Chapter

Functions of Saliva

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Abstract

Saliva is produced and secreted by salivary glands. The basic secretary units of salivary glands are clusters of acini cells. It is fluid that contains water, electrolytes, mucus, and enzymes, all of which flow out of the acinus into collecting ducts, certainly one of the most important components and an integral component to oral health. The protective role and benefits including buffering, remineralization in the healthy oral mucosa, immune defense, digestion, lubrication, diagnostic purpose, and proteome analysis are fulfilled by saliva. It aids in maintaining mucosal integrity and indigestion through salivary enzymes. The functions of saliva in maintaining oral health and the main factors that cause alterations in salivary secretion and the importance of saliva in caries development and bacterial plaque formation are discussed, and also its role and functions and organic and inorganic constituents in saliva are discussed. This is of great importance in ruminants, which have non-secretory forestomachs. Diseases of the salivary glands and ducts are not uncommon in animals and man, and excessive salivation is a symptom of almost any lesions in the oral cavity.

Keywords: functions of saliva, role of lubrication, antimicrobial functions of saliva

1. Introduction

The secretions of the major and minor salivary glands, together with the gingival crevicular fluid, constitute whole saliva which provides the chemical milieu of the teeth and oral soft tissues [1]. Saliva formation can be evoked by sympathetic and parasympathetic stimulations [2]. The critical function of saliva is required for the preservation and maintenance of oral tissue [3]. Saliva is a complex secretion. About 93% by volume is secreted by the major salivary glands and the remaining 7% by the minor glands. About 99% of saliva is water and the other 1% is composed of organic and inorganic molecules [4]. Saliva consists of both full-length and partially degraded forms of mRNA, and its association with macromolecules may protect salivary RNA from degradation [5]. The proteome of the whole saliva will be relevant to oral health and be crucial for the identification of meaningful biomarkers for oral disease [6]. Sialometry and sialochemistry are used to diagnose systemic illnesses, monitoring general health, and as an indicator of risk for diseases creating a close relation between oral and systemic health [7]. Saliva acts as a mirror of the body's health and could constitute the first line of defense against oxidative stress by controlling and/or modulating oxidative damages in the oral cavity [8].

The analysis of salivary transcriptome may be beneficial effects in the detection of oral cancer and salivary diagnostics [9]. Cationic peptides and other defense proteins like lysozyme, bactericidal–/permeability-increasing protein (BPI), BPI-like proteins, PLUNC (palate lung and nasal epithelial clone) proteins, salivary amylase, cystatins, proline-rich proteins, mucins, peroxidases, and statherin are primarily responsible for innate immunity [10]. The protein and ion components make a solution that is 99% water into a viscoelastic solution capable of many roles, such as acting as a lubricant and an antimicrobial, preventing the dissolution of teeth, aiding digestion, and facilitating taste [11]. With the rapid advancement in salivaomics, saliva, as a noninvasive and safe source, could be a substitute for blood in the diagnosis and prognosis of diseases [12]. Saliva has important functions in maintaining mucosal integrity and indigestion through salivary enzymes, buffering, remineralization, and lubrication [13].

Saliva is an aqueous fluid found in the oral cavity playing a fundamental role in the preservation and maintenance of oral health [14]. Saliva acts in relation to taste, mastication, bolus formation, enzymatic digestion, and swallowing. The protective functions of saliva including maintenance of dental and mucosal integrity indirectly influence the digestive process [15]. The review aimed to discuss the different functions that are performed by the saliva.

1.1 Composition of saliva

Saliva is composed of a variety of electrolytes, including sodium, potassium, calcium, magnesium, bicarbonate, and phosphates. Also found in saliva are immunoglobulins, proteins, enzymes, mucins, and nitrogenous products, such as urea and ammonia. These components interact in related functions in the following general area: (1) bicarbonates, phosphates, and urea act to modulate pH and the buffering capacity of saliva; (2) macromolecule proteins and mucins serve to cleanse, aggregate, and/or attach oral microorganisms and contribute to dental plaque metabolism; (3) calcium, phosphate, and proteins work together as an antisolubility factor and modulate demineralization and remineralization; and (4) immunoglobulins, proteins, and enzymes provide antibacterial action. The components listed above generally occur in small amounts, varying with changes in flow; however they continually provide an array of important functions. It is important to stress that saliva, as a unique biologic fluid, must be considered as a whole that is greater than the sum of its parts [3, 16].

Saliva is a very dilute fluid, composed of more than 99% water. Saliva is not considered an ultrafiltrate of plasma [16, 17]; initially, saliva is isotonic; it is formed in the acini, but it becomes hypotonic when it travels through the duct network. The hypotonicity of unstimulated saliva allows the taste buds to perceive different tastes without being masked by normal plasma sodium levels. Hypotonicity, especially during low-flow periods, also allows for expansion and hydration of mucin glycoproteins, which protectively blanket tissues of the mouth [18]; lower levels of glucose, bicarbonate, and urea in unstimulated saliva augment the hypotonic environment to enhance taste.

1.2 Organic and inorganic constituents of saliva

The organic and inorganic compositions of saliva can supply information about alterations in enzymatic activity in response to periodontal inflammation [19]. Alkaline phosphatase (ALP) is a calcium-phosphate binding protein and a phosphor-hydrolytic enzyme. ALP is considered to be an important indicator of bone formation and is a phenotypic marker for osteoblast cells [20]. ALP was detected in the parotid, submandibular, and minor salivary glands, as well as in desquamated epithelial cells, leucocytes, and bacteria from dental plaque. The presence of the ALP in the saliva and in the gingival crevicular fluid is usually indicative of inflammation and/or destruction of the periodontal tissues. Among the several salivary components, urea is an organic compound that represents the final product of the human catabolism of proteins.

The hydrolysis of urea by bacterial urease enzymes generates ammonia and CO_2 and is considered a major pathway for alkali production in the oral cavity. In addition, ammonia is potentially cytotoxic for the periodontal tissues [21]. Ammonia can increase the permeability of the sulcular epithelium to other antigenic and toxic substances, thereby playing a fundamental role in the initiation of gingivitis [22]. The volume of saliva in the oral cavity depends on several factors, such as stimulation, circadian rhythm, diet, age, drugs, and the hydrogen (H+) ion concentration. Meanwhile, these factors can also be altered due to pathological conditions, such as periodontal disease [23] (**Table 1**).

Salivary component	Function
Amylase	Digestive
Bicarbonate	Buffering
Calcium	Remineralization
Salivary antibodies	Antimicrobial
Lactoferrin	Antimicrobial
Lysozyme	Hydrolysis of cell membrane
Mucins	Digestion, lubrication, and pellicle formation
Protease	Digestion
Water	Mucosal integrity

Table 1.
Components and functions of saliva.

2. Saliva functions

2.1 Immune functions

The components like lysozyme, lactoferrin, salivary peroxidase, myeloperoxidase, and thiocyanate concentrations act as a defense mechanism in the whole saliva [24]. The natural defense properties of salivary secretions through clinical modalities such as the development of (1) diagnostic reagents and tests for local and systemic disease, (2) artificial salivas for the treatment of salivary dysfunction, and (3) topical vaccines to combat against oral diseases [25]. Salivary mucins are well recognized as an important factor in the preservation of the health of the oral cavity and are of significance to the processes occurring within the epithelial perimeter of mucosal defense [26]. Human saliva contains a number of physical, physicochemical, and chemical agents that protect oral tissues against noxious compounds. It effectively removes exogenous and endogenous microorganisms and their products into the gut and continuous presence of both nonimmune and immune factors in the mouth [27]. Salivary mucosal pellicle forms the structural basis of the local innate immune defense mechanism of the oral mucosa [28].

2.2 Saliva proteome analysis

The salivary flow rate influences to a high degree the rate of oral and salivary clearance of bacterial substrates included in foods and snacks [29]. Salivary IgA and lysozyme were inversely correlated with self-perceived work-related stress. As these salivary biomarkers are reflective of the mucosal immunity, results support the inverse relation between stress and mucosal immunity [30]. There was an inverse relationship between the presence of hyaluronidase and the presence of hyaluronidase inhibitors particularly in relation to intraoral wound healing and periodontal disease [31]. Human salivary α-amylase (HSA) is a major secretory protein component of saliva and has important biological functions, including the initial digestion of starch [32]. The collagen-cleaving enzyme matrix metalloproteinase-8 (MMP-8) is present in saliva and acts as measurable indicator of periodontal disease [33].

Amylase present in human saliva was one of the first enzymes to be recognized and molecular mechanisms involved in amylolysis of starch and even of the physiological role of the salivary amylase itself [34]. Lactoferrin in saliva represents an important defense factor against bacterial injuries including those related to *Streptococcus mutans* and periodontopathic bacteria through its ability to decrease bacterial growth, biofilm development, iron overload, reactive oxygen formation, and inflammatory processes [35]. Some defense proteins, like salivary immune globulins and salivary chaperokine HSP70/HSPAs, are involved in both innate and acquired immunities [10]. Lactoferrin is a major component of biologically important mucosal fluids and is essential for mucosal-mediated immunity [36].

The antimicrobial in vitro effects of the salivary proteins lactoferrin and lysozyme on microorganisms is involved in the carious process, obtaining their minimum inhibitory concentration and minimum bactericidal concentration [37]. Salivary alpha-amylase has been proposed as a sensitive noninvasive biomarker for stress-induced changes in the body that reflect the activity of the sympathetic nervous system [38]. Salivary α-amylase levels may therefore serve as an effective indicator in the noninvasive assessment of physical stress [39]. Lactoferrin is a multifunctional mammalian immunity protein that limits microbial growth through sequestration of nutrient iron [40]. Lysozyme in saliva is found to have the antibacterial activity against the pathogen, and there is potential for it to serve an antimicrobial role in the specific application of medical industry [41].

Lactoferrin may be a useful agent to prevent irradiation effects in salivary glands [42]. LTF is examined as a first-line mediator in immune defense and response to pathogenic and nonpathogenic injuries as well as a molecule critical for control of oxidative cell function [43]. Salivary and pancreatic amylases hydrolyze starch and involvement of amylase in adiposity and starch metabolism [44]. Lactoferrin is a secretory protein with various physiological functions, and oral lactoferrin may mitigate psychological stress in humans [45].

2.3 Role of lubrication

The complex mix of salivary constituents provides an effective set of systems for lubricating and protecting the soft and hard tissues [46]. The lubricating and antimicrobial functions of saliva are maintained mainly by resting; saliva results in a flushing effect and the clearance of oral debris and noxious agents [47]. Saliva is a complex fluid, which influences oral health through specific and nonspecific physical and chemical properties [48]. Saliva contains numerous antimicrobial proteins that help protect the oral ecosystem from infectious agent [49]. Proteins can move from blood circulation into salivary glands through active transportation, passive diffusion, or ultrafiltration; some of which are then released into saliva and hence can potentially serve as biomarkers for diseases [50]. Saliva covers the oral hard and soft tissues with a conditioning film which governs the initial attachment of microorganisms, a crucial step in the setup of the oral microflora [51].

2.4 Role of digestion

A high quality of saliva is an essential factor to protect the dental elements against attrition and promote the digestion process [52]. Saliva is the principal fluid component of the external environment of the taste receptor cells which is involved in the transport of taste substances and protection of the taste receptor [53]. The role of human saliva and its compositional elements in relation to the GI functions of taste, mastication, bolus formation, enzymatic digestion, and swallowing [54]. Salivary nonesterified fatty acids (NEFA) are proposed to play a role in oral health and oral fat detection, and they may hold diagnostic and prognostic potential [55].

Lingual lipase generates nonesterified fatty acids (NEFA) from dietary fats during oral processing by lipolysis. Lingual lipase in rodents has strong lipolytic activity and plays a critical role in oral detection of fats [56]. Physiological role of salivary lipolytic activity in the regulation of the basal FFA concentration could be involved in fat taste sensitivity [57]. During chewing, saliva helps in preparing the food bolus by agglomerating the formed particles, and it initiates enzymatic food breakdown [58]. Saliva plays a key role in the eating process and on the perception of flavor. Flavor corresponds to the combined effect of taste sensations, aromatics, and chemical feeling factors evoked by food in the oral cavity [59].

2.5 Role of diagnostic properties

Analysis of saliva may be useful for the diagnosis of hereditary disorders, autoimmune diseases, malignant and infectious diseases, and endocrine disorders, as well as in the assessment of therapeutic levels of drugs and the monitoring of illicit drug use [61]. Fluid addition facilitated chewing of dry foods and feeding disorders caused by hyposalivation [62]. Saliva has been demonstrated to be a promising bodily fluid for early detection of diseases, and salivary diagnostics have exhibited tremendous potential in clinical applications [63]. Saliva has the potential to become a first-line diagnostic sample of choice owing to the advancements in detection technologies coupled with combinations of biomolecules with clinical relevance [64]. Saliva is a useful diagnostic fluid for oral-related diseases. Monitoring salivary biomarkers for oral and systemic diseases could become an important complement to clinical examinations in epidemiological surveys [65] (**Figure 1**).

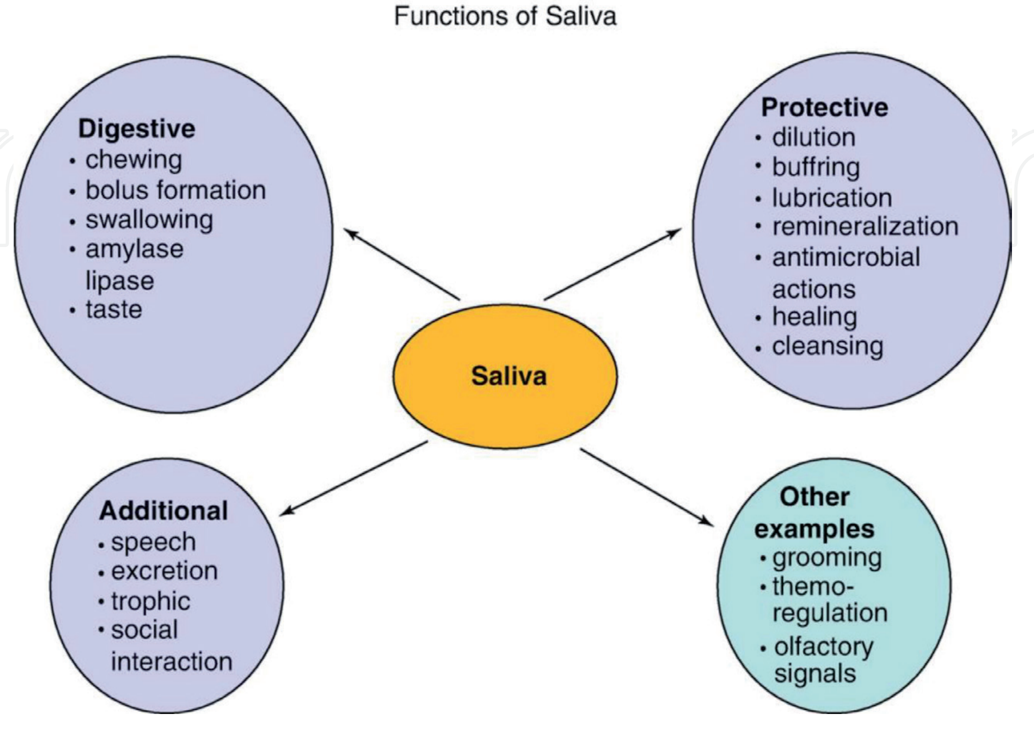

Figure 1.
Different functions of the saliva [60].

The high rate of changes in the composition of saliva can be used for the monitoring of various biorhythms in order to study the physiological characteristics of the human body [66]. The significant influences of the oral environment observed in this study increase the current understanding of the salivary microbiome in caries. These results will be useful for expanding research directions and for improving disease diagnosis, prognosis, and therapy [67].

2.6 Role of maintenance of health teeth

The role of saliva, the prevalence of oral dryness and the consequent importance of salivary flow as well as the relationship between xerostomia and salivary gland hypofunction amongst the causes of oral dryness [68]. Saliva is the medium that bathes the taste receptors in the oral cavity and in which aroma and taste compounds are released when food is eaten. Moreover saliva contains enzymes and molecules that can interact with food [69]. Saliva is an important fluid in the oral cavity as it bathes the teeth and the soft tissues. The salivary pH, buffer capacity and mineral content of calcium (Ca), phosphate (P), sodium (Na), and potassium (K) are important in the tooth de−/remineralization process and calculus formation [70]. Significant change in the pH depends on the severity of the periodontal condition. The salivary pH shows significant changes and thus relevance to the severity of periodontal disease. Salivary pH may thus be used as a quick chairside diagnostic biomarker [71]. Taste perception elicited by food constituents and facilitated by sensory cells in the oral cavity is important for the survival of organisms. In addition to the five basic taste modalities, sweet, umami, bitter, sour, and salty, orosensory perception of stimuli such as fat constituents is intensely investigated [72].

Teeth are exposed to food, drinks, and the microbiota of the mouth and have a high resistance to localized demineralization that is unmatched by bone [73]. The pH of saliva and plaque will result in white spot lesions on the tooth surface which are considered initialization of caries because of demineralization [74]. Saliva is an important biological fluid that aids in mechanically removing food debris and bacteria from the oral cavity and teeth; reduced salivary flow causes ill effects to the oral tissues [13].

2.7 Antimicrobial, antiviral, and antifungal functions

A group of salivary proteins like lysozyme, lactoferrin, and lactoperoxidase working in conjunction with other components of saliva can have an immediate effect on oral bacteria, interfering with their ability to multiply or killing them directly. Lysozyme can cause lysis of bacterial cells, especially *Streptococcus mutans*, by interacting with anions of low charge density chaotropic ions (thiocyanate, perchlorate, iodide, bromide, nitrate, chloride, and fluoride) and with bicarbonate. It has recently been shown that another cationic peptide in saliva the histidine-rich peptide of parotid saliva has growth-inhibitory and bactericidal effects on oral bacteria. The histidine-rich peptides appear to be an effective antifungal agent as well, able to inhibit growth and kill *Candida albicans* at a very low concentration [75].

Lactoferrin, the exocrine gland equivalent of transferrin, is effective against bacteria that require iron for their metabolic processes. It can compete with the bacterial iron-chelating molecules and deprive the bacteria of this essential element. Lactoferrin is also capable of a bactericidal effect that is distinct from simple iron deprivation. Salivary peroxidase is part of an antibacterial system which involves the oxidation of salivary thiocyanate by hydrogen peroxide (generated by oral bacteria) to hypothiocyanite and hypothiocyanous acids. These products, in turn, affect bacterial metabolism (especially acid production) by oxidizing the sulfhydryl groups of the enzymes involved in glycolysis and sugar transport. The antimicrobial effect of salivary peroxidase against *S. mutans* is significantly enhanced by interaction with secretory IgA.

The protective potential of all the antibacterial proteins can be extended by interaction with mucin which can serve to concentrate this defense force at the interface of the mucosa and the inhospitable external environment. When teeth are present, especially if some gingivitis exists, the oral fluids will be augmented by a contribution from the gingival crevice area, the gingival crevicular fluid. This fluid can contribute to the oral defense system by providing (a) serum antibodies against oral bacteria, especially IgG antibodies, (b) phagocytic cells (PMNs), and (c) antibacterial products liberated from the phagocytic cells, e.g., lysozyme, lactoferrin, and myeloperoxidase [27].

The large number of antibacterial and antiviral proteins is present in human saliva. Of interest, most of these antibacterial proteins display antiviral activity, typically against specific viral pathogens. The review focuses on one protein that interacts with both bacteria and viruses, gp340, originally referred to as salivary agglutinin. In the oral cavity, soluble gp340 binds to and aggregates a variety of bacteria, and this is thought to increase bacterial clearance from the mouth. However, when bound to the tooth surface, gp340 promotes bacterial adherence. In the oral cavity, most gp340 proteins are found soluble in saliva and can function as a specific inhibitor of infectivity of HIV-1 and influenza A. In contrast, in the female reproductive track, most gp340 proteins are bound to the cell surface, where it can promote HIV-1 infection [76].

The saliva anti-fungal activity against *Candida albicans* and *Cryptococcus neoformans*. Therefore, the importance of the search for new, broad-spectrum anti-fungals with little or no toxicity cannot be overemphasized. The following properties make histatins promising antifungal therapeutic agents: (1) they have little or no toxicity, (2) they possess high cidal activities against azole-resistant fungal species and most of the fungal species tested, and (3) their candidacidal activity is similar to that of azole-based antifungals. Current research efforts focus on the development of improved histatins with enhanced cidal activity and stability and of suitable and effective histatin delivery systems. These and other approaches may help to outpace the growing list of drug-resistant and opportunistic fungi causing life-threatening, disseminating diseases. The histatins with improved protective properties may also be used as components of artificial saliva for patients with salivary dysfunction [77].

3. Conclusions

Saliva is secreted by salivary glands and has multiple proteins and enzymes. The saliva flow rate and pH are very important for maintenance of oral tissues. The protective role and benefits including buffering, remineralization in the healthy oral mucosa, immune defense, digestion, lubrication, diagnostic purpose, and proteome analysis are fulfilled by saliva. Saliva aids in maintaining mucosal integrity and in digestion through salivary enzymes. Saliva is essential information of the pellicle, which protects the tooth after eruption. Normal salivary composition, flow, and function are extremely important on a daily basis. It occurs in quantities, large or small, and recognition should be given to the many contributions it makes to the preservation and maintenance of health.

Conflict of interest

The authors report no declarations of interest.

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