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The Potential Role of Saliva In Protecting Against Dental Caries

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ABSTRACT: Previously, extensive research studies indicated that the dental caries is the result of microbial infection, as do influence by dietary and host factors. Recently, research studies seek to identify caries risk factors as well as identify natural oral defenses that may protect against and prevent caries progression. The early detected and diagnosed dental disease in pediatric age; the more suitable treatment will be administrated, thus reducing the intensity incidence of caries.Saliva and it is components play a vital role in protecting oral structures. Saliva consists of proteins which can be informative fordisease detection and observation of oral health. Saliva proteins affect the survival of oral microorganisms by multiple innate defensive mechanisms as well, thus modulating the oral microbial flora. Therefore, the proteins composition of saliva involves in the primary line of protection in the oral cavity. Current research has generated abundant information that contributes to a better understanding of theroles salivary proteins in caries occurrence and prevention. This review summarizes the tooth-protective salivary proteins.

I. INTRODUCTION

Dental caries is a multifactorial disease, which causes local destruction of susceptible dental hard tissues by acids derived from fermentation of carbohydrates in the diet by bacterial and numerous host factors including saliva[1]. Basically, caries represent the majorsource of dental pain and missingtooth, as well as affecting the oral health of human beings seriously and also creating heavy economic challenge on society.ECC is a serious problem with such high prevalence which affects nutrition and growth of the child, can also cause damage to the permanent teeth. Due to caries widespread and influence, a caries risk assessment is mandatory to identify caries high-risk children and start preventive measures as early as possible, doing so well have positive influences on reducing costs and pain associated with the progression of the disease, which then can significantly improve the health and the quality of life.

Human saliva is a bodily fluid that contains a lot of molecular biological information and critically played a role inthe conservationof health and balance in the oral cavity [2].Saliva has multiple functions as follows: Food digestion, lubrication, bolus formation, taste facilitation, rinsing food debris, remineralization, neutralizing low plaque pH,maintain tooth integrity, microorganisms aggregation and by its antibacterial properties [3, 4]. The earlier detection and diagnosis of disease play a significant role in decreasing the prevalence of the disorder for the patient; prevent complications that could have undesirable effect on a patient's life welfare and increase success rate of management. Although, three limitations inhibit the totaladvantages of clinical investigation from being recognized: identified markers with various disorders; inexpensive and simple wayswhich are less invasive; and portable, precise and simple to manipulateinvestigativepolicy. Saliva is an attractive medium for disease diagnostic and prognostic purposes because it is characterized by easily collected in noninvasive manner and can be performed without the help of healthcare workers, easy storage, inexpensive and is low risk for both the patient and medical staff, As well as collecting of saliva can be accomplished without stress and pain for the contributor, and the possibility of collecting multiple samples, therefore, representing a suitable bodily fluid that may be collected and analysis in pediatric age[5].Saliva’s utility extends still further, far beyond the oral cavity, with the discovery of oral and systemic disease biomarkers in saliva. The use of salivary biomarkers as diagnostic tools must be preceded by a clear understanding of salivary biochemistry in different conditions and throughout the stages of life. Saliva is a biological fluid containingexcretions of the salivary glands: 90% of whole saliva is formed by three couples of main salivary glands and 10% from numerous minor salivary glands situated submucosa of the mouth, and gingival crevicular fluid [6]. Similarly to serum and different biological fluids, saliva actually comprisesbiomolecules, for instance DNA, courier RNA and miRNA transcripts, proteins, metabolites and microbiota. Therefore, changes in salivary concentration of these biomolecules can be used as biological markersto assistancedetectinitial oral and systemic disorders, estimate diagnosishazard assessment of disease, diagnosis and monitor the response to management [7]. The finding that saliva consists molecular shapeswhichreproduce disorders in the human has released a new noninvasive investigativeways: salivary investigationsas specific and numericalmodifications of saliva contacts with raise ratingof severity thedisorders in the mouth [8].

The definition of the salivary proteome allows not merely the activity characterization of saliva, and thus the explanation of its objective in oral cavity, nonetheless the potential biomarkers of risk disorder.

II. OVERVIEW OF THE SALIVARY GLANDS

Salivary glands are dependable for the production and secretion of theoral fluid that containing proteins. These secretions represent an important contribution to whole saliva. Salivary glands are secreted from two categories: major and minor glands.

The three couplesmain salivary glands in humans are: parotidglands, submandibular and sublingual glands.

Approximately 90% of fluid presented in whole saliva is secreted by major salivary glands, 10% remaining of whole saliva are secreted by minor salivary glands,gingival crevicular, mucosal exudates and oral microflora. Estimated 400-600 minor salivary glands in the mouth, which are situated in the oral submucosa (labial, lingual, buccal and palatal glands) and gingival crevice fluid. In addition,the saliva also containsmicroorganisms, desquamated cells of the oral epithelium, bronchial expectoration remains and food debris [9].Depending on several factors, the influenceof single glands to all saliva is be differenttoo much.Example,throughinactivatedsecretion, the submandibular glands flow 65% of whole saliva, parotid glands flow 20%, sublingual glands flow 5% and minor salivary glands secrete 10% [7]. Nevertheless, throughactivated secretion, the parotid glands flows 50% volume of salivary capacity[10].

III. SALIVA CONSTITUENTS

Saliva is a biological fluid secretion from multiple of salivary glands. The normal salivary secretion is 1000 to 1500mL/day for ahealthy adult,but saliva production qualitatively and quantitatively can modify bysome pathological and physiological conditions [11]. Several conditions modify saliva secretion and production e.g. tasteand smell motivation, mastication, drugs, age, psychosomatic and hormonal status, oral hygiene, geneticeffects and physical training [12]. Saliva is odourless, colourless and has a pH of 6.6 – 7.1 and a relative density of 1.004–1.009 [13]. Principally, saliva consists of 99% water and 1% organic molecules such as salivary mucins,mucopolysaccharide, amylase, and lysozymes, and some inorganic matter such as K^+, Na^+,Cl^-, Ca2+ $HPO^2$3, HCO3, Mg^{2+}, and NH3. Saliva also has a complex composition that includesnitrogenous products (urea and ammonia), uric acid, glucose, fatty acid, cholesterol, triglycerides, neutral lipid, amino acid, glycolipid, steroid hormones, mucin, amylase, glycoprotein, lectin, peroxidase, lysozyme and lactoferrin. In addition, saliva contains an estimated >700 species of microorganisms that are related to oral and systemic diseases. Microorganisms contribute an assortment of enzymes to saliva's composition. Recent proteomic reports have identified more than 3,000 salivary proteins and peptides that are participate in maintenance of oral homeostasis[14]. The major sources of proteins in saliva are salivary glands, but oral microorganisms (particularly bacteria), oral tissues and blood are important contributes of proteins and should include parts of proteome [15]. Among those proteins, the most relevant ones are glandular in origin: Proline-rich proteins (PRPs) (acidic PRPs: 20%, basicPRPs: 12% and glycosylated PRPs: 5%), amylase = 20%, mucins = 20% constitute the most abundant proteins in human saliva [16]. Secretory immunoglobulin A (sIgA) and immunoglobulin (IgG), histatins, cystatins, lactoferrins, mucins, lysozymes and all others are represent 23% of salivary proteins [16]. Bicarbonate plays a vital role inpreventing dissolution of tooth mineral by buffering salivary pH near neutrality. In addition, facilitates solubilization of macromolecules and alters the solubilityand rheological properties of mucins.Calcium and phosphate playing an important role in the mineralization of hard tissue [17].Studies have proposed the concept of saliva omics because the rapid progress made in salivary studies. Saliva omicsinclude epigenome (DNA methylation), (mRNA, microRNA andother noncoding RNAs), transcript me,genomics(human and microbial), proteome and metabolome[18].

Saliva may contain expressed proteins and peptides, and other components that can be used as biomarker of diseases.

IV. SALIVA FUNCTIONS

The fundamental role of saliva is to protecting and maintaining the integrity of the tooth structures in the oral cavity and oral mucosal, as do protecting and maintaining theintegrity of the upper part of the mucous membrane of the gastrointestinal tract that are critical for preserving health and homeostasis in the body andfacilitating important functions.Saliva plays multifunctional roles in oral cavity including lubrication, digestion, cleans the oral cavity, pellicle formation, antimicrobial actions and agglutination, by the multitude of organic and inorganic species including protein and peptides. Saliva alsofacilitates speech, aids taste, mastication, and swallowing.

4.1 Lubrication and protection

Lubrication, defined as the ability of a substance to decrease friction between moving surfaces, is regarded as one of the most vital functions of saliva. Saliva coats hard and soft tissue, which helps to protect against mechanical, thermal and chemical irritation and tooth wear. Lubrication assists also smooth airflow, mastication, speech and swallowingprocesses. Lubrication has been associated with several salivary proteins, including: mucins [19], proline-rich glycoproteins [20], statherin[19, 21], acidic proline-rich proteins [19], and amylase [22].

4.2 Digestionand taste

Saliva is responsible for the initiation of starch and lipid digestion. The salivary α-amylase is the most abundant salivary enzyme; it breaks down of starch into sugars [23]. Saliva acts as a solvent, thus enhancing interaction of food products with taste buds to facilitate taste[23].

4.3 Cleansing and swallowing

Saliva mechanically cleanses non-adherent particles (i.e. food detritus, bacteria, and cellular) from the oral cavity. The clearance of food detritus, in particular excess carbohydrates, results in a reduction of the availability of sugar for microorganism metabolism[24]. Food bolus formation aiding swallowing is also helped by the presence of saliva[23].

4.4 Buffering

Buffer capacity help to neutralize acids produced by acidogenic microorganisms, thus protect the teeth and prevent enamel demineralization by saliva composition such as bicarbonate and phosphate and protein buffer [25]. Bicarbonate is an important component of saliva since it plays a major rolein preventing dissolution of tooth mineral that increases in the presence of protons, by buffering salivary pH near neutrality.

4.5 Maintaining tooth integrity

Maintaining tooth integrity" by balancing demineralization and remineralization process. Demineralized processes happen when acids diffuse into the enamel resulting in crystalline dissolution and occur in a critical pH range (pH 5 - 5.5) for development of caries. Dissolved mineral diffuses from the tooth into the saliva. The mineral diffuses from the tooth into the saliva tooth structure from ions dissolved in the saliva by remineralization process [26]. Statherin and acidic proline-rich proteins in saliva inhibit spontaneous precipitation of calcium phosphate salts.

4.6 Pellicle formation

Acquired pellicle is an organic film depositing on the enamel surfaces as soon as a tooth erupts or is cleaned, derived mainly from salivary proteins and glycoproteins.

The acquired salivary pellicle, a thin acellular (0.5 μm) protective film predominantly consisting of salivary proteins, covers surfaces that are exposed in the oral cavity such as enamel, dentine and oral mucosa, as well as artificial ones such as dental materials. It is known to have an important role in protecting the underlying enamel surfaces[27]. Also it is important in subtraction protection and lubrication. In addition, possesses buffering ability.

Proteins and glycoproteins have been identified as the major components of salivary proteins in the formation of pellicle. Phosphoproteins with a high affinity to hydroxyapatite, such as statherin, histatin and proline-rich proteins (PRPs), have been shown to be among the first proteins, which adsorb onto the hydroxyapatite (HAP) surface from saliva. However, in vivo studies revealed a more diverse and complex pellicle composition, with the presence of high-molecular-weight glycoproteins (MUC5B and MUC7), amylase, cystatins, lysozyme and lactoferrin.

4.7 Antimicrobial actions

Saliva contains many innate defense molecules that participate in the protection of oral tissues by either direct antimicrobial effect or interference with microbial colonization.Saliva contains several immunologic and non-immunologic proteins with antimicrobial properties. Among immunologic components of saliva, Secretory immunoglobulin A (IgA) is the largest proportion, which can neutralize bacterial, viruses, and enzyme toxins. The non-immunologic salivary proteins also act as antibacterial agents; for example lysozymes and thiocyanate ions in the saliva are bactericidal, making saliva an important part of the nonspecific immune system of humans.

V. SALIVARYPROTEINSAS APROTECTIVE FACTOR FOR ECC

The components of saliva are important in the maintenance of oral health. Patients who suffer from a decrease salivary flow rate are more susceptible to dental caries and fungal infections than healthy individuals[28].The critical importance of saliva is strikingly evident in individuals with decreased salivary flow who experience: acute irritation of oral mucosa, tooth caries and severe difficulties with speaking, swallowing, food clearance and taste.Evidently saliva prevents unlimited colonization of the oral tissues by oral microorganisms, rather than completely extirpating the oral microflora. Below we will discuss different antimicrobial mechanisms by which saliva modulates the microbial colonization of the oral tissues Table 1.

5.1 Modulation of Bacterial Attachment

The enamel of tooth is coated with a film of salivary proteinsthatcalled AEP.
Pellicle formation starts with binding of phosphoproteins including proline-rich proteins, statherin and histatins, which have been implicated in mineral homeostasis.

The antimicrobial mechanisms in saliva are listed in Table 1 and described below.

Salivary components	**MW**	**Sources**	**Main functions**	**Conc. in whole saliva**
Immunoglobulins A	60 kDa	Major and minor salivary glands	Immune response, microbial agglutination	76.1µg /mL
Mucins[24, 29]	120-1000 kDa	Submandibular, Sublingual glandsand minor mucous glands	Promotes growth of a complex microflora which suppresses colonization by exogenous microorganisms, microbial agglutination	10-500 µg/mL
Statherin[30, 31]	5.4 kDa	Produced by acinar cells	Inhibition of hypha formation of Candida albicans, microbial receptors on dental surface	2-12 µg/mL
Lactoperoxidase[32]	78-280 kDa	GCF and neutrophil granulocytes (Myeloperoxidase), Salivary glands (Lactoperoxidase	Formation of microbicidal products (OSCN–)	1-5 µg/mL
Lysozyme[33, 34]	14.3 kDa	Salivary glands, neutrophil granulocytes and gingival crevicular fluid	Degradation of cell wall	28.9 µg /mL
Lactoferin[35]	~ 80 kDa	Salivary glands, mucosal epithelial cells and neutrophil granulocytes	Inhibition of biofilm formation, iron depletion,	0.4-7 µg/mL
Agglutinin[36]	~340 kDa	Parotid, submandibular and sublingual glands	Microbial agglutination	
LL-37[37]	18-kDa	Salivary glands and duct, neutrophil leukocytes and gingival sulcus	Pore formation in microbial membranes	2–5 µg/mL
Defensins[38]	4–5 kDa	Neutrophil granulocytes, mucosal cells	Pore formation in microbial membranes	
Histatins[31, 39, 40]	3-6 kDa	Parotid and submandibular salivary duct cells	Pore formation in microbial membranes	2-8 µg/mL

5.1.1 Immunoglobulins

Human saliva contains several constituents with antimicrobial or protective properties in the oral cavity. Usually, constituents in saliva are classified as either immunoglobulins or non-immunoglobulins. Salivary immunoglobulinscompose ~ 5–15% of whole salivary proteins[41]. Salivary immunoglobulins are salivary antibodies that act as the first line of defense; they include two major antibodies namely secretory IgA (50%–60%) found in the saliva,and the rest belong to the IgG. [42].IgA scan neutralize bacterial toxins and enzymes, interferewith the adherence of the bacteria to the tooth surface by physicallyblocking bacterial adhesions, inhibiting bacterial metabolism, reducingthe hydrophobicity of bacteria and aggregating or clumping thebacteria together, which aids in the antibacterial action of thesaliva[41, 43].Many investigations reported significant higher levels of salivary IgA in caries-active children that probably to provide protective mechanism against cariogenic bacteria especially *S. mutans*[44-49]. IgA prevent the interaction of bacteria and virus with oral surfaces without triggering an immune response[50]. This mechanism,neutralization of antigens without causing an inflammatoryresponse, is called immune exclusion.

5.1.2 Mucin MUC7

MUC7 (mucin MG2) is a glycoprotein secretion from submandibular and labial glands, with molecular weight 150-200kDa. Mucins found in human saliva protect teeth from demineralization induced by the acid produced from microbial metabolism[51].In addition, mucins play roles in lubrication, healing of the oral mucosa, formation of the food bolus, and phonation[52].

Many studies have reported that MG2can interact with oral microorganisms by promoting their binding and agglutination [53, 54]. Binding is mediated by both the carbohydrate side chains of MUC7, in particular unglycosylated peptide domains [55] and sialic acid [56, 57].Thus, MG2 may be an important antimicrobialagent. Levine et al. [58]reported that salivary mucins agglutinated *S. mutans* and *S. sanguis*.

5.1.3 Agglutinin

Agglutinin: Salivary agglutinin (SAG) is a high-molecular-mass (~340 kDa) component of human salivathat is secreted by the parotid gland, sublingual gland and submandibular gland. SAG was originally characterized as an *S. mutans*agglutinating glycoprotein[36].Like MUC7; SAG is capable to binds a wide variety of bacteria[59]. SAG is highly glycosylated and extremely sticky, potentially binding to the pellicle and interacting with unattached bacteria, resulting in the aggregation of bacteria that are more easilyswallowed or flushed away [60-62]. Thus, SAG plays a role in the oralclearance of bacteria. Some studies have reported a correlationbetween increased levels of agglutinin in saliva and increased numbersof *S. mutans*in dental plaque and susceptibility to dental caries [63].
Saliva-mediated aggregation and adherence plays a direct role in caries resistance.

5.2 Inhibition of Microbial Growth

Saliva contains many components that exhibit in vitro antibacterial properties. Their function is to keep the oral microflora within certain limits by preventing excessive colonization of the oral cavity in combination with the bacteria-agglutinating factors.

5.2.1 Statherin

Statherin is a low molecular weight (5.4 kDa) acidic protein. Statherin has various functions, including binding tohydroxyapatite(HAP), inhibiting the spontaneous precipitation of calcium and phosphate salts from the supersaturated saliva, and inhibiting HAP crystal growth. Maintaining saliva supersaturated with calcium phosphate salts is achieved by statherin, which enhances enamel remineralization, thereby maintaining the integrity of the tooth and inhibiting caries progression[10].

The hyphae form isconsidered the most invasive form of the fungus. The antimicrobial mechanismfor statherin has been discovered, which inhibits hyphal formation of C. albicansand may thus contribute to the oral defense against candidiasis [64].Statherin reduces bacterial and fungal colonization by aggregating the microbes. This clumping process reduces the ability of bacteria to adhere to intraoral hard and soft tissue surfaces[10]. Vitorino et al.[65]reported a strong correlation between high levels of statherin and the absence of dental caries in children. This finding implies a protective role of statherin against caries.

5.2.2 Lactoperoxidase

Lactoperoxidaseis aninnate human salivary defense protein that known to exert a wide antimicrobial activity against a number of bacterial, viral and fungal pathogens *in vitro*[66]. Some studies reported that the increased of thiocyanate ions in saliva reduce the number of cariogenic microflora in children with ECC [67]. The study investigated by Ravi et al. [68] revealed that toothpaste-containinglactoperoxidase was highly significant in reducing the salivary levels of *L. acidophilus* and mutans Streptococciin children with S-ECC ($p<0.001$).

5.2.3 Lysozyme

Lysozyme is an antibacterial enzyme found in high amounts in body fluids such as saliva, serum, tears and amniotic fluid, as well as in low amounts in bile, urine and cerebrospinal fluid.Lysozyme promotes bacterial clearance through aggregation and adherence. Furthermore, it has the ability to destroy and inhibit bacterial growth [10, 69]. In an *in vitro* study, *S. mutans* and *L. casei* were inhibited by lysozyme [70].

5.2.2 Lactoferrin

LF is an iron-binding cationic glycoprotein that is present in various mucosal secretionssuch as parotid and submandibularsaliva,tears and milk. LF possesses potent activity against *S. mutans*, fungi, parasites and viruses[35]. LF has the ability to bind and kill bacteria via direct interactions through the strongly basic N-terminal region of the glycoprotein that consists of 47 amino acids [71]. In addition, LF and other cationic peptides are capable of neutralizing the interaction between bacterial lipopolysaccharides (LPS) and host defense cells [72]. This interaction can alter the permeability of the outer membrane of Gram-negative bacteria and release LPS[73]. Because of its antimicrobial activity, salivary LF is thought to play a major role in caries susceptibility.

5.3 Antimicrobial Peptides

Antimicrobial Peptides **(**AMPs) are essential components of innate immunity, providing the first line of defense against oral microbial colonization and infection[74]. The smaller size of AMPs facilitates the rapid diffusion and secretion of peptide outside the cells, which is required for eliciting immediate defence response against pathogenic microbes [75].

5.3.1 Histatins

Histatins are small cationic peptideswith high histidine content. Histatins have been reported to exhibit both direct and indirect antimicrobial activities and play major roles in innate immunity. Therefore, histatins are considered to be important components of the non-immune host defense system of the oral cavity [76-78]. Histatins, especially histatin 1, may play a role in reducing bacterial colonization on tooth surfaces because it has the ability to incorporate into the acquired pellicle and block the binding site of bacteria on tooth surfaces[79][80]. In an in vitro study, histatin 1 reduced *S. mutans* adhesion onto HAP surfaces by inhibiting the adsorption of salivary high-molecular-weight glycoproteins [80]. Some studies demonstrated a significant correlation between high levels of salivary histatin 1 and the absence of dental caries[65].

5.3.2 Defensins

Defensins are antimicrobial (prototype) cations, low molecular weight (4– 5 kDa) peptides. Depending on the pattern of cysteine pairing, two types of defensins are recognized, namely, the α-defensins and theβ-defensins[38].α-defensins are present in saliva and gingival crevicular fluid[81].β-Defensins (hBDs) are cationic peptides of 30– 45 amino acids[82], which are secreted by gingival keratinocytes.They interact with bacterial wall due to their positive electronic charge; they then integrate with the bacterial membrane, forming ion channels and transmembrane pores, which causes leakage and destruction of bacteria [34, 74].In a more recent study, conducted by Ahn et al. hBD-3 showed antimicrobial activity by inhibiting biofilm formation by *S. mutans*and other dentinophilic bacteria such as *Enterococcus faecalis*and *streptococcus gordonii*[83].
Many of studies support the association between reduction of alpha-defensins (HNP1–3) and high caries rate and suggested that these are biological factors that can be used for caries risk assessment in children[81, 84]. However, another study has shown no statistic difference of HNP1-3 salivary levels between S-ECC group and caries-free group [85].

5.3.3 Human Cathelicidin peptide LL-37

Cathelicidins are antimicrobial host defense peptides.LL-37 is the only member in the cathelicidin family that expressed in humans. Cationic alpha-helical peptide, with 18kDa, is found in neutrophils and inflamed epithelia, as well as in saliva [37]. The antibacterial effect of LL-37 and its derivatives is based on their cationic property. These molecules aggregate on microbial membranes to form ion channels and transmembrane pores to ultimately cause membrane leakage and membrane rupture [74]. Moreover, LL-37 has the ability to prevent biofilm formation of *Pseudomonas aeruginosa* at sub-minimum inhibitory concentrations by decreasing the attachment of bacterial cells and stimulating twitching motility [86]. In addition, LL-37 inhibits biofilm production of *Staphylococcus epidermidis*[87]. In a longitudinal study, 57 toddlers (12 to 24 months old) were followed for 2–3 years. The study showed a positive correlation between elevated concentrations of salivary LL-37 ($r= 0.336$, $P <0.05$) and higher numbers of *S. mutans*[88]. This result suggests that increases in the concentration of salivary LL-37 may be a response to higher bacterial colonization.

VI. SALIVARY PROTEOME IN RELATION TO DENTAL CARIES

Dental caries are one of the most common chronic infectious oral diseases, characterized by the destruction of tooth tissues by synergistic complex effects among acids generated from the fermentation of dietary carbohydrates by bacteria and susceptible host factors, such as teeth and saliva [1]. This process can ultimately lead to tooth loss. Saliva is an important factor in the development of dental caries[46].Since the last decades, salivary diagnostics have been developed to monitor dental caries,periodontal disease and other oral diseases[89, 90].Evaluating alterations biomarkers of saliva can be applied to the early detection of oral and systemic diseases.Saliva is actively being investigated as abundant source of protein biomarkers [90], capable of discriminating healthy from diseased individuals[91].Early diagnosis and early preventive are important for disease control.

The potential of salivary components as biomarkers in the diagnosis of several oraldiseases have been recognized.Vitorino et al.[65]utilizing the HPLC-MS, found a significant correlation between high levels of salivaryhistatin 1, statherin and PRP1/3 and the absence of dental caries in children. Also in another study using 2D gel electrophoresis, reported higher concentrations of cystatin S in caries-free children[45].The concentration of proteins and polypeptides present in saliva is important in the maintenance of oral health and homeostasis, as increased frequency and severity of oral disease are often associated with qualitative and quantitative changes of the saliva proteome [8, 16]. Proteomic molecules, such as histatins, mucin, lactoperoxidase, defensins, proline-rich peptides and lactoferrin (LF) regulate the microbial flora of the oral cavity by exerting direct antibacterial effects [41]. Many of the proteins present in saliva are critical for the protection of oral tissues against fungal or viral infections [31]. Therefore, salivary protein composition may play an important role in the etiology of oral disease prevalence and dental caries development [41].Inrecent studies, saliva was used to evaluate the incidence of caries byexamining bacterial abundance, protein identity and concentration,and buffer capacity within the saliva samples. Saliva is known to play a protective role against caries since it contains several antibacterial agents, can mechanically clear the pathogens and has a buffering capacity to decrease the acid concentration on tooth surfaces.Therefore, changes in quantity and composition of saliva can also provide potential tools to detect and monitor caries.

VII. CONCLUSION

Various functions of saliva are implicated in the protection of teeth against caries and the maintenance of oral health. Salivacontains many of proteins that involve in the first line of defense in the oral cavity.

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