



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

Available online at: <http://www.iajps.com>

Review Article

**REVIEW ON PROPERTIES OF *STREPTOCOCCUS SALIVARIUS***Anas Tariq<sup>1</sup>, Maged Al mezgagi<sup>1</sup>, Irum Saleem<sup>2</sup>, Wang Qianqian<sup>1</sup>, Xing Jiangwa<sup>\*1</sup><sup>1</sup>Research Center of Basic Science, Medical College, Qinghai University, Xining 810016,  
anastariq@hotmail.co.uk<sup>1</sup>Research Center of Basic Science, Medical College, Qinghai University, Xining 810016  
1902244017@qq.com<sup>2</sup>Physics Department of zakariya University, Multan , Pakistan  
imschims@gmail.com<sup>1</sup>Research Center of Basic Science, Medical College, Qinghai University, Xining 810016  
1498619249@qq.com<sup>1</sup>Research Center of Basic Science, Medical College, Qinghai University, Xining 810016  
xingjiangwa@qhu.edu.cn**Abstract:**

*Streptococcus salivarius* is present in the oral cavity of healthy people within a few hours of birth, which is an opportunistic pathogen that can infect people with impaired immune systems. At the same time, *S. salivarius* also secretes antimicrobial peptides, which can be employed as a probiotic to promote dental health. This review mainly focuses on the properties of *S. salivarius*, which is widely recognized for its probiotic and anti-inflammatory properties. However, *S. salivarius* also can cause some diseases, such as meningitis, endocarditis, and neonatal sepsis. In conclusion, these bacteria have numerous beneficial characteristics, but they also have some functions in causing diseases, which need to be studied more thoroughly.

**Keywords:** *Streptococcus salivarius*, probiotics, anti-inflammatory, antimicrobial peptides, Immune systems.

**Corresponding author:**

**Xing Jiangwa,**  
Research Center of Basic Science,  
Medical College, Qinghai University, Xining 810016  
[xingjiangwa@qhu.edu.cn](mailto:xingjiangwa@qhu.edu.cn)

QR code



Please cite this article in press Xing Jiangwa et al., *Review On Properties Of Streptococcus Salivarius*, 2024; 11 (02).

## INTRODUCTION:

### *Streptococcus Salivarius*

*Streptococcus salivarius* is a gram-positive bacterium which is spherical, non-motile, non-sporing, and catalase-negative. It is a common member of the oral cavity in healthy individuals after a few hours of birth. *S. salivarius* is an opportunistic pathogen capable of infecting individuals with compromised immune systems. Studies showed *Streptococcus salivarius* secretes antimicrobial peptides, which can be used as a probiotic to improve oral health [1]. Electively anaerobic microorganisms that are found in the oral cavity have been studied for their probiotic properties and antimicrobial activity in the oral cavity and upper respiratory tract of humans [2].

*S. salivarius* K12 was the first strain used commercially to develop oral probiotics, and it helps to improve oral health and reduces halitosis, or bad breath [3][4]. *S. salivarius* is also present in the stomach and jejunum and plays an important role in digestive tract ecology [5]. The infection rate caused by *S. salivarius* is low in normal conditions; however, it may be higher in institutionalized persons, such as those staying in hospitals or long-term care institutions, immunocompromised patients, and those with poor dental hygiene or periodontal disease [23]. Biofilm formation by *S. salivarius* may also play a role in dental plaque formation and oral biofilm development, which can lead to dental caries and periodontal disease [25].

### 1.1 Properties of *S. Salivarius*

#### 1.1.1 Anti-Inflammatory properties

*Streptococcus salivarius* is one of the first colonizers of the human oral cavity and gut after birth and therefore may contribute to establishing immune homeostasis and regulating host inflammatory responses. The anti-inflammatory potential of *S. salivarius* was first evaluated in vitro on human intestinal epithelial cells and human peripheral blood mononuclear cells[30].

Therefore they play a significant role in the tendency of the immune system to protect internal stability and also in regulating inflammation tendencies and responses [9,27]. Nowadays, as per the demand for health issues, discussion and research on the actions, reactions, and role of the microbiota are increasing [10].

When *S. salivarius* is segregated from the mouth or oral cavity, it shows inflammatory responses both in lab results and when applied to living organisms [11].

#### 1.1.2 Probiotic

Probiotics are beneficial live bacteria that can improve our overall health when consumed in the right amount. It's essential to maintain a balance of these bacteria in our gut for a healthy digestive system[31].

They play a vital role in boosting the host's health. It is observed that *S. salivarius* secretes antimicrobial peptides that have rich probiotic properties [12,32].

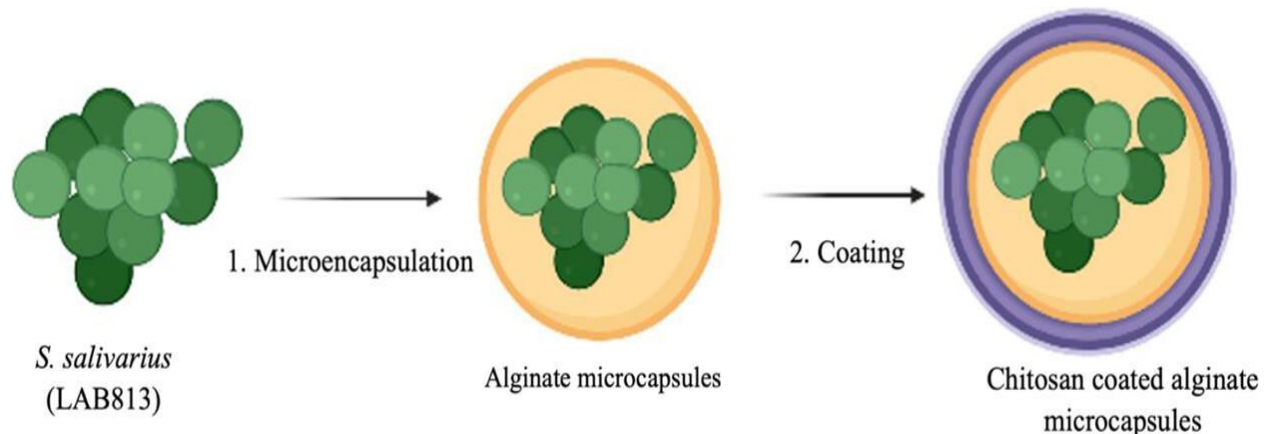


Fig. 1 : Microencapsulation of *S. salivarius* LAB813 [26].

The novel strain of *Streptococcus salivarius* was micro capsulated, as shown in [Fig. 1], which was first identified in the laboratory. These microcapsules enhance oral health due to their robust and prolonged inhibitory effects. *S. salivarius* generates bacteriocins to combat *Streptococcus pyogenes*. This production is highly influenced by the adhesive ability of bacteria on Kappa B (KB) cells. Few strains of *S. salivarius* produce bacteriocins, which can shield young children in school from pharyngeal infections. [13] M18 is a *S. salivarius* strain that was obtained from adult humans. It is extremely benign for humans since it does not possess any virulence factors or antibiotic resistance. [14] As per advanced research, there is another isolated strain called BIO5 that is also non-toxic and could be used as a probiotic therapy for different oral diseases like tonsils or sore throats. [15]

### 1.1.3 Antibiotic Resistance

Macrolides and tetracycline are the most widely used antibiotics for the treatment of infections caused by *Streptococci*. When some clinical, pathogenic, and commensal strains were isolated and analyzed using advanced techniques and methods like multilocus sequence typing (MLST), they exhibited astounding resistance to these antibiotics. Therefore, *S. salivarius* affects the oral and gastrointestinal dissemination of antibiotic-resistance genes [16].

When samples were collected from saliva and tissues around the tooth of the patient, its strains were analyzed using Active Pharmaceutical Ingredient (API) test systems to check their credibility against resistance to different drugs. E-tests and PCRs prove that *S. salivarius* is responsive to linezolid and meropenem. Surprisingly, *S. salivarius* also shows 23.5% resistance to penicillin, which is a notable figure. Other considerable resistances are to erythromycin, which is 47.9%; 44.4% to tetracycline; and last but not least, ofloxacin, which is 41%. It is of great importance to know how prone these organisms are to different antimicrobial drugs because they play a very vital role in the transmission of resistance determinants to more pathogenic and clinically relevant germs. [17]

Also, the above-mentioned resistance level is quite high in infants (2–8 months) and higher in 12- to 18-month-olds. There is a possibility that antibiotic-resistance genes are stored in the oral microbiome of healthy newborns by *S. salivarius*. That is why it is way more important to comprehend and track levels and their changes to resistance in this group of age. [18]

## 1.2 Role of *S. Salivarius* in Diseases

*S. salivarius* is part of the normal oral cavity and gastrointestinal tract microflora and an unusual cause of acute bacterial meningitis. Although this bacterium is usually nonpathogenic, in rare cases, it causes bacteremia, endocarditis, and meningitis. [19]

### 1.2.1 Meningitis

*S. salivarius* could be the originator of meningitis in some cases. [21] Though that is rare, reported cases of infection are spreading worldwide. Initial symptoms are the same as those of bacterial meningitis. These symptoms may include fever, pain in the neck, headaches, head spinning, etc. [20] Numerous investigations and case reports demonstrate that gastrointestinal cancer may be the source of the *S. salivarius* infection in cases of non-iatrogenic meningitis. The key cause of these phenomena is a disorder of the gastrointestinal mucosa [4].

Also, during different surgical procedures, vascular bleeding may occur. It sometimes allows peripheral blood to taint Cerebrospinal fluid (CSF). This contamination is one of the major causes of *S. salivarius* meningitis.

### 1.2.2 Endocarditis

The relationship between endocarditis and *S. salivarius* is quite certain [5]. It has been observed in a few cases that *S. salivarius* leads to endocarditis [29]. Owing to its hypoallergenic and nonirritating properties, this viridian species is a failure to catch. But it does not mean that it can be ignored, since *S. salivarius* can result in serious intricacy. It is observed in some cases that this bacterium may cause infective endocarditis, which in any case plays a role in originating mycotic aneurysms. So this peaceful bacterium that usually belongs to guts and oral issues must not be given the benefit of the doubt, but it should be diagnosed properly and seriously. [6] As reported in some cases, if cerebral mycotic aneurysms burst, it could be a lethal drawback of endocarditis. And it may also accompany a seriously deadly acute subarachnoid hemorrhage (SAH) [7].

### 1.2.3 Neonatal Sepsis

*S. salivarius* is typically located in the oral microbiota. Rarely and surprisingly, it may cause neonatal sepsis [22][23]. Neonatal sepsis is a kind of blood infection in infants younger than 90 days [8]. It could be a significant cause of death in neonates. It could be diagnosed by blood culture and saliva. The blood culture method is quite time-consuming and

expensive, whereas saliva is non-invasive, approachable, and easygoing [33].

Conclusion: *S. salivarius* is well-known for its probiotics and anti-inflammatory qualities. Besides, these bacteria have antibiotic resistance against some commonly used antibiotics. However, further research is required to fully understand the roles that these bacteria play in meningitis, endocarditis, and neonatal sepsis.

#### Declaration by Authors

**Ethical Approval:** Approved

**Acknowledgment:** None

**Source of Funding:** None

**Conflict of Interest:** The authors declare no conflict of interest.

#### REFERENCES:

- [1] McCarthy C, Snyder ML, and Parker RB. The indigenous oral flora of man. I. The newborn to the 1-year-old infants. Arch Oral Biol. 1965 Jan-Feb;10(1):61-7
- [2] Bidossi, A., De Grandi, R., Toscano, M., Bottagisio, M., De Vecchi, E., Gelardi, M., & Drago, L. (2018). Probiotics *Streptococcus salivarius* 24SMB and *Streptococcus oralis* 89a interfere with the biofilm formation of pathogens of the upper respiratory tract. BMC Infectious Diseases, 18, 1-11.
- [3] Cernioglo, K., Kalanetra, K. M., Meier, A., Lewis, Z. T., Underwood, M. A., Mills, D. A., & Smilowitz, J. T. (2021). Multi-Strain Probiotic Supplementation with a Product Containing Human-Native *S. salivarius* K12 in Healthy Adults Increases Oral *S. salivarius*. *Nutrients*, 13(12), 4392.
- [4] Carley NH. Streptococcus salivarius Bacteremia and Meningitis following Upper Gastrointestinal Endoscopy and Cauterization for Gastric Bleeding Get access Arrow. Clin Infect Dis 14: 947-948, 1992
- [5] Nilson, Bo; Olaison, L; Rasmussen, Magnus ; Published in: European Journal of Clinical Microbiology & Infectious Diseases; DOI: 10.1007/s10096-015-2532-5; 2016
- [6] Saad Ahmad, David Song, Jonathan Vincent M Reyes, and Adrian Whiting +2 more •Institutions (2) Icahn School of Medicine at Mount Sinai<sup>1</sup>, Royal College of Surgeons in Ireland<sup>2</sup> 01 Sep 2021: Annals of medicine and surgery (Ann Med Surg (Lond))-Vol. 69, pp. 102798
- [7] F. R. Prandi, Malcolm Anastasius, Stavros Matsoukas, and Lily Zhang: Concurrent cardiac and central nervous system complications of acute infective endocarditis, published in European Heart Journal, Case Reports, Vol. 6, Iss. 8
- [8] Seale AC, Blencowe H, Manu AA, Nair H, Bahl R, Qazi SA, Zaidi AK, Berkley JA, Cousens SN, Lawn JE., pSBI Investigator Group. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. Lancet Infect Dis. 2014 Aug;14(8):731-741.
- [9] Harry Sokol<sup>1</sup>, Bénédicte Pigneur, Laurie Watterlot, and Omar Lakhdari, Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. 28 Oct 2008- Proceedings of the National Academy of Sciences of the United States of America (National Academy of Sciences), Vol. 105, Issue 43, pp. 16731-16736
- [10] Peter P. Bradley, Dennis A. Priebe, Robert D. Christensen, Gerald Rothstein, Mar 1982- Measurement of Cutaneous Inflammation: Estimation of Neutrophil Content with an Enzyme Marker; Journal of Investigative Dermatology (Elsevier)-Vol. 78, Issue 3, pp. 206-209
- [11] Michael. Gasson , 01 Apr 1983- Plasmid complements of *Streptococcus lactis* NCDO 712 and other lactic streptococci after protoplast-induced curing. Journal of Bacteriology (American Society for Microbiology)-Vol. 154, Iss: 1, pp 1-9.
- [12] Priyadarshani Choudhary, Heinz-Bernhard Kraatz, Céline M. Lévesque, and Siew-Ging Gon, ACS Omega. Microencapsulation of Probiotic *Streptococcus salivarius* LAB813, 2023, 8, 13, 12011-12018 Publication Date: March 23, 2023
- [13] Vera Fantinato<sup>1</sup>, Heloísa Ramalho Camargo, Ana Lúcia Orlandinni Pilleggi de Sousa, Probiotics study with *Streptococcus salivarius* and its ability to produce bacteriocins and adherence to KB cells , •Institutions (1) 29 Aug 2019- Revista de Odontologia da UNESP (Revista de Odontologia da UNESP/Universidade Estadual Paulista Júlio de Mesquita Filho)-Vol. 48

- [14] John, R., Tagg, Liam, K., Harold., Rohit, Jain., John, D., F., Hale. (2023). Beneficial modulation of human health in the oral cavity and beyond using bacteriocin-like inhibitory substance-producing streptococcal probiotics. *Frontiers in Microbiology*, doi: 10.3389/fmicb.2023.1161155
- [15] Vera Fantinato, Camargo Hr, Sousa ALOPilleggi. Streptococcus Salivarius Subsp Salivarius BIO5: Toxicity Evaluation of a Possible Probiotic Strain,01 May 2020-The Journal of medical research (Global Journals)-pp 51-56
- [16] . Fanny Chaffanel, Florence Charron-Bourgoin, University of Lorraine,Resistance Genes and Genetic Elements Associated with Antibiotic Resistance in Clinical and Commensal Isolates of Streptococcus salivarius Institut national de la recherche agronomique. 15 Jun 2015-Applied and Environmental Microbiology (American Society for Microbiology)-Vol. 81, Iss: 12, pp 4155-4163
- [17] Nataliia Valerievna Davidovich, A S Galieva, N G Davydova, O G Malygina +3 more,Spectrum and resistance determinants of oral streptococci clinical isolates;17 Sep 2020-Klinicheskaia laboratornaia diagnostika (Klin Lab Diagn)-Vol. 65, Iss: 10, pp 632-637
- [18] Thais Palma, Erika N. Harth-Chu, Jodie C. Scott, Rafael Nobrega Stipp,Oral cavities of healthy infants harbour high proportions of Streptococcus salivarius strains with phenotypic and genotypic resistance to multiple classes of antibiotics 16 Dec 2016-Journal of Medical Microbiology (Microbiology Society)-Vol. 65, Iss: 12, pp 1456-1464
- [19] Wilson M, Martin R, Walk ST, et al. Clinical and Laboratory Features of Streptococcus salivarius meningitis: A Case Report and Literature Review. *Clin Med Res*10: 15-25, 2012.
- [20] K. Camps, C. Brands, M. Van de Vyvere, P. Bruynseels, A. Mertens, Streptococcus salivarius meningitis,Clinical Microbiology Newsletter,Volume 25, Issue 15, 2003,
- [21] Hosoi, Y., Yamanaka, Y., Baba, T., & Ito, M.. (2023). *Noniatrogenic Meningitis Caused by Streptococcus salivarius Associated with Early Esophageal Cancer and Early Gastric Cancer*. <https://doi.org/10.2169/internalmedicine.1304-22>.
- [22] Keerthi, S., & Banu, S. N.. (2020). *Streptococcus salivarius: an unusual etiology of neonatal sepsis*. <https://doi.org/10.36106/IJAR/6311464>
- Bin, S., & Im, S.. (2023). *Early-onset neonatal sepsis due to Streptococcus salivarius: A case report*, 11(1). <https://doi.org/10.1002/ccr3.6837>
- [24] Shenep, J. L. (2000). Viridans-group streptococcal infections in immunocompromised hosts. *International journal of antimicrobial agents*, 14(2), 129-135.
- [25] Colombo, A. P. V., & Tanner, A. C. R. (2019). The role of bacterial biofilms in dental caries and periodontal and peri-implant diseases: a historical perspective. *Journal of Dental Research*, 98(4), 373-385.
- [26] Priyadarshani Choudhary, Heinz-Bernhard Kraatz, Céline M. Lévesque, and Siew-Ging Gong ACS Omega 2023 8 (13), 12011-12018 DOI: 10.1021/acsomega.2c07721.
- [27] MacDonald, K.W., Chanyi, R.M., Macklaim, J.M. et al. Streptococcus salivarius inhibits immune activation by periodontal disease pathogens. *BMC Oral Health* 21, 245 (2021). <https://doi.org/10.1186/s12903-021-01606-z>
- [29] Gil, Hevroni., Andrii, Maryniak., Diego, Cepeda-Mora., Moro, O., Salifu., Samy, I., McFarlane. (2020). Paravalvular Abscess as a Complication of Streptococcus Salivarius Infective Endocarditis of a Bioprosthetic Aortic Valve.. *American Journal of Medical Case Reports*, doi: 10.12691/AJMCR-8-11-7
- [30] Fanny, Chaffanel., Florence, Charron-Bourgoin., Claire, Soligot., Mounira, Kebouchi., Stéphane, Bertin., Sophie, Payot., Yves, Le, Roux., Nathalie, Leblond-Bourget. (2018). Surface proteins involved in the adhesion of Streptococcus salivarius to human intestinal epithelial cells. *Applied Microbiology and Biotechnology*, doi: 10.1007/S00253-018-8794-
- [31] Y K., S., Babina., Dilara, Salikhova., M, A, Polyakova., Oxana, Svitich., R., Samoylikov., S., A., Ahmad, El-Abed., A., Zaytsev., N., E., Novozhilova. (2022). The Effect of Oral Probiotics (Streptococcus Salivarius k12) on the Salivary Level of Secretory Immunoglobulin A, Salivation Rate, and Oral Biofilm: A Pilot Randomized Clinical Trial. *Nutrients*, doi: 10.3390/nu14051124
- [32] Andrea, Stašková., Miriam, Sondorová., Radomíra, Nemcová., Jana, Kačírová., Marián, Maďar. (2021). Antimicrobial and Antibiofilm Activity of the Probiotic Strain Streptococcus salivarius K12 against Oral Potential Pathogens. *The Journal of Antibiotics*, doi: 10.3390/ANTIBIOTICS10070793.
- [33] S., Keerthi., S., Nasreen, Banu. (2020). *Streptococcus salivarius: an unusual etiology of*

neonatal sepsis. Indian journal of applied  
research, doi: 10.36106/IJAR/6311464.