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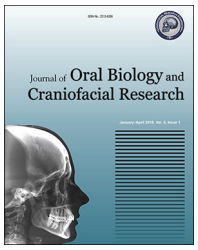

Review Article

Saliva as a diagnostic tool for oral and systemic diseases

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ABSTRACT

Early disease detection is not only vital to reduce disease severity and prevent complications, but also critical to increase success rate of therapy. Saliva has been studied extensively as a potential diagnostic tool over the last decade due to its ease and non-invasive accessibility along with its abundance of biomarkers, such as genetic material and proteins. This review will update the clinician on recent advances in salivary biomarkers to diagnose autoimmune diseases (Sjogren's syndrome, cystic fibrosis), cardiovascular diseases, diabetes, HIV, oral cancer, caries and periodontal diseases. Considering their accuracy, efficacy, ease of use and cost effectiveness, salivary diagnostic tests will be available in dental offices. It is expected that the advent of sensitive and specific salivary diagnostic tools and the establishment of defined guidelines and results following rigorous testing will allow salivary diagnostics to be used as chair-side tests for several oral and systemic diseases in the near future.

1. Introduction

Early diagnosis of diseases is crucial to prevent complications that could have a negative impact on a patient's quality of life. For instance, ovarian cancer, the fifth most common cancer and cause of death in females, has a 5-year-survival rate of 10% when detected at stage 4 in comparison to 93% if diagnosed at stage 1.[1] Similarly, type 2 diabetes, which affects 7% of the adult population, can be solely controlled by diet and change in lifestyle if the diagnosis is made earlier.[2] Furthermore, despite the regular screenings and check-ups, many diseases are undetected until a late phase where morbid symptoms become apparent. To overcome these challenges, researchers are unravelling biomarkers. These biomarkers include genetic material (e.g. DNA, RNA) and protein molecules that reflect the current physiological state of an individual and hence help scientists to better understand the underlying cause of a disease.[3] Over the years, studies have shown that alterations in human genetics can be detected by molecular diagnostics, and anomalies in nucleic acids and proteins present in the patient's body fluids such as blood, cerebrospinal fluid (CSF) and urine can be used as effective biomarkers for disease diagnosis.[4–6] However, many obstacles remain such as lack of

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definite biomarkers for specific diseases, absence of inexpensive sample collection methods incurring minimal discomfort, and paucity of accurate and portable detection systems.[3] Fortunately, some of these limitations can be overcome by analysing one's saliva. Due to its ease and non-invasive accessibility along with its abundance of biomarkers such as genetic material and proteins,[3] saliva has been studied extensively as a potential diagnostic tool over the last decade.[7]

2. Properties of saliva as a diagnostic fluid

Although the utility and advantages of saliva as a screening tool for cystic fibrosis has been identified in the early 1960s,[8] its full diagnostic potential was discovered three decades later when studies revealed distinct advantages of saliva over serum.[9,10] Like serum, saliva also contains hormones, antibodies, growth factors, enzymes, microbes and their products.[7,11] As shown in Fig. 1, many of these constituents enter saliva through blood via passive diffusion, active transport or extracellular ultra filtration.[7,12] Therefore, saliva can be seen in many cases as a reflection of the physiological function of the body.[13] There have been concerns about the use of saliva for diagnostic purposes due to its low concentration of analytes in comparison to blood.[14] However, with the advent of highly sensitive molecular methods and nanotechnology, this is no longer a limitation.[15] Saliva as a diagnostic tool should be sought due to a multitude of compelling reasons summarized in Table 1. All these characteristics make saliva an appealing diagnostic candidate for the detection and monitoring of several biomarkers in infants, children, adults and uncooperative patients.[16]

Table 1 – Advantages of salivary testing for diagnosis.

Advantages[3,69–72]
Non-invasive, easy to use, inexpensive
Safer to administer than serum sampling (no needles)
Real-time diagnostic values
No need for trained medical staff
Multiple samples can be obtained easily
Collection and screening can be done at home
Minimal risks of cross-contamination
More economical sampling, shipping and storage compared to serum
Requires less manipulation during diagnostic procedures compared to serum
Commercial availability of screening assays

3. Autoimmune disorders

3.1. *Sjogren's syndrome*

Sjogren's syndrome (SS) is a chronic autoimmune disease characterized by salivary and lacrimal dysfunction, multiple organ abnormalities and serological changes.[17] Salivary secretions from these patients exhibit elevated levels of antibodies and cytokines such as IgA, IgG, prostaglandin-E2, and interleukin-6. This is accompanied by a reduction in oral phosphate levels and xerostomia due to reduced salivary flow, which can lead to infections, progressive caries, dysphagia and oral pain.[18] Current tests for SS include sialometry or salivary flow rate determination, salivary scintigraphy, sialography, serological tests or minor salivary gland biopsies. Although useful, these tests are invasive, expensive or in many cases non-conclusive.[17,19] Salivary proteomics represent a valuable tool to diagnose SS. It is based on the detection of several biomarkers that are simultaneously influenced by the disease. Recently, a panel of candidate salivary biomarkers of SS was investigated.[20] Twenty-eight proteins were found to be significantly modified by SS. The authors concluded that these tests, when performed on whole saliva, can diagnose SS, although larger clinical trials are warranted before they are brought to the market. Recently, salivary proteomics have gained attention with their advanced proteins for diagnoses, classification and/or predicting the prognosis of SS. Although saliva proteomics could provide new insights, however, still several questions remained unanswered. A study found salivary proteomics such as pSS biomarker as a potential

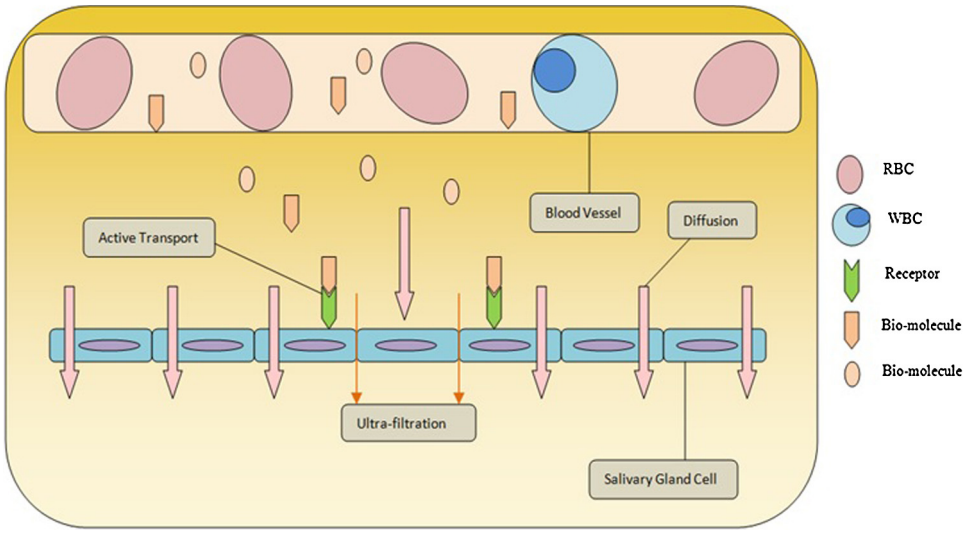

Fig. 1 – Schematic diagram illustrating key routes through which serum molecules enter saliva. This movement of constituents makes saliva functionally equal to serum for potential diagnosis of various diseases.