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# COMPOSITION AND FUNCTION OF SALIVA: A REVIEW

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## ABSTRACT

Saliva is a secretion produced by exocrine gland called the salivary gland. 1-1.5L of saliva is produced daily on average in a normal person. Oral mucosal cells that need to be lubricated all the time so that aberrations and injuries to the oral cells could be lowered thus oral cavity has a constant flow of saliva all the time and it's important to omit infections in the salivary gland entering through the mouth. Saliva plays and important role in scattering the food all over the oral cavity and taking the tastant toward the specified region of taste while the salivary enzymes help in digestion of food. Saliva also help control buildup of plaque or dental carries and protect the enamel of teeth at the same time. Salivary proteins also have protective functions against bacteria, viruses and fungi and it's also involved in healing processes. In this review we will discuss the major functions and composition of saliva and this will help the future and current researchers.

**KEYWORDS:** Exocrine gland, Infections, Bacteria, Viruses and Fungi.

## INTRODUCTION

Saliva is a secretion produced by exocrine gland called the salivary gland. The saliva producing glands include major glands i.e. parotid gland, submandibular gland and sublingual gland while others are also present called the minor salivary glands. It consists mainly of

water along with salivary enzymes, some electrolytes, antibodies and other chemicals important for oral health.[1]

Saliva is produced every time when there is no stimulation, in resting form, produced mainly from the basal area under the tongue to lubricate the oral tissues. When there is a muscular activity, or some olfactory stimulation is there (food) it will also result in the production of saliva (stimulated) produced from all the sides of face which is the most part of the average production of saliva per day.[2,3]

1-1.5L of saliva is produced daily on average in a normal person. The index used to measure the level of salivation by both resting and stimulated production is called SF as in table 1.[4]

**Table 1: saliva flow range for stimulated and unstimulated conditions.[4]**

| SF (stimulated) | Range |
|---|---|
| Normal | 1-3mL/min |
| Low | 0.7-1 mL/min |
| Hyposalivation | >0.7 mL/min |
| SF (unstimulated) | Range |
| Normal | 0.25-0.35 mL/min |
| Low | 0.1-0.25 mL/min |
| Hyposalivation | >0.1 mL/min |

Saliva is very important for the well-being of oral hygiene and health. As it has enzymes, it plays an important role in metabolism and along with that, its also very important for drug elimination.[5]

Saliva also play an important role in diagnosis of diseases. The basic techniques used are sialometry and sialochemistry for monitoring the health of a person and to determine any systematic disease and general health. A comparison between general health and systematic illness can be used as an important indicator of the risk.[6]

**Composition and Functions**

**1. Lubrication and moistening**

Oral cavity is lined with oral mucosal cells that need to be lubricated all the time so that aberrations and injuries to the oral cells could be lowered. For this purpose, oral cavity has a constant flow of saliva all the time (unstimulated).[7] Along with this, a constant flow of saliva is also important to omit infections in the salivary gland entering through the mouth.[8]

Salivary flow rate changes throughout the day in a rhythmic fashion i.e. the flow rate is highest in the afternoon and is the lowest during the sleep time to overcome the need to swallow and that's why mouth feels dry during the night mostly.[9]

The saliva produced per day is the measure of amount produced by the salivary glands minus the amount that is evaporated (breathing) and absorbed (mucosal lining). Absorption takes place all the time due to the composition of saliva, as its mostly composed of water, the concentration is always hypotonic while the mucosal cells are more permeable which makes the absorption more efficient.[10]

In those species that don't have sweat gland, they use the salivary evaporation to balance their body temperature, i.e. dogs put their tongues out when their body temperature rises, saliva evaporates and give a cooling effect. Similarly, rats spread saliva on their body which evaporates and gives cooling effect.[11]

Saliva consists mostly of water (almost 99%), but it also contains secretions called mucins from sun-lingual and sub-mandibular glands. Mucin is also produced by some minor mucosal glands present in buccal, labial and palatal mucosa. Most common mucin found in saliva are MUC5B & MUC7.[12] During eating processes i.e. mastication and swallowing, these mucins form a slimy fluid which coat the surface f oral cavity providing the lubrication omitting the aberrations caused by the activity.[13,14]

**2. Smell and taste**

For any kind of taste, taste buds are present all over the tongue, but for a specific taste there is a specific region of tongue having the taste buds. Similarly, the taste buds are also scattered all over the oral cavity i.e. on papillae, on soft palate, in the nasopharynx, esophagus and epiglottis. When food enters the mouth, saliva plays and important role in scattering the food all over the oral cavity and taking the tastant toward the specified region of taste.[15]

There are 5 basic tastes that are recognized i.e. sweet, sour, bitter, salty and savory. In order of stimulation of saliva production, sour stimulate the most while bitter produce the smallest amount of saliva production. The receptors of bitter taste are also present in the nasopharynx and esophagus and act as second line of defense by initiating anti-peristaltic movement and coughing which expel out the noxious material out of the system.

Saliva, act as first line of defense and dilutes any thing that come from outside environment, and at this point if anything tastes bad/noxious, it will be spat out now and will not reach the digestive system.[16,17]

The taste receptors for salty and sour taste are ion channels and the presence of more types for each receptor is still unknown. For sweet taste, there is present a co-expression of 2 receptors, i.e. T1R2 and T1R3 and similarly, for umami/savory taste 2 co-expression of T1R1 and T1R3 are responsible while, there are 25 receptors for bitter taste.[18]

The secretions produced by acinar cells present in the salivary glands is alike to the plasma (ultrafiltrate). This secretion travel through the duct system of the salivary gland to reach the main exit duct. During this flow from acinar cells to the main exit duct, ions are reabsorbed from the secretion and the final secretion (unstimulated saliva) that exits becomes hypotonic and osmotic pressure becomes lower by 1/6 as compared to the secretion produced in acinar cells.[19]

For the taste buildup, the fact that saliva is hypotonic is very advantageous. It is because the taste receptors are very sensitive and they adapt very quickly, so if the saliva were to be more concentrated with ions, the taste buds would have been unable to taste any salty flavor which is more dilute than the secretions produced by acinar cells.

Unstimulated saliva also contains urea (bitter taste), glucose (sweet taste) and some bicarbonates that act as buffers for the acids. All of these can produce taste but are not recognized as their concentration in saliva is much lower than the threshold level to produce taste as in table 2.[20]

**Table 2: A relation between plasma and saliva concentration if tastant.[21]**

| Tastant | Level in saliva | Level in plasma | Threshold for taste |
|---|---|---|---|
| Sour (Hcl) | 0.00004 | 0.0001 | 3 |
| Sweet (sucrose) | 4.5 | 0.08 | 12 |
| Bitter (urea) | 6 | 4 | 120 |
| Salty (Nacl) | $Na^+$ 145<br>$Cl^-$ 101 | $Na^+$ 6<br>$Cl^-$ 16 | 12<br>12 |

Aromatic receptor are present mostly present nose and nasopharynx for gas products, but for liquid and solid product, it has been recently tested with 4 types of cheeses in solid from releasing it aroma during the process of mastication in the mouth, while during the process of

swallowing, the release of aroma stops. Saliva is important in such cases because its effecting directly the release of aroma by helping to make bolus during mastication which tend to help in release of aroma prior to swallowing. So, if chewing process will take, the more will be the release of aroma and similarly the more will be the release of saliva in turn as the process tends to stimulate the flow of saliva. This can be proved by chewing a gum. When the chewing gum is flavored, more saliva is produced during mastication but as it starts losing flavor, the flow rate of saliva will decrease accordingly.[22,23]

### 3. Digestion

The main digestive enzyme present in the saliva is called amylase which is also the major enzyme present in saliva. Amylase is present as 6 isoenzymes in saliva that can convert starch into maltotriose, maltotetrose, maltose and some other oligosaccharide. As compared to the saliva produced by sublingual and submandibular glands, the saliva produced by parotid gland contains a higher concentration of amylase while the lowest concentration is present in secretions produced by minor salivary glands.[24,25]

Although, the bolus produced in mouth when swallowed it is exposed to the gastric secretions which are mostly acidic turning the amylase inactive so, the actual role of amylase in starch digestion becomes uncertain. In a recent study, bolus was spat out and taken as a sample while to compare a similar crushed food was taken without exposure of saliva, when the starch digestion was checked, in bolus 17% of starch was digested while in the former there was no starch digestion.[26]

Another important enzyme that is discovered in rat's saliva is called lingual lipase which act as a very important enzyme in the digestion of lipids in the rat's stomach. But, in humans, when the action of lipase is compared, the gastric lipase shows promising results in digestion of lipids in the stomach as compared to the lingual lipase of saliva.[27,28]

Saliva plays an important role in digestion by converting the food into bolus which is much easy to swallow and digest as compared to the solid food entering the mouth. Also, presence of enzymes in the saliva aid the process of digestion. Saliva is also important for the indirect stimulation of production of secretion in the stomach by distributing the food tastant all over the taste receptor which trigger the production of gastric secretions (cephalic phase).[29]

**4. Mucosa protection**

Food entering the mouth may have harmful effects which is protected by the mucosal lining to move things smoothly, but this lining can also be damaged and for its protection adequate amount of saliva is present in the mouth. Also, if a food is noxious, it spat out without swallowing which stops any damage to esophagus.

Bicarbonates are present in saliva for buffering the acidity of food but the concentration of bicarbonate in saliva is very low and is not adequate to buffer the acidity. To overcome the concentration, more saliva is produced in response to the acidic stimulus from the food.[30]

Bicarbonates present in saliva hen are exposed to acids, they react with hydrogen to make carbonic acids which is then converted to water and $CO_2$ by the action of another enzyme present in saliva called the carbonic anhydrase. By this reaction, no contents of acids are accumulated in the process which makes bicarbonates the perfect buffer for saliva.[31]

Saliva soften the food when it enters the mouth and this bolus products omit any physical aberrations caused by the rough and hard food. There are up to 600-700 mucous glands present that make a mucous layer of 95 micrometer thickness. The food mixed with saliva makes bolus, bolus is covered with a layer of salivary mucin which help to reduce any physical harm in the esophagus.

GORD (gastro-esophageal reflux disease) is caused lower esophageal sphincter relaxes more than usual. In such case, the gastric secretions having hydrochloric acid along with pepsin start moving toward the esophagus causing the lining of esophagus to be damaged. In some cases, bile may also enter the esophagus which have a detergent effect that act specifically on the mucosal lining. The flow of unstimulated saliva makes this acidity to be lowered by buffering out the acids. Also, saliva helps in replenishing of the mucosal lining of esophagus.[32]

Epidermal growth factor (EGF) id produced in the saliva with the highest concentration in the parotid glands in humans while in rodents, its reported to be produced by submandibular glands in highest concentration. The receptors for EGF are present in the mucosal lining of esophagus and they reach in by the flow of saliva into the esophagus. EGF attach to these receptors and promote growth of the mucosal cells.[33,34]

**5. Protection of teeth**

➢ **Enamel pellicle formation**

Acquired enamel pellicle (AEP) is a thin layer of protein which covers all the surfaces having enamel. It also covers the layers of dentine and cementum of tooth when enamel is lost to protect the teeth from wearing.[35]

It was first thought that all the proteins of this layer are salivary in origin but after extensive research it has been found that AEP is composed of more than 130 proteins out of which 14.4% are originated from the salivary glands.[36]

Depending on the susceptibility of the surfaces towards aberrations, the thickness of AEP varies from 0.3 to 1.1 micrometer at different locations in the mouth. As soon as the AEP wears off, enamel is reformed in seconds when saliva is exposed to the surface. This property of saliva to reform so quickly on wearer surfaces makes it the most efficient renewable lubricant of mouth.[37]

The AEP is reported to lower the friction coefficient by 20-fold between opposing teeth. Thus, we can say that AEP provides protection to enamel by aberrations caused by foreign objects i.e. food and toothbrush as well as by attrition that is caused by contact between opposing teeth.[38]

The enamel is composed of calcium and phosphorus in the form of crystalline structure formed exactly of $(Ca)_{10}$ $(PO4)_6$ $(OH)_2$. Saliva have both Ca and P ions in supersaturated form. In the absence of AEP, there could be deposition of Ca and P making crystals causing the teeth to be enlarged with the passage of time. The presence of AEP not only stop the crystallization but due to its permeable nature, it let Ca and P ion to permeate to the enamel for re-mineralization.[39]

➢ **Clearance**

Removal of food debris is one of the most important function of saliva. The average amount of saliva before swallowing is 1.1 mL while the amount of saliva after swallowing is 0.8mL which is not much of a difference. It means that there is only a small amount of saliva which is swallowed each time swallowing.

The removal of fermentable carbohydrates i.e. acidic food, drinks, glucose and sucrose soon after intake is very important for oral health. It has been calculated, that stimulated and

unstimulated flow of saliva plays a major role in removal of such residues from mouth after swallowing, by computer modeling.[40]

People having problem/diseases due to which their salivary glands are affected can't produce adequate amount of saliva have very low rate for clearance. This make them more vulnerable to dental problems as they have a prolonged exposure to sugars. Also, sugar stimulates least amount of saliva normally which makes it even more hard to remove sugar residues completely.[41]

- **Dental caries and erosion of teeth**

Calcium, bicarbonates and phosphorus are the main components present in saliva that are involved in the protection of teeth. As compared to hypoxyapatite (major mineral present in dentine and enamel), both calcium and phosphorus are present in supersaturated form in the saliva. Thus, when mouth is empty (no food), saliva provides Ca and P for remineralization and at the same time APE protect the crystallization of hypoxyapatite crystals.

$10Ca + + 6PO_4 + 2OH \longrightarrow Ca_{10}(PO4)_6(OH)_2$ (A)

If the pH of saliva decreases by the presence of H+ then the equation changes as:

$PO_4 + H \longrightarrow HPO_4$

$HPO_4 + H \longrightarrow H_2PO_4$

$H_2PO_4 + H \longrightarrow H_3PO_4$

$OH + H \longrightarrow H_2O$

Similarly, if the pH of saliva increases in the presence of OH and $PO_4$ Equation A will be reversed i.e. solubility of minerals increase.[42]

As compared to fluorapatite formed in teeth as a result of fluoride product and food containing fluoride, the concentration of fluoride in saliva always remain supersaturated and is equal to 1 micro mole per liter of saliva. Although, the minerals are present in supersaturated form but still the do not precipitate in saliva, this is due to presence of special proteins in saliva which binds the minerals even to small amount of hydroxyapatite or fluorapatite called, statherin.[43]

Dental plaque has acidogenic microorganisms which when are exposed to fermentable carbohydrates, initiate a mineral dissolution by acids which cause dental caries.

Hyposalivation cause more susceptibility towards the production of dental caries due to loss of protective substances that are present in saliva.[44]

The microorganism converts fermentable carbohydrates into lactic acid and other organic acids and incorporate them into dental plaque. This will lead to reduction of pH causing the leaking of acid and formation of base as a film. If the pH is reduced to more than the threshold value, the dissolution of teeth will begin leading to the formation of lesions. The threshold of pH is 5.2-5.6.[45]

Another important constituent of saliva is urea which has anti-carcinogenic properties and its concentration in saliva is slightly less than concentration in blood. Microorganism present in plaque produce urease which break urea present in saliva converting it into ammonia and carbon dioxide leading to increase of pH in plaque.[46]

## 6. Protective functions of salivary proteins

Proteins present in saliva are known to be protective in function having anti-viral, anti-fungal and anti-bacterial properties. Although, normal flora of mouth contains more than 700 species of microorganisms which shows that the anti-microbial proteins are not enough to eradicate the normal flora from mouth as in table 3.[47]

**Table 3: protective properties of some salivary proteins.[48]**

| Proteins | Functions |
|---|---|
| Cathelicidin | Anti-bacterial |
| Agglutinin | Agglutination of bacteria |
| Cystatins | Prevent activity of protease |
| Histatins | Anti-bacterial |
| Immunoglobulins | Bacterial inactivation and aggregation |
| Defensins | Anti-bacterial |
| Lysozyme | Killing of microbes |
| Lactoferrin | Inhibit growth |
| MUC5B | Inhibit diffusion of H+ in pellicle |
| Proline-rich proteins | Help in attachment |
| MUC7 | Involved in aggregation process |
| Statherin | For adherence |

Porphyromonas gingivalis is a pathogenic bacteria and amylase (salivary protein) is the growth inhibitor for this bacterium but it still survives in the mouth. This shows that the antibacterial activity is not enough to maintain good oral health and personal hygiene plays an important role to lower the harms produced by oral flora.[49]

Cationic proteins are also present in saliva like histatin and statherins and defensins. Histatin 1, 3 and 5 are present richly and are known to inhibit the growth of CandIida Albicans that is an oral fungus.[50]

Primarily, statherin is involved in the inhibition of calcium phosphate crystallization but it is also involved to eradicate the anerobic bacteria from the mouth.103 Similarly, alpha and beta defensins are produced by neutrophils and epithelial cells respectively and they are involved in both anti-bacterial and anti-viral effects.[51]

In saliva, there are also present some proteins that are involved in agglutination and agglutinate the bacteria which makes them incapable to attach to mouth surface and easy to remove from mouth by swallowing. These proteins are; MUC7, salivary agglutinins and proteins rich in proline.[52]

Iron is important for the growth of many microorganisms and by removal of iron thus stops the growth of many harmful microorganisms. Lactoferrin present in saliva are involved in removal of iron from the mouth inhibiting growth by inhibiting the metabolism of microbes. With a similar effect, there are also present some other proteins like, cystatins and secretory leucocyte protease inhibitor that inhibit the metabolism of microbes making them unable to grow.

Another enzyme present in saliva is called lysozyme which is cationic in nature and is involved in breaking the cell wall of bacteria.[53] HIV-1 is also inhibited by flow of unstimulated saliva.[54]

Myeloperoxidase and salivary peroxidase are the 2 types of peroxidase present in saliva which use hydrogen peroxide that is involved in the conversion of salivary thiocyanate into hypothiocyanite that is more anti-bacterial as compared to hydrogen peroxide.[55]

The main antibody present in saliva is secretory IgA but sometimes a smaller amount of IgM may also be present in saliva. Some miRNA present in saliva are known to have anti-viral properties as in table 4.[56]

**Table 4: Origin of some anti-bacterial salivary proteins.[48]**

| Anti-bacterial proteins | Origin |
|---|---|
| MUC7 | Mucous glands |
| MUC5B | Mucous glands |
| Immunoglobulins | Lymphocytes |
| Cystatins | Sub-mandibular glands<br>Sub-lingual glands |
| Proline-rich proteins | Parotids glands |
| Histatins | Sub-mandibular<br>Parotid glands |
| Agglutinin | All major salivary glands |
| Lactoferrin | All major salivary glands |
| Cathelicidin | Neutrophils |
| Defensins | Epithelial cells<br>Neutrophils<br>Salivary glands |
| Lactoperoxidase | Sub-mandibular<br>Parotid gland |
| Lactoferrin | All major salivary glands<br>Serous glands |

## 7. Healing properties

Mouth is susceptible to injuries by biting or tooth extraction etc. and the saliva plays an important role in the healing process. Saliva contains many growth factors i.e. EGF, VEGF etc. Other factors include SLP1 which can inhibit protease activity and is also involved in anti-bacterial activities. Histatin 1 are also involved in promoting growth by migration of epithelial cells as in figure 1.[57]

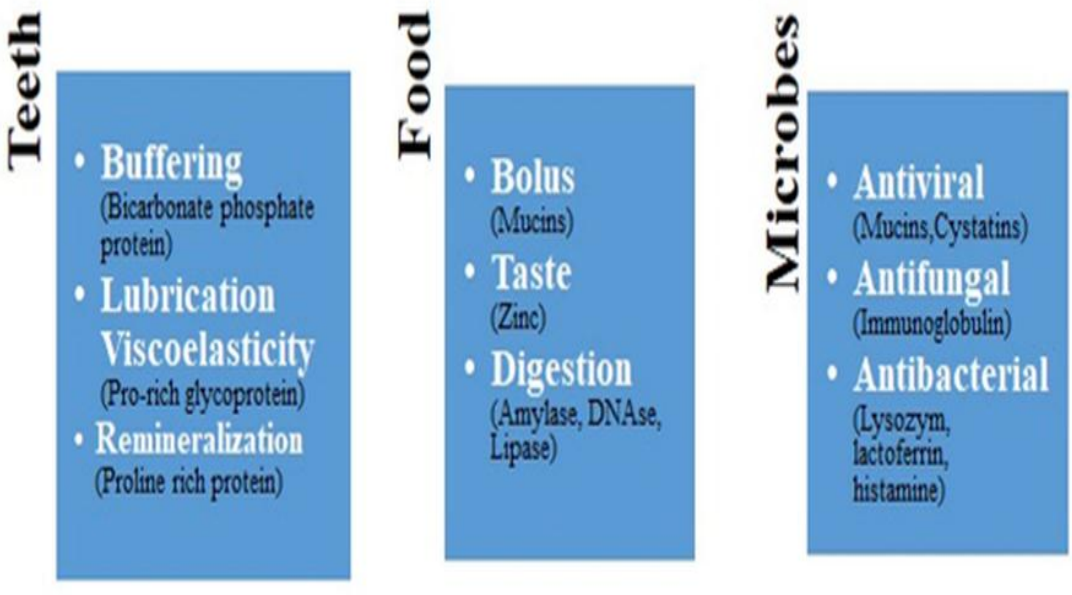


**Figure 1: Functions of saliva.**

## CONCLUSION

Saliva is very complex secretion produced by the salivary glands and have many functions which makes it very important. It is important for basic oral hygine as well as general health of a person. Secretion of saliva is dependent on many factors which may increase or decrease the level of saliva to be produced thus to check the proper function in specific time, sialo chemistry and sialometry should be done. This will also make it more clinically significant.

**Conflict of Interest**: None declared.

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