

## Sialochemistry A Valuable Tool In Diagnosis Of Systemic Diseases

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**ABSTRACT:** Saliva has proven to be a diagnostic element in forensic medicine, an effective indicator of acute diseases of salivary glands, and a promising probe in drug monitoring. With the advent of sensitive immunochemical assays, the compositional profile of human salivary secretions has been expanded considerably. Saliva contains a variety of growth factors and antimicrobial constituents.

**KEYWORDS:** Saliva. diagnosis, sialochemistry, diseases.

### INTRODUCTION

The diagnostic use of saliva has attracted the attention of numerous investigators because of the relative simplicity of collection and noninvasive nature. Saliva is a perfect medium to be explored for health and disease surveillance.<sup>[1]</sup> The clinical use of saliva range from the drug monitoring to forensic field and diagnosis of systemic and local conditions affecting salivary glands. Saliva is of great importance for forensic experts<sup>[1]</sup>.

It is a complex fluid containing an entire library of hormones, enzymes, proteins, antibodies, cytokines, antimicrobial constituents.<sup>[2]</sup> Sialochemistry provides qualitative information on certain important parameters of saliva which are used for diagnostic and research purposes.<sup>[3]</sup> Methods for determining salivary gland dysfunction include salivary flow rate measurements (sialometry) and analysis of salivary composition (sialo-chemistry) analyzed by using radioimmunoassay (RIA), for which whole saliva (oral fluid) is most frequently used. The concentration of IgA was somewhat elevated

(commensurate with reduced flow rate); the levels of IgG, IgM, and albumin were normal. The major functional abnormality of the parotid gland in Sjogren's syndrome appears to be luminal transport in the ductal region; leakage of serum components is minimal. Sialochemistry can be helpful in differentiating Sjogren's disease from other diseases of the salivary gland and in assessing degree of pathologic change.<sup>[3]</sup> p53 antibody is a tumor suppressor protein which is produced in cells exposed to various types of DNA-damaging stress, can also be detected in the saliva of patients diagnosed with oral squamous cell carcinoma (SCC), and can thus assist in the early detection and screening for this tumor.<sup>[5]</sup>

The use of human saliva as a diagnostic and prognostic fluid has until recently somewhat disregarded. Whole saliva (WS) is a mixture of the secretions of the minor and major salivary glands, gingival crevicular fluid, mucosal transudations, serum and blood derivatives from oral wounds, desquamated epithelial cells, bacteria and bacterial products, viruses and fungi, other cellular

components, and expectorated bronchial and nasal secretions and food debris.<sup>[4]</sup>

## **SALIVA AS A DIAGNOSTIC BIOFLUID**

### **Advantages of using Saliva as a Diagnostic Fluid-**

Saliva can be easily collected by non-invasive techniques and contains many analytes of interest for diagnosis, screening, and monitoring.

1. Levels of certain markers in saliva are not always a reliable reflection of the levels of these markers in serum.
2. Salivary composition can be influenced by degree of stimulation of salivary flow and by the method of collection.
3. Variability in salivary flow rate is expected between individuals and in the same individual under different conditions.
4. Changes in salivary flow rate may affect the concentration of salivary markers and also their availability due to changes in salivary pH.
5. In addition, many serum markers can reach whole saliva in an unpredictable way (i.e. gingival crevicular fluid flow and through oral wounds). These parameters will affect the diagnostic value of many salivary constituents.
6. Whole saliva also contains proteolytic enzymes derived from the host and from oral microorganisms. These enzymes can affect the stability of diagnostic markers. During intracellular diffusion into saliva some molecules are also degraded.

7. Furthermore, certain systemic disorders, numerous medications and radiation may affect salivary gland function and consequently the quantity and composition of saliva.<sup>[4]</sup>

### **Limitations**

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**Different types of markers found in saliva with their uses are listed, many of which are currently being used for development of an effective test-**

<b>Biomarker class</b>	<b>Potential applications</b>
<b>DNA</b>	Standard genotyping ,Bacterial infection, Head and neck cancer diagnosis , Forensics
<b>RNA</b>	Viral /bacterial identification, Oral cancer diagnosis
<b>Proteins</b>	Periodontitis diagnosis, Cancer diagnosis, Caries susceptibility
<b>Mucins/ glycoproteins</b>	Head and neck cancer diagnosis , Caries susceptibility
<b>Immunoglobulins</b>	Viral infection[HIV,Hepatitis B and C]
<b>Metabolites</b>	Various endocrine conditions, Stress, Psychological status, cystic fibrosis, periodontitis diagnosis
<b>Drugs and their metabolites</b>	Monitor drug abuse, monitor patient compliance to therapy
<b>Viruses</b>	Epstein – Barr virus reactivation[mononucleosis]
<b>Bacteria</b>	Oral cancer diagnosis, caries susceptibility
<b>Cellular material</b>	Head and neck cancer diagnosis <sup>[6]</sup>

Salivary analysis can be done for the diagnosis of the following diseases.

1. Hereditary disease
2. Autoimmune disease
3. Malignancy
4. Infection
5. Monitoring of levels of drug.
6. Monitoring of levels of hormones
7. Bone turnover marker in saliva
8. Sjögren’s syndrome

9. Forensic Evidence

10. Oral diseases.<sup>[4]</sup>

Sialochemistry is a useful means of chronologically monitoring quantitative changes of chemicals which are present in saliva.

The stimulated saliva or the mixed saliva collected from the mouth is a complex mixture, which is secreted in response to masticatory or gustatory stimulation. The resting flow rate of the whole saliva is 0.2-0.4 mL/min and on stimulation, the rates increase to 0.2-0.6 mL/min for the saliva. The pH of the whole saliva varies from 6.4 to 7.4.

1. **Hereditary diseases** Cystic fibrosis (CF) is a genetically transmitted disease of young adults and children, which is considered a generalized exocrinopathy. An electrolyte transport in epithelial cells and viscous mucus secretions from glands and epithelia characterize this disease. The organs most affected in CF are the lungs, sweat glands and the pancreas. Elevations in electrolytes (chloride, calcium ,sodium and phosphorus) total protein and lipids, urea and uric acid were observed in the submandibular saliva of CF patients.<sup>[8]</sup>

2. **Multiple Sclerosis (MS)** is an inflammatory disease characterized by loss of myelin and scarring caused due to destruction of myelin producing cells by the immune system. SDs shows no significant change in the saliva of patients with multiple sclerosis except for a reduction in IgA production. <sup>[9]</sup>

3. **Infectious diseases** Oral cavity may be the source of infection. There was considerable variation in the detection rate of H. pylori DNA in salivary samples. Saliva contains immunoglobulins

(IgM, IgA, IgG) that originate from two sources the salivary glands and serum. Antibodies against bacteria, viruses, fungi and parasites can be detected in saliva and can aid in the diagnosis of infections. Bacterial infections *Helicobacter pylori* infection has been associated with peptic ulcer and chronic gastritis.<sup>[10]</sup>

ELISA offers a valuable complement to conventional diagnostic methods and detection of Pneumococcal pneumonia C polysaccharide in saliva.<sup>[7]</sup>

#### 4. Bone Turnover Marker in Saliva

McGehee and Johnson used commercially available ELISA to test for the presence of pyridinoline (PYD) and osteocalcin (OC) in the whole human saliva of women. Level of PYD and OC in saliva correlated reasonably well with calcaneus bone mineral density BMD/t scores.<sup>[13]</sup>

#### 5. Occupational and Environmental Medicine

**Salivary biomarkers** play a role in the diagnosis of occupational stress (OS) and heavy metal toxin poisoning. OS is classified into two types: decreased level of salivary IgA and lysozyme and Chronic stress is associated with increased levels of salivary cortisol. Saliva chromogranin A and alpha-amylase are markers of acute stress. The concentration of cadmium in saliva is more than in blood, but the level of salivary lead analysis is limited to higher levels of lead exposure poisoning. Occupational toxins such as cadmium and lead are analyzed from the saliva.<sup>[14]</sup>

**6. Detecting Hormonal Levels** The other major use of saliva is quantification of steroid hormone levels for which assays are available commercially

for estradiol, testosterone, cortisol etc. The only drawback is salivary levels does not correlate with the serum levels of the conjugated steroid hormones.<sup>[7]</sup>

#### 7. Discovering Genetic Cause of the Disease

Stress and pain are interrelated events. It has been found that cognitive behavior serotonin levels tryptophan and in saliva are related. Certain biomarkers levels in saliva like, salivary amylase, secretory IgA, substance P, cortisol are influenced by pain and stress and even the pain responses in dental pulp correlated with neuropeptides including neurokinin A, neurokinin calcitonin gene related peptide (CGRP).<sup>[21]</sup> Mouth cancer in advanced stages can usually be detected by inspection of the oral cavity. Initial oral carcinomas are not visible and cannot be diagnosed and treated on time. The salivary proteome can also be used for tumor detection.<sup>[8]</sup>

**8. Autoimmune diseases** Sjogrens syndrome (SS), a chronic autoimmune disease characterized by dysfunction of salivary and, keratoconjunctivitis sicca, lacrimal glands and xerostomia. Interleukin 6 and 2 are found in levels significantly high in individual that suffers from this disease. Sialochemistry may be used to assist in the diagnosis of SS. A consistent finding is increased concentrations of sodium and chloride. Elevated levels of IgA, IgM, lactoferrin, and albumin, and decreased concentration of phosphate were also seen in saliva of patient with SS. Sarcoidosis, is an inflammatory disease of the lungs, lymph nodes, liver, eyes, skin, or other tissues.

A decrease in secretion volume of saliva in addition to a reduction in the enzyme activity of

kallikrin and alpha – amylase is seen in most of the patients diagnosed of sarcoidosis.<sup>[12]</sup>

**9. Dental caries** Caries is a result of demineralization of the tooth surface initiated by acid production of cariogenic bacteria. This process caused to tooth loss. High number of *S. mutans*, and *Lactobacillus* indicate a shift in oral microflora from healthy to cariogenic. It is demonstrated in various studies that *S. mutans* initiates dental caries; while *Lactobacilli* have a role in progression of carious lesions. High salivary levels of both pathogens have shown a positive correlation with the presence of caries in both children and adults. Buffering capacity and Saliva secretion rate have proven to be sensitive parameters in caries production.<sup>[12]</sup>

**10. Cardiovascular diseases** Atherosclerosis is triggered by the presence of inflammation which results in deposition of lipids in the arterial walls and progressive narrowing of the arterial lumen. This condition might turn into acute myocardial infarction (AMI). It is possible to detect cardiac troponin, a biomarker for the detection of AMI in saliva that is released in response to cardiac cell necrosis.<sup>[15]</sup>

Diseases showing alteration in organic substances in saliva-

DISEASE	ORGANIC SUBSTANCES
Sjogrens syndrome	Increased lactoferrin, kalikerin ,20 folds increase in phospholipid. Raised total protein, $\beta_2$ microglobulin in parotid saliva.
Cystic fibrosis	Raised total protein, amylase, lysozyme in submandibular saliva. Glycoprotein in parotid saliva
Sarcoidosis	Decreased amylase and lysozyme

Hyperparathyroidism	Raised total protein
Diabetes mellitus	Raised total protein, IgA, IgG, IgM and increased glucose levels.
Cirrhosis	Raised total protein & amylase in parotid saliva <sup>[16]</sup>

Diseases showing alteration in inorganic ions in saliva-

DISEASE	INORGANIC ION
Sialadenitis	Increased sodium, potassium, calcium, phosphate levels
Radiation damage	Increased sodium, calcium, magnesium and chlorine
Sjogrens syndrome	Increased sodium, chlorine, phosphate in parotid saliva
Cystic fibrosis	Increased sodium, calcium, phosphate and Calcium phosphate concentration forms a diagnostic index
Aldosteronism	Decreased sodium, increased potassium. Sodium/ Potassium ratio is of diagnostic value
Hypertension	Decreased sodium
Alcoholic cirrhosis	Increased potassium
Hyperparathyroidism	Increased calcium levels.
Diabetes mellitus	Increased calcium levels
Psychiatric illness	Possibly increased sodium levels
Chronic pancreatitis	Decreased bicarbonate levels. ( $\text{Hco}_3$ ).
Digitalis intoxication	Raised $\text{Na}^+$ and $\text{K}^+$ product is of diagnostic value <sup>[16]</sup>

## CONCLISION-

Our mouth is a key to the pathological and disease diagnostic biomarker library hidden inside our bodies. Saliva is the source to all the information. Salivary diagnostics is a dynamic field that is being incorporated as part of disease diagnosis, clinical monitoring and for making clinical decisions for patient care. Oral cavity is the mirror of health

understanding saliva based biomarkers could have a considerable role in establishing oral fluids as a credible diagnostic and prognostic biofluid.

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