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NANOTECHNOLOGY POWERED SALIVARY DIAGNOSTIC LABORATORY FOR ORAL AND SYSTEMIC DISEASES: A MINI REVIEW

Dental Science

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ABSTRACT

Advances in the use of saliva as a diagnostic fluid have been affected by current technological developments: enzyme–linked fluorescence technique, Western blot assays, polymerase chain reaction (PCR). Salivary diagnostics is a dynamic and emerging field utilizing nanotechnology and molecular diagnostics to aid in the diagnosis of oral and systemic diseases and using the salivary biomarkers for disease detection. With a salivary specimen, one can collect multiple specimens from the same individual at the optimum times for diagnostic information. Saliva can be considered as gland-specific saliva and whole saliva. Whole saliva is a mixed fluid that is derived predominantly from major and minor salivary glands. Analysis of saliva done for the diagnosis of Hereditary disease, Autoimmune disease, Malignancy, Infection, Monitoring of levels of hormones and drugs, Bone turnover marker in saliva, Forensic Evidence, Dental caries and periodontal disease and in diagnosis of Oral Disease with Relevance for Systemic Diseases. This paper aims to impart and share knowledge on the role of saliva in diagnosis of oral and systemic disease using nanotechnology.

KEYWORDS

Saliva, Nanotechnology, Salivary diagnostics, MEMS/NEMS, OFNASET.

INTRODUCTION:

Most commonly used laboratory diagnostic procedures involve the analyses of the cellular and chemical constituents of blood. On the other hand Saliva offers some distinctive advantages like being sample collected non-invasively, and by individuals with limited training, including the patient. Saliva is an informative, biological complex fluid which like serum consists of pool of hormones, proteins, enzymes, antibodies, antimicrobial constituents, and cytokines. Due to this property of saliva, whole saliva or gland specific saliva is used commonly as biomarker for diagnosis of multiple oral and systemic diseases. Transcellular, passive intracellular diffusion and active transport, or para-cellular routes by extra cellular ultrafiltration within the salivary glands or through the gingival crevice are the methods or mechanism which allows transport of these constituents from blood into saliva.[1,2] Advantages of salivary sample collection over serum sample collection includes being non-invasive, easy to use and inexpensive. Also multiple samples can be obtained immediately and no trained medical/paramedical staff is required. Salivary sample collection and screening can be done at home with minimal chances of cross-contamination and cheaper storage/shipping as compared to serum samples.[1,3] But the widespread implementation of salivary diagnostics met with challenges and barriers such as technological problems related to achieving high sensitivity, high specificity, miniaturization, high throughput where large number of samples are assayed concurrently, automation, portability, low cost, high functionality and speed. These barriers are overpowered by newer technologies and nanotechnology from a combination of miniaturization technologies like **MEMS/NEMS** biosensors (Micro/Nano electro mechanical systems), **"lab on a chip"** and **OFNASET** (Oral Fluid Nano Sensor Test, Figure-1) which has enabled researchers to detect and measure multiple salivary disease markers or salivary biomarkers as these systems/techniques provide ultrasensitive and ultraspecific detection of salivary diagnostic analytes (measures proteins, DNA, gene transcripts (mRNA), electrolytes and small molecules in saliva). With the invent of these nano techniques real-time and simultaneous assessment of various diseases (by rapid detection of multiple salivary protein and nucleic acid targets) can be done with the use of minute amounts of saliva to produce critical patient information that reflects health and disease status of patients.[4,5,6]

Thus nowadays improved efficiency and accuracy of genomic and proteomic biomarker discovery with invent of nanotechnologies are turning saliva into advanced diagnostic laboratory as a new frontier in diagnosis of various oral and systemic diseases.

Nano-Salivary Analysis/Proteomics/biomarkers for Systemic Diseases[7,8,9,10,11]

Cardiovascular diseases: Coronary artery disease (CAD), forms component of cardiovascular diseases where Oral Fluid-based Lab-on-a-chip testing is done for early detection of Acute myocardial infarction (AMI) as survival and good prognosis depends upon early diagnosis and intervention. Cardiac biomarkers/proteins such as C-reactive protein (CRP), myeloperoxidase (MPO), interleukins, matrix metallo-perteinase-9 (MMP-9), and cellular adhesion molecule-1 (sICAM-1), can be easily detected in saliva using nanotechnology which along with electrocardiogram (ECG) findings makes early diagnosis of disease. **Sjögren's syndrome (SS)** (dysfunction of salivary and lacrimal glands, keratoconjuctivitis and xerostomia) is systemic autoimmune disease. Dysfunction due to damage of glandular cells and inflammation of the oral cavity in patients of this disease is shown by 16 down-regulated and 25 up-regulated proteins. In Systemic sclerosis (): pathological role of keratin 6l, psoriasin, TPi, and arp2/3 complex was observed by Giusti and colleagues.

Nano-Salivary Analysis/ proteomics/ biomarkers for Oral Diseases[3,7,12,13]

Oral cancer: Exfoliative cytology based on nano-bio-chip sensor platform for oral cancer detection can be used for early detection of oral cancer. Overexpression of proteins like M2BP (Tumor antigen), MRP14 (Calcium binding protein), CD59 (Enables the tumor cells to escape from complement dependent and antibody mediated killing) and Prifilin1 (Regulator of microfilament system and is involved in various signaling pathways Catalase Protects against oxidative stress) is of diagnostic value for oral cancer. Again detection of telomerase activity in saliva samples is assistance for diagnosis of oral squamous cell carcinoma**.** The intended use of the OFNASET is for the point-of-care multiplex detection of salivary biomarkers for oral cancer. **Premalignant conditions** like *oral lichen planus* higher salivary levels of CD44s and CD44v5 (isoforms of CD44) are diagnostic as compared to controls. Secondly severity of oral lichen planus depends upon high salivary IL-4 levels.

In **Dental caries,** salivary phosphopeptides (PRP1/3, histatin-1 & statherin) were found to maintain sound tooth as they were absent in carious lesions. Higher number of proline-rich protein bands can be seen in caries free patients whereas lesser number is seen in subjects

with early childhood caries, highlighting protective role of this protein. In **Periodontal disease,** IL (Interleukin)-1β and matrix metalloproteinase (MMP)-8 combined increased levels increases the risk of periodontal destruction by 45 folds. Also MMP-1 (interstitial collagenase) along with MMP-2, MMP-3 and MMP-9 also appeared to be activated in periodontitis. Higher values of Immunoglobulin IgA, IgG and IgM are specific to periodontal disease. More Acid Phosphatase (ACP) and Alkaline phosphatase (ALP) levels are associated with more calculus formation and interdental/alveolar bone loss repectively.

CONCLUSION:

To conclude salivary diagnosis is preferred over serum diagnosis because salivary sample collection is non-invasive, of low cost, easy to handle and is time saving. Further nanotechnology synergistically added ultra sensitivity, ultra specificity, point of care diagnosis and multiple disease indicator property to salivary diagnosis. Nano sensor devices aim to improve the ease and effectiveness of oral physician to get early diagnosis of oral and systemic diseases.

Figure-1: Oral Fluid Nano Sensor

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