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SYSTEMATIC REVIEW ON THE ROLE OF SALIVARY PROTEIN IN ORAL HOMEOSTASIS

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ABSTRACT: Background: Saliva serves plenty of critical functions. These encompass oral mucosa and enamel protection, antimicrobial action, nutrient facilitation, bodily washing, and buffering. Cross-sectional studies of human salivary proteins quickly reveal a great deal of variation in the levels of various proteins between individuals. Methods: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Science Direct, and Lilac were used to conduct a literature search Scopus using MeSH terms-role of salivary protein, oral homeostasis, the role of Saliva, and Oral health care. Of a total of 178articles screened, 83 were full-text articles assessed for eligibility and five were taken for qualitative analysis. This review was reported according to the PRISMA guidelines. Results: the role of salivary protein among different groups of people in all studies showed a statistically significant impact. And they are responsible for oral hygiene and oral homeostasis. Conclusion: salivary protein has a significant role in maintaining oral hygiene, antimicrobial action enamel protection and buffering action.

Keywords: Salivary protein, Oral homeostasis, Role of Saliva.

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1.INTRODUCTION

Saliva serves plenty of critical functions. These encompass oral mucosa and enamel protection, antimicrobial action, nutrient facilitation, bodily washing, and buffering. Although it's feasible to stay without Saliva, having inadequate salivary features could make residing difficult. The significance of this physical fluid is high-quality, understood via way of means of inspecting the ones that've reduced salivary flow. They have an extensive variety of complaints, which include dryness, adjustments in taste (commonly indicating pain), and chewing and swallowing difficulties. [1]Understanding the utility of full Saliva as a diagnostic fluid, in addition to its software, has a lot of promise. Its structure is highly dependent on our ability to set it up. Most of the proteins and peptides in complete Saliva have passed through a transformation. A complicated set of molecular mechanisms that decide their frameworks [2] The transcription and translation of salivary protein genes in the salivary glands is the first step in salivary protein production. Glands, followed by internal post-translational processing. Protein glycosylation, phosphorylation, sulfation, and proteolysis are all processes that occur in acinar cells. Saliva contains a large number of glycoproteins, such as mucin, which are responsible for bacterial agglutination and lubrication of oral cavity tissues [3]The acquired pellicle (AP) is a protein integument that forms on the oral surface after Saliva is exposed to the oral environment for a short period. Specific physical linkages cause this protein coating to develop on the dental enamel. Because various salivary pellicle proteins observed in vivo can restrict or boost oral microbiota growth, the AP may regulate pathogenic microbe attachment to oral surfaces. At amounts observed in salivary secretions of healthy people, the carboxyl-terminal of histatin 5 has powerful fungistatic and fungicidal actions against pathogenic fungi, such as Candida albicans. Histatin 5's antibacterial effect is attributed to numerous basic amino acid residues (arginine and lysine), which give this salivary protein a basic character capable of breaking the cell membrane. [4]Amylase, a carbohydrate digesting enzyme secreted by the salivary glands, is significant. It can, however, encourage streptococcal plaque production and adhesion to the teeth. Amylase is also a stress-related salivary sign and a biomarker for diseases such as type 2 diabetes. Histatins are tiny, cationic, histidine-rich proteins produced in the parotid glands that inhibit proteases, have bactericidal and fungicidal activity, and aid in the healing of oral wounds. Statin S is an oral defence protein produced largely in the submandibular glands and implicated in innate immunity. Patients with Sjögren's syndrome had lower levels of cystatin S, suggesting that this protein could be used as a diagnostic for other oral conditions. [5]Maintaining oral homeostasis requires a high level of salivary buffer capacity. The bicarbonate and phosphate systems, as well as those dependent on proteins, are known to contribute to Saliva's total buffer capacity. The epithelial pellicle is hypothesized to protect epithelial cells from proteases released by bacteria attached to mucosal surfaces and degenerating

polymorphonuclear leukocytes by providing a lubricating layer and an effective barrier against desiccation and environmental influences. [6] Cross-sectional studies of human salivary proteins quickly reveal a great deal of variation in the levels of various proteins between individuals. SDS PAGE of parotid salivary proteins demonstrates this variance, particularly in protein-rich proteins. These proteins are unique to Saliva and are most prevalent in parotid saliva, accounting for up to 80% of total saliva protein. It has been demonstrated that these proteins have a significant degree of genetic polymorphism. There are two types of protein-rich protein [7]Biomarkers assessed in Saliva are clinically beneficial in children with diabetes and obesity and children with chronic renal disease. However, no studies on salivary redox biomarkers in children with hypertension have been published. The secretory function of salivary glands in hypertensive children has also not been studied. Salivary gland function and protein release in Saliva are likely to be disrupted, as they are in other oxidative stress-related illnesses. Because redox homeostasis isn't defined by a single biomarker [8], The term "stable" or "climax" community does not imply that conditions are static. Homeostasis provides stability. This means compensating mechanisms that act to keep the system running. Various controls maintain steady-state conditions by counteracting perturbations that would upset the steady state. [9] It is well understood that Saliva plays an important role in the balance of de- and remineralization of enamel In an oral environment that may be cariogenic [10]

2. MATERIALS AND METHODS

Eligibility criteria:

Study Design: Systemic review of randomized controlled trails

Inclusions:

• original articles

• Full-text articles

• Studies on Role of salivary protein in oral homeostasis

Exclusions:

• Animal studies

•Articles without full text

Search strategy:

Original articles and research papers are among the published literature on assessing the role of salivary protein in oral homeostasis in databases such as Pub med, Google Scholar, science direct, lilacs, Wiley and Cochrane. Literature research was done with the help of the MeSH term SALIVARY PROTEIN, AND ORAL HOMEOSTASIS was done to collect relevant data for the study. According to the Prisma guideline, the MeSH term was altered in each search engine.

SEARCH ENGINE:

• Pubmed

• Google Scholar

• Science Direct

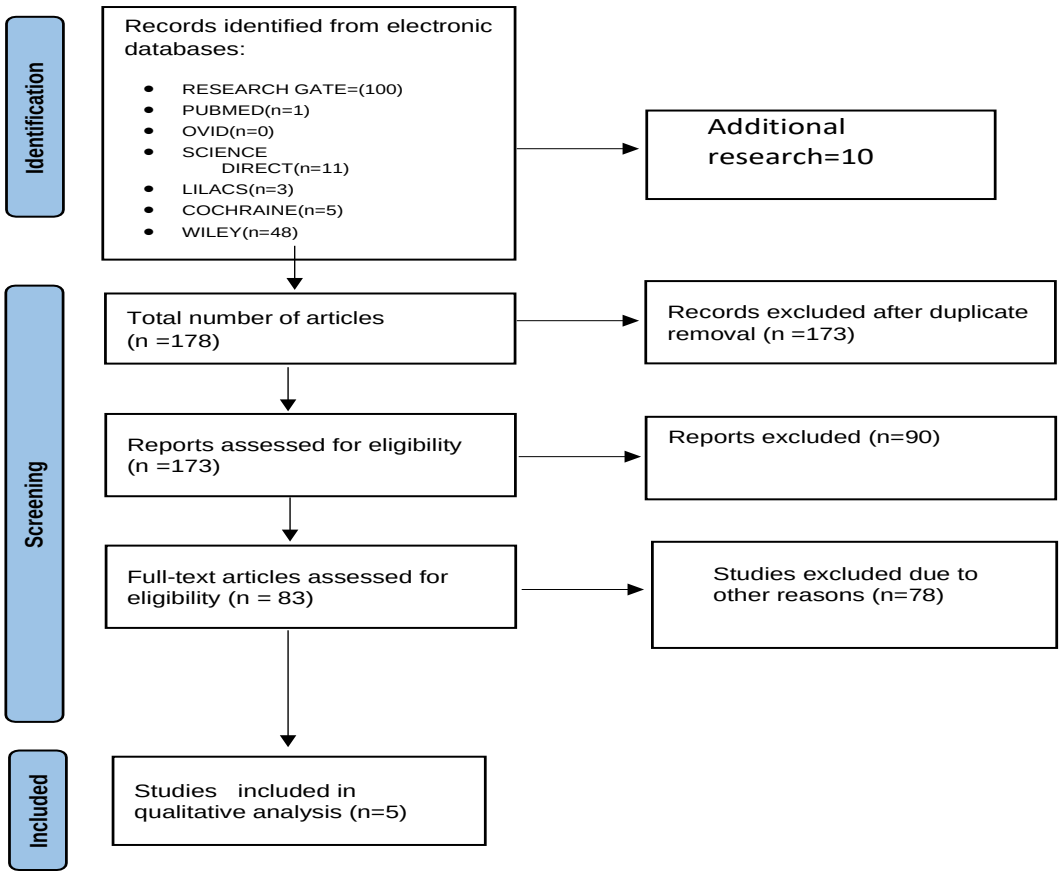
• Lilacs

• Wiley

Results:

The search yielded 310 records,

Figure 1: Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review



and 83 articles were independently assessed. Among these 83 articles, five themes were included in the review.

Table 1 shows the characteristics of the interventions in the included studies. All five studies, the role of salivary protein in the oral health of a screened population. The studies differed individually regarding the sample size, age of the screened population and duration of the intervention. Four of the studies were performed on school children, while one study was conducted on people who belonged to any age group.

Table 1: Characteristic Of Interventions In Included Studies

AUTHOR NAME	YEAR	SAMPLE SIZE	PATIENT CHARACTERISTICS	DURATION	NUMBER(CASE/CONTROL)
Su, Haixiang et al. [11]	2012	696	I)Diabetes types (type 1 or type 2) II) medication use (i) insulin, (ii) metformin, (iii) insulin and metformin, and (iv) insulin and metformin, as as well as diet-controlled	20min	i) TEST GROUP(DM)=215: GROUP1(DM1) =87 GROUP2(DM2) =128 ii)CONTROL GROUP=481

Huang, Xuelian, et al. [12]	2015	14	Supragingival dental plaque was collected from Caries free subjects who had no clinical or reported evidence of current or past caries experience [decayed, missing, and filled teeth (DMFT) = 0) and Caries active subjects who had at least four involved, cavitated (dentin level), and unrestored caries lesions (DT 4, MFT 0).	5days	i)GROUP1= caries free =11 ii)GROUP2=Caries active=3
Basiri, T., et al. [13]	2017	60	Human permanent first molars free of flaws were cleaned, rinsed, and sectioned after having the roots removed.	12days	i)GROUP1(n=10) =DR9-DR9 PROTEIN ii)GROUP2(n=10) =DR9-RR14 iii)GROUP3(n=10) =RR14 iv)GROUP4(n=10) =DR9 v)GROUP5(n=10) =Statherin vi)GROUP6(n=10) =histatin

Shimomura-Kuroki, Junko, et al. [14]	2020	37	Subjects aged 3-16 years in the Patients from The Nippon Dental University's Pediatric Dental Clinic with primary, mixed, or permanent dentition were chosen.	-----	i)GROUP1=19 MALES ii)GROUP2=18 FEMALES
Tlus tenko, Vladimir, et al. [15]	2021	85	mild chronic generalized periodontitis and with mild dental peri-implantitis	-----	i) GROUP TEST1 = 30 mild chronic periodontitis ii)TEST GROUP2=35mild dental peri implants iii)CONTROL GROUP=20, comparable in gender and age, healthy in terms of dental and bodily health

Table 2: Outcome Data From Included Studies

AUTHOR NAME	YEAR	EFFECT MEASURE	RESULTS
Su, Haixiang et al. [11]	2012	Oxidative DNA damage level, protein carbonyl levels in Saliva	Mean log of biomarker concentrations among Diabetes Groups (DM1 and DM2) compared to controls. *P < 0.05, **P < 00.1,***P < 0.001.
Huang, Xuelian, et al. [12]	2015	Screening of ADS-Positive Strains, Isolation of Bacterial Strains	There were 2,328 strains, 288 of which were ADS-positive, for a ratio of 20.5 stresses per subject or 15.8 strains per CF subject (minimum of 5 ADS-positive and 5 ADS-negative). Within these caries, there are a total of 51 ADS-positive strains. group) and 38 strains per CA subject (minimum of 6). ADS-positive, with a maximum of 84 ADS-positive strains within this group of caries).
Tlus tenkoVladimir, et al. [13]	2021	Total albumin concentration, Albumin binding capacity.	The total albumin concentration was higher in the control groups and patients with chronic generalized periodontitis, but it was lower in patients with

			dental peri-implantitis group1=(P=1.000), group2=(P=<0.001), group3=(P=<0.001), albumin-binding capacity was the lowest in patients with mild dental peri-implantitis (p=0.003)
Basiri, T., et al. [14]	2017	Phosphate level and calcium level	The Catherine and DR9 groups had significantly lower phosphate loss than DR9-RR14 and histatin one groups, with DR9-DR9 having the smallest phosphate loss of any group (P 0.05). . DR9-DR9 treatment resulted in the lowest calcium loss, followed by the Catherine and DR9 groups
Shimomura-Kuroki, Junko, et al. [15]	2020	multiple regression analysis, RT-PCR	Amylase protein=(p=0.141) Histatin protein=(p=0.007) BPIFB1 p=(p=0.014)

Table 2 shows the outcome data of the role of salivary protein in periodontitis and dental caries scores in the included studies. There was a progressive decrease in salivary protein levels for the screened population. Table 3 shows the bias assessment of the included studies.

Table 3: Bias Assessment As Included In The Studies

Author name, year	Random sequence generation	Allocation concealment	Blinding of outcome	Incomplete outcome data	Blinding of participants and personnel	Selective reporting	Judgemental Bias
Su, Haixiang et al., 2012	+	-	+	+	?	-	+
Huang, Xuelian, et al., 2015	+	-	+	+	-	-	+
Basiri, T., et al.,2017	+	+	+	+	?	+	+
Shimomura-Kuroki, Junko, et al., 2020	+	+	+	+	+	+	+
Tlus tenko, Vladimir, et al, 2021	+	+	?	?	-	+	?

+ = Low risk of bias; - = High risk of bias; ? = unclear risk of bias

3. RESULTS AND DISCUSSION

The buffering capacity was significantly increased by increasing the salivary flow rate. Previous research has found that children with active caries have a slightly lower salivary flow rate. Salivary RNA was analyzed to determine the levels of candidate biomarkers related to oral health status. RT-PCR methods demonstrated that these factors could be detected and potentially monitored. Individual expression levels of the antimicrobial proteins analyzed in the study may have been too low to affect saliva pH. However, salivary proteins may contribute to Saliva buffering capacity due to their ampholytic properties. However, increased expression of various proteins, including antibacterial proteins, may result in salivary homeostasis. The western blotting analysis revealed that an increase in the proteins histatin-1 and BPIFB1 was associated with an increase in buffering capacity. [15]Human

Saliva contains oxidative damage products (e.g., protein carbonyls, 8-OHdG, 4-hydroxyalkenals, malondialdehyde) and antioxidant enzyme activities (e.g., superoxide dismutase, glutathione peroxidase, catalase). Levels of salivary 8-OHdG and significantly higher levels of protein carbonyls in type 2 diabetes patients compared to type 1 diabetes patients. Oxidative DNA damage in type 2 diabetes may be caused by low levels of reduced glutathione (GSH) associated with chronic hyperglycemia. The results are comparable to Sena et al., who found that metformin supplementation significantly reduces 8-OHdG and protein carbonyl levels. [11]Compared to mild dental peri-implantitis, chronic generalized periodontitis causes more significant disturbances in protein and mineral metabolism. A decrease in the effective concentration of albumin corresponds to a reduction in its free binding centre. Their number aided in determining the protein's level of protection. This transport protein's effective concentration describes its ability to participate in detoxification. In mild chronic generalized periodontitis and mild dental peri-implantitis, albumin-binding capacity decreased significantly. Which can be considered a pathogenetically significant link within inflammation[13]The metabolism of arginine in oral biofilms allows for the development of novel anticaries approaches that may be beneficial for short-term moderation of acid challenges to teeth and long-term effects on the persistence of desirable bacteria in dental plaque. Streptococci that are abundant are likely to have a dominant influence on the arginolytic capacity of human oral biofilm. [12] The presence of -amylase in acquired enamel pellicle suggests that it plays a role in bacterial adhesion. [16] Following the completion of hemodialysis sessions, there was an increase in salivary flow rate. [17] Histatin, a human salivary protein, has antifungal activity and is susceptible to enzymatic degradation when released into the oral cavity. Histatin has an antifungal effect by decreasing cell metabolism in Candida albicans. [18] Saliva has been used to detect dental caries, gingivitis, periodontitis (chronic/aggressive), oral cancers, cleft palate, salivary gland diseases, Bechet disease, and oral leukoplakia[19]. Proline was the most abundant amino acid in Saliva, and a 3:2:2 ratio of proline, glycine and glutamic acid was found in both parotid and submandibular secretions. [20]When duplicated, DR9, a recently identified and characterized AEP phosphorylated statherin peptide, may also show enhanced biological function in the oral cavity. The importance of creating novel constructs with increased adhesion to enamel is that it increases their substantivity, which is related to the rate of clearance of a biologically active molecule from its site of action. It has also been established that salivary molecules that are more retentive to oral surfaces degrade slower. [14]

4. CONCLUSION

Salivary proteins and peptides have a wide range of antimicrobial activity, but a reduction in salivary protein content, especially secretory immunoglobulin (Ig) A, weakens the body's ability to fight off

caries. This leads to more frequent oral bacterial and fungal infections (especially Candida albicans), periodontal inflammation, traumatic oral lesions with angular cheilitis, high rates of caries, and earlier tooth loss.Some defence proteins, like salivary immunoglobulins, are involved in innate and acquired immune activation. Salivary cationic peptides and other salivary defence proteins, like lysozyme, salivary amylase, cystatins, proline-rich proteins,histatin, mucins, peroxidases, Catherine are primarily responsible for innate immunity.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

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CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

Authors have no conflict of interest.

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