugs and monitoring illicit drug use.

Conclusion The various tasks that saliva completes in the oral cavity are accomplished by the biochemical, physical, and interaction characteristics of these salivary constituents. These days, there are numerous assays available to examine different salivary parameters; nevertheless, in order to get significant data, collection and storage procedures must be standardized.

Keywords: Saliva; Composition; Oral; Systemic diseases

1 Introduction

Every illness deviates from optimal health, and effective treatment and elimination of the illness depend on early detection. Because saliva is non-invasive, inexpensive, easy to store, and easy to collect, saliva-based diagnostics has received a lot of interest [1]. There are issues with collecting other body fluids, such as blood and urine, which are frequently used to diagnose disorders. Important elements found in saliva may serve as prospective biomarkers. Saliva will therefore complement the diagnostic toolbox by offering crucial details regarding digestive and dental health [2]. Salivary biomarkers span a variety of scientific domains, including transcriptomics, metabolomics, and proteomics [3]. This study highlights the potential of saliva as a diagnostic specimen by examining its varied capacities and exploring studies connected to saliva-related diagnostics and its association with systemic disorders [2, 4]. Significant advancements have been achieved in the early detection and screening of numerous illnesses, particularly cancerous disorders, in the past few decades [5]. Accurate testing are still unavailable in many situations, and some of these techniques are costly or invasive. This is the situation with oral cancer, the sixth most common cancer globally, which has a 50% 5-year survival rate and is often identified at an advanced stage [5, 6]. A biomarker is a feature that can be objectively measured and assessed as a sign of healthy or pathological processes, or as a sign of how a medication is responding to therapeutic measures, according to the 2011 Biomarker Definitions Working Group [7]. One of the most ambitious goals of modern research is to develop salivary biomarkers and employ them in clinical practice in the near future [6].

1.1 Properties of saliva as a diagnostic fluid

Saliva is a crucial bodily fluid that includes a variety of proteins, many of which have the potential to be linked to certain disease phenotypes and are therefore highly valuable in the detection of human diseases [8]. Whole saliva is often the type of sample that is investigated most frequently since it can be obtained quickly, easily, and without the use of specialized equipment [9]. Roughly 30% of blood proteins are detected in human saliva, along with other proteins that are clinically significant. In contrast to blood or urine, he emphasizes that saliva can be used for clinical purposes [10]. These advantageous proteins could function as biomarkers, paving the way for the use of non-invasive biofluids for illness monitoring and detection if they are found and proven [11, 12].

Saliva has been used for diagnostic purposes since the turn of the century. The use of saliva testing to assess pathological or medical problems is becoming more and more significant [13]. One of the biological fluids in the human body, saliva is clear, somewhat acidic (pH = 6.0–7.0), and heterogeneous in composition.3. The gingival spinal fluid and the secretions of the major and minor salivary glands together make about In addition to saliva [4, 13].

There are two types of saliva: total saliva and gland-specific saliva [2]. Human saliva is an indicator of overall health and wellbeing. Because saliva contains about 20% of the proteins found in blood, it provides a non-invasive method of identifying biomarkers associated with a particular illness state [2, 14].

When used as a diagnostic fluid, saliva has a number of advantages over blood that make specimen collection non-invasive, easy, and secure. Its makeup represents the body's state of health and illness and can be used to diagnose systemic disorders [2, 15].

1.2 Factors affecting the diagnosis of saliva

Technology for detecting saliva biomarkers has been widely employed in the healthcare system to diagnose diseases. Figure 2 [16] Saliva has been used much more frequently as a diagnostic or screening tool throughout the last ten years. The favored approach for diagnosing conditions is now to use saliva samples because they are simple and non-invasive to obtain. It has been determined that saliva diagnosis may be used in place of serum protein vital signs. But the best method for gathering saliva hasn't been decided upon yet [8].

1.3 Saliva composition

Saliva is a complex biological fluid that is primarily made up of cell debris, plasma discharges, salivary gland and upper respiratory tract secretions [17], gingival spinal fluid, and microbial components [18]. Saliva samples are now the preferred method for identifying illnesses due to their ease of collection and non-invasive nature. Saliva diagnosis has been found to be a viable alternative to serum protein vital signs. However, the optimal technique for collecting saliva has not yet been determined [18]. Saliva contains a wide range of molecules, including metabolites, DNA from mRNA, or miRNA, a proteins (cytokines, enzymes, chemokines, immunoglobulin, etc.), and inorganic ions. These molecules' variations in concentration can be used as biomarkers to identify oral diseases early on or track how well treatment is working [19].

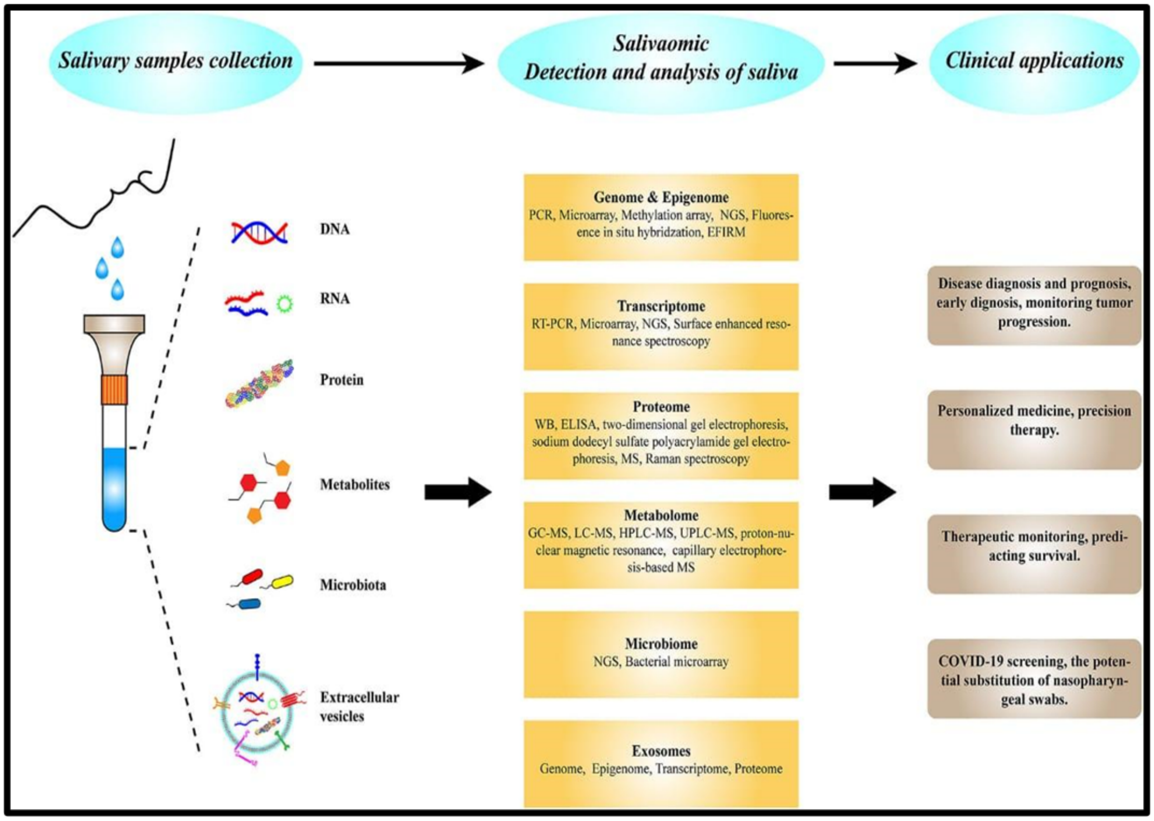

Figure 1: Process and application of saliva diagnosis.

2 Materials and Methods

The basis for this research was the existence of bioactive components in saliva that can be exploited as biomarkers for early diagnosis and detection of oral health issues as well as possible links to systemic and oral disorders. Are there any alterations in the biological components of saliva that could be utilized for diagnosis? is the primary inquiry that this evaluation addresses. Electronic databases such as PubMed, Researcher, Science Direct, Web of Science, and other websites such as Wiley Online Library and Google Scholar were considered in this review. Focus only on the available literature. We used the keywords "saliva," "saliva," "biomarkers," "oral diseases," "systemic diseases," and relationships between terms to search the PubMed database. We only chose English-language articles. To find the best papers for our topic, we first looked at the titles and abstracts of the submitted papers. The full-text articles were then examined and made part of the review.

2.1 Collection methods

Saliva can be collected using six different methods, as Figure 2 illustrates. The effects of various saliva collecting locations on various saliva biomarkers vary. Numerous scientific contexts, such as controlled trials conducted at random Processing samples from healthy volunteers frequently results in sampling errors as well as statistical inaccuracies [8]. Saliva can be collected using six different methods, as Picture 2 illustrates. The effects of various saliva collecting locations on various saliva biomarkers vary. Numerous scientific contexts, such as controlled trials conducted at random Processing samples from healthy volunteers frequently results in sampling errors as well as statistical inaccuracies [20]. Furthermore, unlike blood, saliva collection is non-invasive, its transportation and preservation are very convenient, and the risk of cross-contamination is relatively low [21]. All these are the advantage of saliva as a diagnostic fluid. However, compared with blood, the content of biomolecules in saliva is lower, and the microbial environment in saliva is more complex, which will have an unexpected impact on the detection results [9]. However, the construction and development of a highly sensitive detection platform will gradually solve these problems, and saliva testing may also become a new opportunity for disease screening, detection, and monitoring [16].

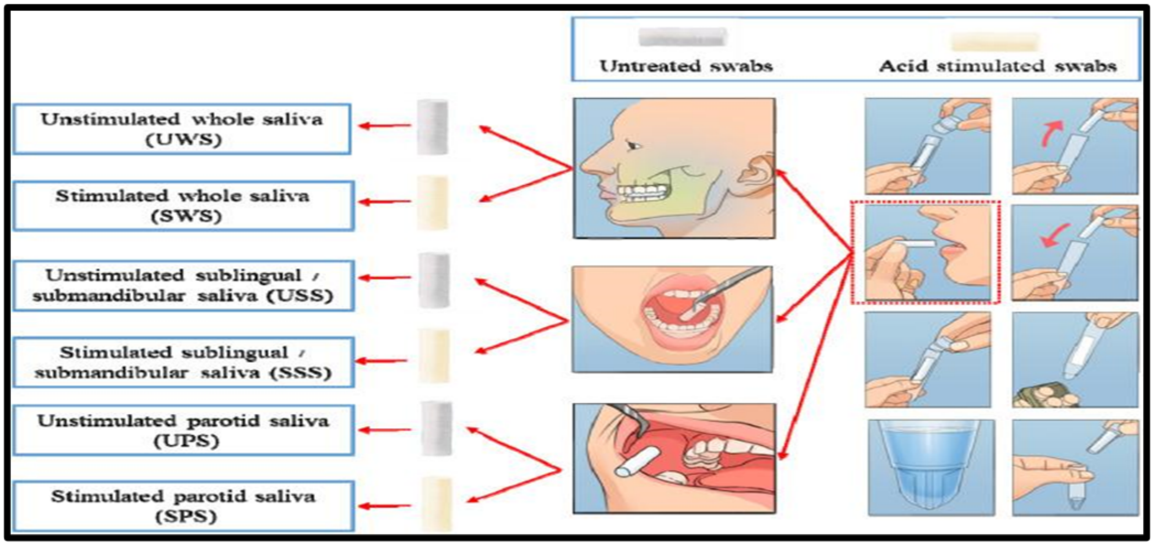

Figure 2: An illustrative overview of the different methods of collecting saliva.

3 Saliva in Disease Management

Saliva has a major role in prognostic outcome evaluations such as recurrence prediction, intervention evaluation, risk assessment, and disease screening [8]. Establishing clinical value from macromolecules and low molecular weight components is also necessary for saliva diagnostic advancement [20]. In this context, salivary variations noted in particular clinical circumstances have been contrasted with those of blood or other substances [22]. A.I. Lorenzo Busso et al. provide an overview of the salivary biomarkers found in various oral disorders using molecular biology techniques [23]. Saliva has been shown by Colak-Pegda et al. to be a good material for biochemical, toxicological, and immunological diagnostics of systemic disorders, the oral cavity, and the uncharted realm of neuropsychiatry [24, 25].

4 Diagnosis of Oral Diseases Using Saliva

The terms "oral diseases," or "oral and maxillofacial diseases," relate to conditions affecting the jaw ("condyle") and mouth ("stoma"). Periodontal disease and dental caries have long been regarded as two of the biggest worldwide oral health concerns [6]. It's crucial to remember that the main obstacles in oral diagnostics are figuring out the clinical usefulness of prospective biomarkers for screening (in asymptomatic individuals)***, forecasting the early start of disease (diagnostic tests), and evaluating the effectiveness of treatment and disease activity. via cutting-edge diagnostic procedures**. In theory, oral diagnostic testing ought to yield useful data for infection severity, disease localization, and differential diagnosis. This information can then be used by the doctor to develop treatments and will give them a way to assess how well they are working [26].

* **Salivary Biomarkers: Toward Future Clinical and Diagnostic Utilities**

4.1 Periodontitis

The irreversible loss of gingival attachment and the subsequent degradation of alveolar bone are hallmarks of periodontitis, a chronic inflammatory disease. Adverse cardiovascular events are a considerable risk related with periodontitis, as they are with other chronic inflammatory autoimmune diseases [27]. Since numerous microorganisms have been linked to Parkinson's disease (PD), pathogens are first detected by PCR or culture methods prior to receiving antibiotic treatment. Nevertheless, this element of saliva analysis has gained new significance due to the recent focus on the possible role of Parkinson's disease (PD) as a risk factor for cardiovascular and cerebrovascular disorders [14, 28] "Any measurable substance, structure, or process in the body or its products that can influence or predict the occurrence of outcomes or diseases" is what is meant to be understood as a biomarker [29].

4.2 Caries

Studies have been conducted on human saliva as a possible diagnostic tool for tooth decay and other disorders. A host, environmental, and microbial component imbalance leads to the multifactorial illness known as caries. The correlation between caries activity and salivary alpha-amylase renders it a significant indicator of host-associated variables [30]. The goal of this research is to identify the patient population at risk for saliva-based dental caries by developing a caries host predictor [31].

4.3 Salivary biomarkers of oral cancer

Reliable salivary biomarkers for OSCC screening have been identified thanks to frequent and non-invasive saliva collection [32]. Disease-related pathophysiological tissue alterations might manifest as changes in metabolism, proteins, or genes. More than 100 possible saliva biomarkers for OSCC have already been published in the literature as a result of the scientific community's increased efforts in the field of saliva research, which have yielded several studies [21]. Potential biomarker options include circulating cancer cells, microRNA, and cell-free DNA (cDNA). The majority of them can be easily tested because they are detected in saliva and are delivered straight into the bloodstream by the tumor [33]. Some possible possibilities are secreted into the blood in response to the tumor's surrounding microenvironment rather than coming from the cancer cells themselves. These biomarkers generally belong to the messenger RNA and proteins (mostly secretary) classes [34].

4.4 Sjögren's syndrome

It is a long-term autoimmune disease of the exocrine glands characterized by lymphocyte infiltration from the glands that are impacted. An infection of the salivary and tear glands causes dry mouth and eyes. Because these glands are biopsy-accessible, the molecular biology of the tissue-specific autoimmune process can be studied. Endocrinopathy can occur either in isolation (primary Sjögren's syndrome) or in conjunction with another autoimmune disease (rheumatoid arthritis, for example) [35].

5 Diagnosis of Systemic Diseases Using Saliva

A number of systemic illnesses can impact the salivary glands directly or indirectly, which can have an impact on both the volume and makeup of saliva produced. certain distinctive alterations could aid in the early identification and diagnosis of certain illnesses [36]. The following conditions can be diagnosed with saliva analysis [37]:

5.1 Genetic disease

1. Cystic fibrosis (CF) It is a genetically defined illness brought on by a CFTR gene mutation. In patients with cystic fibrosis, saliva is altered. The expression of the CFTR protein in the parotid gland's epithelial cells causes the gland to become involved. Before secretion is triggered with paraffin pledgets, the saliva of individuals with cystic fibrosis has significantly greater levels of cathepsin-D activity than that of healthy controls [33]. Saliva can be used as a diagnostic test for cystic fibrosis since the results for salt, potassium, and chloride concentrations were significantly greater than in healthy people. When comparing saliva from cystic fibrosis patients with that of healthy controls, there were higher concentrations of calcium, magnesium, and lactate dehydrogenase in the saliva from these individuals [38].

2. Ectodermal dysplasia: X-linked hypodense ectodermal dysplasia (HED) is the most prevalent type of ectodermal dysplasia. A study on the composition and flow of entire saliva in males with HED and female carriers was done by Lexner et al. Whole saliva flow was found to have decreased, and total protein and inorganic component concentrations were found to be high. However, salivary alpha-amylase activity and concentration fell [39].

5.2 Autoimmune disease

1. Serological abnormalities, keratoconjunctivitis sicca, xerostomia, and malfunction of the salivary and tear glands are the hallmarks of Sjögren's syndrome (SS), a chronic autoimmune disease. In order to potentially aid in the diagnosis of SS patients, researchers have evaluated particular cytokine concentrations in their saliva. Because this condition is associated with noticeably high levels of interleukins 2 and 6 [14].

2. Multiple sclerosis (MS)is an inflammatory disease marked by scarring and loss of myelin, which is caused by the immune system's inability to properly destroy or function myelin-producing cells. The only discernible difference in the saliva of MS patients according to standard deviations (SD) is a decrease in IgA production [14, 40].

3. Sarcoidosis is an inflammatory illness that can impact the skin, eyes, liver, lymph nodes, lungs, and other tissues. In the majority of these patients, SDs reveal a decrease in the volume of saliva secreted as well as in the activities of kallikrein and alpha-amylase [14].

5.3 Malignancy

Head and neck cancer may aid in the early screening and identification of certain malignant tumors as well as the tracking of treatment efficacy [12]. Saliva from individuals with head and neck cancer has increased amounts of certain protein's mRNA. Tumor suppressor protein p53 is created by cells that are subjected to different kinds of stress that damage DNA. Antibodies against this p53 protein are produced as a result of the accumulation of inactive p53 protein. Patients with oral squamous cell carcinoma (OSCC) have anti-p53 antibodies in their saliva, which can help with early screening and identification [14].

5.4 Infection

Immunoglobulins (IgA, IgM, and IgG) found in saliva come from two sources: serum and salivary glands. Saliva contains antibodies against bacteria, fungi, viruses, and parasites that can be used to diagnose illnesses [14].

5.5 Cardiovascular diseases

The main emphasis of research on cardiovascular disease is on proteins. The most often investigated salivary proteins include C-reactive protein (CRP), salivary creatinine kinase, myocardial band (CK-MB), myoglobin (MYO), troponin-1 (Tn1), myeloperoxidase (MPO), and matrix metalloproteinase-9 (MMP-9). cardiovascular disease biomarkers. The most promising biomarkers include CRP, CK-MB, MYO, and Tn1, but the outcomes of other biomarkers are debatable. Serum and saliva have been investigated by Miller et al. as diagnostic fluids to find biomarkers of acute myocardial infarction (AMI) [16]. Patients who have undergone cardiovascular surgery are managed postoperatively using markers of cardiovascular illness discovered in their saliva, such as amylase [14].

5.6 Diabetes

Both the World Health Organization and the International Diabetes Federation have reported that diabetes is the chronic illness that has affected the greatest number of people this century [41]. Saliva from diabetic individuals varies in several ways, including in terms of proteins, glucose levels, peroxidase, and buffering ability, all of which are important for diagnosing diabetes. As a result, screening, diagnosing, and tracking diabetes can be done more affordably and non-invasively with saliva glucose testing. It has long been the subject of discussion and investigation [42]. Figure 2 lists the variations in biochemical analytes found in saliva under various clinical circumstances [15]:

Condition	Specific salivary markers
Malignancies	SA↑, Long non-coding RNA↑, p53 antibodies*, CA15-3↑, Cellular erythroblastosis oncogene B-2↑, Cancer antigen 125↑, Fibroblast growth factor 2↑, Fibroblast growth factor receptor 1↑, Prostate specific antigen↑, Cortisol↑, LD↑, Nitrate↑, Adenosine deaminase↑, Alpha-defensins↑, Beta-defensins↑, Endothelins↑, Statherins↓, Interleukin-8↑, Thioredoxin↑
DM	Glucose↑
Renal condition	Cortisol↑, Nitrite*, UA*, Alpha-amylase*, Lactoferrin*, Creatinine↑
Sjogren's Syndrome	Lactoferrin↑, Beta-2-microglobulin↑, Lysozyme C↑, Cystatin C↑, Amylase↓, Carbonic anhydrase↓
Multiple sclerosis	IgA↓
Sarcoidosis	Alpha-amylase↓, Kallikrein↓
Bone turnover markers	Deoxypyridinium↑, Osteocalcin↑, Hepatocyte growth factor↑, Interleukin-1-beta↑, Alkaline phosphatase↑
Cardiovascular diseases	C-reactive protein↑, Myoglobin↑, Creatinine kinase myocardial band↑, Cardiac troponins↑, Myeloperoxidase↑, Tumor necrosis factor α↑, Matrix metalloproteinase–9↑, Intercellular adhesion molecule-1↑, Soluble CD40 ligand↑, Lysozyme↑
Dental caries and periodontal diseases	Aspartate aminotransferase↑, Alkaline phosphatase↑, UA↓, Albumin↓, Polymeric immunoglobulin receptor↓, Actin-related protein 3↓, Carbonic anhydrase VI↓, Interleukin 1 Receptor antagonist↓, Plastin-2↑, Leukocyte elastase inhibitor↑, Immunoglobulin J↑, Immunoglobulin↑, Cystatin S↑, Amylase*, Calprotectin*, Histatins*, Lysozyme↑, Lactoferrin↑, Defensins*, Peroxidases*, PRPs*, MUC*, Prostaglandin E(2)*, Albumin↑, LD↑
Diseases of the adrenal cortex	Cortisol↑
Psychological conditions	SAA↑, Cortisol*, Substance P*, Lysozyme↑, Secretory IgA↓, Testosterone↑
Occupational and environmental medicine	Cortisol↑, IgA↓, Lysozyme↓, Chromogranin↑, SAA↑, Lead↑, Cadmium↑
Infections (bacterial, fungal, viral)	Measles virus-specific IgM↑, HIV—HIV-1*, HIV-2—antibodies*, *Mycobacterium tuberculosis*↑, MUC 5B↑, MUC 7↑, Candidiasis immunoglobulins*, Hsp 70*, Calprotectin*, Histatins*, MUC*, Basic PRPs*, Peroxidases*, IgM↑, IgG (dengue) ↑
Cystic fibrosis	Cathepsin-D↑, LD↑
Ectodermal dysplasia	Inorganic constituents↑, Total protein↑
Obesity	CRP↑, Leptin↑, Insulin↑, Adiponectin↓
Metabolic Syndrome	UA↑

Figure 3: Disease-specific biochemical analyzers in saliva.

6 Conclusion

Saliva is a biological fluid that is dynamic and complicated, made up of many different substances. The various tasks that saliva completes in the oral cavity are accomplished by the biochemical, physical, and interaction characteristics of these salivary constituents. These days, there are numerous assays available to examine different salivary parameters; nevertheless, in order to get significant data, collection and storage procedures must be standardized. Saliva has drawn more and more attention from scientists in recent years.

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References

[1] Li Y, Guan C, Liu C, Li Z, Han G. Disease diagnosis and application analysis of molecularly imprinted polymers (MIPs) in saliva detection. Talanta. 2023:125394. doi:10.1016/j.talanta.2023.125394. [Backref page 1]

[2] Kumari S, Samara M, Ampadi Ramachandran R, Gosh S, George H, Wang R, et al. A review on saliva-based health diagnostics: biomarker selection and future directions. Biomedical Materials & Devices. 2024;2(1):121-38. doi:10.1007/s44174-023-00090-z. [Backref page 1], [Backref page 33]

[3] Shakeeb N, Varkey P, Ajit A. Human saliva as a diagnostic specimen for early detection of inflammatory biomarkers by real-time RT-PCR. Inflammation. 2021;44(5):1713-23. doi:10.1007/s10753-021-01484-1. [Backref page 33]

[4] Anjum A, Hosein M. Diagnostic Importance of Saliva-An Overview. Journal of the Pakistan Dental Association. 2019;28(3). doi:10.2530/JPDA.283.129. [Backref page 33]

[5] Rebaudi F, De Rosa A, Greppi M, Pistilli R, Pucci R, Govoni FA, et al. A new method for oral cancer biomarkers detection with a non-invasive cyto-salivary sampling and rapid-highly sensitive ELISA immunoassay: a pilot study in humans. Frontiers in Immunology. 2023;14:1216107. doi:10.3389/fimmu.2023.1216107. [Backref page 33]

[6] Martina E, Campanati A, Diotallevi F, Offidani A. Saliva and oral diseases. Journal of clinical medicine. 2020;9(2):466. doi:10.3390/jcm9020466. [Backref page 33], [Backref page 35]

[7] Naik N, Rallapalli Y, Krishna M, Vellara AS, KShetty D, Patil V, et al. Demystifying the advancements of big data analytics in medical diagnosis: an overview. Engineered Science. 2021;19:42-58. doi:10.30919/es8d580. [Backref page 33]

[8] Cui Y, Yang M, Zhu J, Zhang H, Duan Z, Wang S, et al. Developments in diagnostic applications of saliva in human organ diseases. Medicine in Novel Technology and Devices. 2022;13:100115. doi:10.1016/j.medntd.2022.100115. [Backref page 33], [Backref page 34], [Backref page 35]

[9] d'Amone L, Matzeu G, Omenetto FG. Stabilization of salivary biomarkers. ACS Biomaterials Science & Engineering. 2021;7(12):5451-73. doi:10.1021/acsbiomaterials.1c01138. [Backref page 33], [Backref page 34]

[10] Schulz BL, Cooper-White J, Punyadeera CK. Saliva proteome research: current status and future outlook. Critical reviews in biotechnology. 2013;33(3):246-59. doi:10.3109/07388551.2012.687361. [Backref page 33]

[11] Zhang A, Sun H, Wang P, Wang X. Salivary proteomics in biomedical research. Clinica chimica acta. 2013;415:261-5. doi:10.1016/j.cca.2012.11.001. [Backref page 33]

[12] Arellano M, Jiang J, Zhou X, Zhang L, Ye H, Wong DT, et al. Current advances in identification of cancer biomarkers in saliva. Front Biosci (Schol Ed). 2009;1(1):296-303. [Backref page 33], [Backref page 36]

[13] Iqbal A, Hanif S, Arif F. Oral Profile of Patient Effected by Chikungunya Virus: A Case Report. JPDA. 2019;28(03):150. doi:10.25301/JPDA.283.149. [Backref page 33]

[14] Arunkumar S, Arunkumar J, Krishna N, Shakunthala G. Developments in diagnostic applications of saliva in oral and systemic diseases-A comprehensive review. J Sci Innov Res. 2014;3(3):372-87. [Backref page 33], [Backref page 35], [Backref page 36], [Backref page 37]

[15] Soares Nunes LA, Mussavira S, Sukumaran Bindhu O. Clinical and diagnostic utility of saliva as a non-invasive diagnostic fluid: a systematic review. Biochemia medica. 2015;25(2):177-92. doi:10.11613/BM.2015.018. [Backref page 33], [Backref page 37]

[16] Huang Z, Yang X, Huang Y, Tang Z, Chen Y, Liu H, et al. Saliva–a new opportunity for fluid biopsy. Clinical Chemistry and Laboratory Medicine (CCLM). 2023;61(1):4-32. doi:10.1515/cclm-2022-0793. [Backref page 33], [Backref page 34], [Backref page 37]

[17] Punj A. Secretions of human salivary gland. In: Salivary glands-new approaches in diagnostics and treatment. IntechOpen; 2018. doi:10.5772/intechopen.75538. [Backref page 33]

[18] Zhou Y, Liu Z. Saliva biomarkers in oral disease. Clinica Chimica Acta. 2023:117503. doi:10.1016/j.cca.2023.117503. [Backref page 33]

[19] Dongiovanni P, Meroni M, Casati S, Goldoni R, Thomaz DV, Kehr NS, et al. Salivary biomarkers: novel noninvasive tools to diagnose chronic inflammation. International journal of oral science. 2023;15(1):27. doi:10.1038/s41368-023-00231-6. [Backref page 33]

[20] Spinelli MA, Haberer JE, Chai PR, Castillo-Mancilla J, Anderson PL, Gandhi M. Approaches to objectively measure antiretroviral medication adherence and drive adherence interventions. Current Hiv/Aids Reports. 2020;17:301-14. doi:10.1007/s11904-020-00502-5. [Backref page 34], [Backref page 35]

[21] Gug IT, Tertis M, Hosu O, Cristea C. Salivary biomarkers detection: Analytical and immunological methods overview. TrAC Trends in Analytical Chemistry. 2019;113:301-16. doi:10.1016/j.trac.2019.02.020. [Backref page 34], [Backref page 36]

[22] Mortha N, Uppala D, Kothia NR, Majumdar S, Kotina S, Sravya K. A systematic review of saliva on its diagnostic utility. Journal of Dr NTR University of Health Sciences. 2018;7(2):115-9. doi:10.4103/JDRNTRUHS.JDRNTRUHS_91_17. [Backref page 35]

[23] Lorenzo-Pouso AI, Pérez-Sayáns M, Bravo SB, López-Jornet P, García-Vence M, Alonso-Sampedro M, et al. Protein-based salivary profiles as novel biomarkers for oral diseases. Disease markers. 2018;2018(1):6141845. doi:10.1155/2018/6141845. [Backref page 35]

[24] Zalewska A, Waszkiewicz N, López-Pintor RM. The use of saliva in the diagnosis of oral and systemic diseases. Disease markers. 2019;2019. doi:10.1155/2019/9149503. [Backref page 35]

[25] Zalewska A, Waszkiewicz N, López-Pintor RM. The use of saliva in the diagnosis of oral and systemic diseases. Disease markers. 2019;2019. doi:10.1155/2019/9149503. [Backref page 35]

[26] Zhang X, Kulasinghe A, Karim RS, Punyadeera C. Saliva diagnostics for oral diseases. Advances in salivary diagnostics. 2015:131-56. doi:10.1007/978-3-662-45399-5_7. [Backref page 35]

[27] Buzalaf MAR, Ortiz AdC, Carvalho TS, Fideles SOM, Araujo TT, Moraes SM, et al. Saliva as a diagnostic tool for dental caries, periodontal disease and cancer: is there a need for more biomarkers? Expert review of molecular diagnostics. 2020;20(5):543-55. doi:10.1080/14737159.2020.1743686. [Backref page 35]

[28] Malathi N, Mythili S, Vasanthi HR. Salivary diagnostics: a brief review. International Scholarly Research Notices. 2014;2014(1):158786. doi:10.1155/2014/158786. [Backref page 35]

[29] Papale F, Santonocito S, Polizzi A, Giudice AL, Capodiferro S, Favia G, et al. The new era of salivaomics in dentistry: frontiers and facts in the early diagnosis and prevention of oral diseases and cancer. Metabolites. 2022;12(7):638. doi:10.3390/metabo12070638. [Backref page 35]

[30] Prodan A. Salivary biochemistry of the healthy oral ecosystem [Ph.D thesis]. Amsterdam: Vrije Universiteit; 2017. [Backref page 35]

[31] Yazid F, Zain M, Yusof Z, Ghazali F, Zulkifli S, Nadri N, et al.; AIP Publishing. Caries detection analysis in human saliva alpha amylase. AIP Conference Proceedings. 2020;2203(1). doi:10.1063/1.5142106. [Backref page 36]

[32] Khurshid Z, Zafar MS, Khan RS, Najeeb S, Slowey PD, Rehman IU. Role of salivary biomarkers in oral cancer detection. Advances in clinical chemistry. 2018;86:23-70. doi:10.1016/bs.acc.2018.05.002. [Backref page 36]

[33] Yakob M, Fuentes L, Wang MB, Abemayor E, Wong DT. Salivary biomarkers for detection of oral squamous cell carcinoma: current state and recent advances. Current oral health reports. 2014;1:133-41. doi:10.1007/s40496-014-0014-y. [Backref page 36]

[34] Goldoni R, Scolaro A, Boccalari E, Dolci C, Scarano A, Inchingolo F, et al. Malignancies and biosensors: A focus on oral cancer detection through salivary biomarkers. Biosensors. 2021;11(10):396. doi:10.3390/bios11100396. [Backref page 36]

[35] Mavragani CP, Fragoulis GE, Moutsopoulos HM. Sjögren's syndrome. The Autoimmune Diseases. 2014:495-510. doi:10.1016/B978-0-12-384929-8.00035-6. [Backref page 36]

[36] Kaufman E, Lamster IB. The diagnostic applications of saliva—a review. Critical Reviews in oral biology & medicine. 2002;13(2):197-212. doi:10.1016/B978-0-12-384929-8.00035-6. [Backref page 36]

[37] Mittal S, Bansal V, Garg S, Atreja G, Bansal S. The diagnostic role of Saliva—a review. J Clin Exp Dent. 2011;3(4):e314-20. [Backref page 36]

[38] Gonçalves AC, Marson FAdL, Mendonça RMdH, Ribeiro JD, Ribeiro AF, Paschoal IA, et al. Saliva as a potential tool for cystic fibrosis diagnosis. Diagnostic pathology. 2013;8:1-7. doi:10.1186/1746-1596-8-46. [Backref page 36]

[39] Lexner MO, Bardow A, Hertz JM, Almer L, Nauntofte B, Kreiborg S. Whole saliva in X-linked hypohidrotic ectodermal dysplasia. International Journal of Paediatric Dentistry. 2007;17(3):155-62. doi:10.1111/j.1365-263X.2006.00812.x. [Backref page 36]

[40] Goswami Y, Mishra R, Agrawal AP, Agrawal LA. Salivary biomarkers: A review of powerful diagnostic tool. IOSR J Dental Med Sci. 2015;14(3):80-7. doi:10.9790/0853-14378087. [Backref page 36]

[41] Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes research and clinical practice. 2019;157:107843. doi:10.1016/j.diabres.2019.107843. [Backref page 37]

[42] Fares S, Said MSM, Ibrahim W, Amin TT, Saad NES. Accuracy of salivary glucose assessment in diagnosis of diabetes and prediabestes. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019;13(2):1543-7. doi:10.1016/j.dsx.2019.03.010. [Backref page 37]

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