

Differences in the Effectiveness of the Antibacterial Power of Chlorhexidine 0.2% and Povidone Iodine 10% against the Growth of Porphyromonas Gingivalis Bacteria

Dwi Leni Yuliana^{1*}, Fitrotus Bela Arofah²
Bhakti Wiyata Institute of Health Sciences, Indonesia
*Corresponding Email: dwi.leni@iik.ac.id

Article History

Received: 10-08-2023
Accepted: 20-08-2023
Published: 20-09-2023

Abstract

One of the causes of gingivitis and periodontitis is the bacteria Porphyromonas Gingivalis. Chlorhexidine and povidone iodine liquids are liquids that contain antibacterial properties against the growth of Porphyromonas Gingivalis bacteria. This research was conducted to determine the difference in the effectiveness of the antibacterial power of Chlorhexidine and povidone iodine liquids on the growth of Porphyromonas Gingivalis bacteria. The method used was an in vitro laboratory experiment with a posttest only group design, with a population of Porphyromonas Gingivalis bacteria using a simple random sampling technique, where the number of samples was 7 samples for each treatment and divided into 3 groups. The normality test uses the Shapiro Wilk test and statistical tests use the Independent sample t-test. The results of the Independent sample t-test show a p value < 0.05 , which indicates that overall there is a significant difference in the antibacterial activity of chlorhexidine solution and povidone iodine solution against the growth of Porphyromonas Gingivalis bacteria, so it can be concluded that administering the povidone iodine solution is more effective than the chlorhexidine solution. as an antibacterial against the growth of Porphyromonas Gingivalis bacteria.

Keywords: Chlorhexidine, Povidone Iodine, Gingivitis, Periodontitis, Porphyromonas Gingivalis

How to Cite: Yuliana, D., L., & Arofah, F., B. (2023). Differences in the Effectiveness of the Antibacterial Power of Chlorhexidine 0.2% Liquid and Povidone Iodine 10% Against the Growth of Porphyromonas Gingivalis Bacteria. Cigarskruiie: Journal of Educational & Islamic Research. Pages, 1-8. Vol. 1, No. 1, 2023.

Introduction

Periodontal disease is inflammation of the tissues supporting the teeth which include the gingiva, alveolar bone, periodontal ligament and cementum (Tsuchida & Nakayama, 2023). The most common periodontal diseases are gingivitis and periodontitis which often occur at the age of 35 years and over (Chatzopoulos et al., 2023). In the 2010 National Health Survey, periodontitis was in second place with 42.8% of the Indonesian population suffering (Sukhabogi et al., 2023). The results of the 2013 Basic Health Research (Riskesdas) also show that gingivitis and periodontitis are the most common periodontal tissue diseases, namely 23.4% in Indonesia (Rachmawati et al., 2023).

Gingivitis is a mild form of periodontitis with clinical symptoms of red, swollen gums that bleed easily and without damage to the alveolar bone (Kumar et al., 2023), while *periodontitis* is an inflammatory disease of the periodontal tissue that causes gradual damage

to the periodontal ligament and alveoli and progressive recession (Ni et al., 2023). One of the causes of gingivitis and periodontitis is the bacteria *Porphyromonas Gingivalis* (Chen et al., 2023). *Porphyromonas Gingivalis* bacteria were found in periodontitis patients by 85.75% (Huang et al., 2024). In Asian regions such as Indonesia, the prevalence of the disease periodontal disease is also high, namely 96.58% in all age groups (Harefa et al., 2022).

The pathogenic bacteria *Porphyromonas Gingivalis* has virulence factors that enable it to attack the immune system and bloodstream (Shahoumi et al., 2023). These bacteria can cause damage to periodontal tissue by penetrating into the gingival sulcus which ultimately causes an increase in sulcus depth. The treatment mechanism used for bacterial infections focuses on the process of eliminating bacteria in the area of infection by surface debridement accompanied by supporting therapy using antibacterial (Zhong et al., 2023). Antibacterial that can be used are usually available in liquid form (Ardila et al., 2023). Several debridement fluids that can inhibit the growth of *Porphyromonas Gingivalis* bacteria include Chlorhexidine and Povidone iodine (Alves et al., 2023).

Chlorhexidine has been proven to be effective against oral bacteria because it can reduce plaque microorganisms, prevent plaque growth and prevent periodontitis (Gergeta et al., 2024). This is because chlorhexidine is bactericidal and bacteriostatic against various types of bacteria, including bacteria in plaque (Álvarez et al., 2023). Long-term use of this drug is not recommended, because it has side effects of taste disturbance, burning sensation, changes in tooth colour, fillings and mucous membranes and increased tartar formation. Povidone Iodine is a type of mouthwash used to treat mild oral mucosal infections and pharyngitis (Zhang et al., 2023). Side effects that arise when using povidone iodine are irritation, toxic reactions to skin fibroblasts, lungs, keratinocytes and osteoblasts. Long-term use causes systemic effects such as metabolic acidosis and kidney disorders. It is not recommended for use in children under 6 years and for routine use in thyroid sufferers, breastfeeding mothers and pregnant women (De Angelis et al., 2024).

Several studies have been carried out previously regarding etrates with *Porphyromonas Gingivalis* bacteria, such as (Rams et al., 2023), (Yavagal et al., 2023), (Gadde et al., 2023), (Brookes et al., 2023), and (Prasetya et al., 2024). The trend in this research focuses on the effects of *Porphyromonas Gingivalis* bacteria on other types of bacteria. Very few have focused on the anti-bacterial effect of chlorhexidine and povidone iodine liquids. Novelty of this research focuses on the effectiveness of antibacterial data on chlorhexidine and povidone iodine liquids on the growth of *Porphyromonas Gingivalis* bacteria.

Research Method

This type of research is experimental laboratory (in vitro). The research design used was a posttest only group design. The population in this study was *Porphyromonas Gingivalis* bacteria using a simple random sampling technique, where The number of samples for this research is 7 samples per treatment. Group 1 is the control group (negative) without treatment, group 2 is the treatment group which was given Chlorhexidine liquid and group 3 is the treatment group which was given Povidone Iodine liquid. *Porphyromonas Gingivalis* bacteria (ATCC No.33277) were put into a test tube containing BHIB, and incubated for 48 hours at room temperature 37 °C , then the bacteria were wiped evenly on MHA media with *Porphyromonas Gingivalis* bacteria (ATCC No.33277) put into the tube reaction containing BHIB and incubated for 48 hours at room temperature 37 °C , then the bacteria were wiped evenly on MHA media with a round oases on a petri dish, after that the sample was treated, by administering Chlorhexidine and Povidone iodine liquid and incubated for 24 hours at temperature room 37 °C . The Normality Test uses the Shapiro Wilk test to determine whether the data distribution is normal or not, provided that the sample subjects are ≤ 50 . Then, a statistical test was carried out using the independent sample t-test, with the condition that the data distribution was normal and the data variance had to be the same, to see the area of the inhibition zone between treatment groups. The test is fulfilled if the significant value (2-tailed) is below 0.05 ($p < 0.05$).

Results and Discussion

The results of the research (Table 1) showed that the results of the colony count test showed that the growth of *Porphyromonas Gingivalis* bacteria started from the control group with an average of 165 colonies, the 0.2% chlorhexidine liquid group with an average of 30 colonies and the povidone iodine liquid group 10 % with an average of 11 colonies. From the colony count test table it can be concluded that 10% povidone iodine solution is more effective than 0.2% chlorhexidine solution as an antibacterial against the growth of *Porphyromonas Gingivalis* bacterial colonies.

Table 1. Colony Test Results

No.	K(-)	Chlorhexidine 0.2%	Povidone iodine 10%
1.	142	33	8
2.	156	32	10
3.	162	28	12
4.	172	22	11
5.	168	29	14
6.	174	34	15
7.	178	31	9
Average	165	30	11

In (Table 2) it was found that the results of the inhibitory zone test for the growth of *Porphyromonas Gingivalis* bacteria were seen starting from the 0.2% Chlorhexidine liquid group with an average of 20.10 mm and had a difference for each sample of 1-0.5 mm while the liquid group Povidone Iodine 10% with an average of 22.3 mm and a difference between each sample of 0.5-0.3 mm. From the colony count test table it can be concluded that 10% Povidone iodine liquid is more effective than 0.2% Chlorhexidine liquid as an antibacterial against the growth of *Porphyromonas Gingivalis* bacterial colonies.

Table 2. Inhibition Zone Test Results

No.	Chlorhexidine 0.2%	Povidone iodine 10%
	(-)	
1.	20,20	22.35
2.	20.05	22.40
3.	20.40	22,20
4.	20.15	22.55
5.	19.80	22.05
6.	20,20	22.40
7.	19.95	22.15
Average	20.10	22.30

The results of the normality test using Shapiro-Wilk, all groups were normally distributed because the p value was > 0.05 . Based on these values, the results of the normality test for *Chlorhexidine* and *Povidone iodine fluids* on the growth of *Porphyromonas Gingivalis* bacteria are normally distributed (Table 3).

Table 3. Colony Test Results

Colonies & Inhibition Zones	Shapiro-Wilk P value
Colony chlorhexidine	0.312
Povidone iodine colony	0.837
Chlorhexidine inhibition zone	0.937
Povidone iodine inhibition zone	0.812

The significant value resulting from the independent t-test for colonies on the chlorhexidine and povidone iodine liquid treatment data was 0.000 sig. (2-tailed). This value is smaller than the specified research error level, namely 95% (0.05), meaning that there is a significant influence (Table 4).

Table 4. Independent T-Test Colony Test Results

Number of Colonies	<i>P value</i>
Equal variances assumed	0,000
Equal variances not assumed	0,000

p value from the Independent t test for the bacterial inhibition zone is $p > 0.05$ so it is significant. To determine significance, it can be done using the p value = 0.000 where the p value < 0.05 so it is meaningful (it is recommended to write this) because it is based on the p value where the critical value is 0.05 (Table 5).

Table 5. Results of the Independent T-Test for Bacterial Inhibition Zones

Number of Colonies	<i>P value</i>
Equal variances assumed	0,000
Equal variances not assumed	0,000

The research results showed that Povidone iodine had the strongest antibacterial effect compared to Chlorhexidine. Povidone iodine is more effective in inhibiting the growth of Porphyromonas Gingivalis bacteria and mixed bacteria in plaque. These results are in line with research conducted by (Shreenidhi & Rajasekar, 2024) Povidone Iodine reduced the average plaque index value to a greater extent compared to Chlorhexidine but was not statistically significant. Another study by (Langgartner et al., 2023) found lower bacterial colony growth in the Chlorhexidine alcohol group when compared with Povidone Iodine (4.7% vs 30.8%). In similar research conducted by (Suhadi et al., 2023), Povidone Iodine liquid has an inhibitory zone for bacterial growth with a diameter in the strong category of 11.50-15.00 mm, Medium 6.00-9.50 mm, Weak 0.00 mm and the liquid contains the active ingredient methyl salicylate such as Chlorhexidine which has the ability to inhibit bacterial growth with a diameter category of Strong from 11.00-15.00, Medium 5.50-8.50 mm, Weak 4.50 mm. Of the two liquids containing the active ingredients povidone iodine and methyl salicylate, there was no significant difference in inhibitory power on bacterial growth.

Povidone Iodine is a germicidal that works quickly, bacteria are killed within 1 minute and bacterial spores will be killed after 15 minutes (Lesmanawati et al., 2023). Povidone iodine can also treat wounds and fight fungal infections and parasites. Povidone Iodine has anti-bacterial properties mainly through a mechanism where it carries free iodine compounds through cell membranes (Xu et al., 2023). Iodine compounds have cytotoxic properties so they can kill bacterial cells. Povidone iodine is able to inhibit the synthesis of

glucosyltransferase (GTF) and fructosyltransferase (FTF) by bacteria (Rahmatika et al., 2024). GTF and FTF are extracellular enzymes that synthesize the polysaccharides glucans and fructans which play an important role in the process of bacterial attachment and biofilm formation on the tooth surface (Jeong et al., 2024).

The antimicrobial mechanism of action of iodine is that iodine actively reacts in an electrophilic reaction with respiratory chain enzymes and with amino acids in bacterial cell membrane proteins (Faleye et al., 2024). As a result, the tertiary structures needed to maintain the respiratory chain are damaged. The respiratory chain is a metabolic pathway for electron transport in cellular respiration. This creates an electrochemical proton gradient that drives ATP synthesis. By disrupting ATP synthesis, bacterial growth can be inhibited (Courbon et al., 2023). This damage affects the structure and function of enzymes and bacterial cell proteins, thus damaging the function of bacterial cells. This reaction causes rapid death of microbes and prevents the development of bacterial resistance.

The mechanism of Chlorhexidine as an antimicrobial is to interact with phospholipids and lipopolysaccharides (Waller et al., 2023), in bacterial cell membranes and enter cells via active or passive transport mechanisms. The interaction of the positive charge of the Chlorhexidine molecule with the negatively charged phosphate groups on the microbial cell wall, changes the osmotic balance of the cell which disrupts bacterial growth. Increases cell wall permeability, so that Chlorhexidine molecules can enter the bacteria. Membrane damage is followed by leakage of intracellular elements such as *adenosine triphosphate* and nucleic acids. As a result, the bacterial cytoplasm becomes clotted and then the bacterial cells lyse (Nosrati et al., 2023).

The bactericidal effect of chlorhexidine is due to the rupture of cell membranes and the consequent loss of intracellular substances such as potassium (at low concentrations) or to the inhibition of respiration and loss of nucleic acids (at high concentrations). In addition, due to the interaction of chlorhexidine with cytoplasmic proteins, protein and nucleic acid deposition occurs. chlorhexidine inhibits glucosyltransferase and phosphoenolpyruvate phosphotransferase, the latter being an enzyme essential for the function and maintenance of the bacterial glycolytic pathway. It is active against both Gram-positive and Gram-negative bacteria and Gram-positive bacteria are more sensitive than Gram-negative bacteria, possibly due to the absence of an outer membrane and the presence of teichoic acids in their cell walls.

Conclusion

Chlorhexidine 0.2% and povidone iodine 10% are antimicrobials which have the ability to kill *Porphyromonas Gingivalis* bacteria which are the most resistant bacteria and are one of the causes of periodontal disease. Thus it can be concluded that *Chlorhexidine 0.2%* and *Povidone iodine 10%* can kill *Porphyromonas Gingivalis* bacteria. However, Povidone iodine 10% has greater antibacterial power than Chlorhexidine 0.2% against *Porphyromonas Gingivalis* bacteria.

References

- Álvarez, G., Soler-Ollé, A., Isabal, S., León, R., & Blanc, V. (2023). Bacterial decontamination of toothbrushes by immersion in a mouthwash containing 0.05% chlorhexidine and 0.05% cetylpyridinium chloride: A randomized controlled trial. *International Journal of Dental Hygiene*, 21(2), 357–364. <https://doi.org/10.1111/idh.12652>
- Alves, P. J., Gryson, L., Hajjar, J., Lepelletier, D., Reners, M., Rodríguez Salazar, J., & Simon, A. (2023). Role of antiseptics in the prevention and treatment of infections in nursing homes. *Journal of Hospital Infection*, 131, 58–69. <https://doi.org/10.1016/j.jhin.2022.09.021>
- Ardila, S., Wahab, A., & Candra, A. (2023). Antibacterial Effectiveness Test of Kersen Leaves (*Muntingia Calabural* L) on *Escherichia Coli*. *Medalion Journal: Medical Research, Nursing, Health and Midwife Participation*, 4(3), Article 3. <https://doi.org/10.59733/medalion.v4i3.81>
- Brookes, Z., Teoh, L., Cieplik, F., & Kumar, P. (2023). Mouthwash Effects on the Oral Microbiome: Are They Good, Bad, or Balanced? *International Dental Journal*, 73, S74–S81. <https://doi.org/10.1016/j.identj.2023.08.010>
- Chatzopoulos, G. S., Jiang, Z., Marka, N., & Wolff, L. F. (2023). Periodontal Disease, Tooth Loss, and Systemic Conditions: An Exploratory Study. *International Dental Journal*. <https://doi.org/10.1016/j.identj.2023.08.002>
- Chen, W. A., Dou, Y., Fletcher, H. M., & Boskovic, D. S. (2023). Local and Systemic Effects of *Porphyromonas gingivalis* Infection. *Microorganisms*, 11(2), Article 2. <https://doi.org/10.3390/microorganisms11020470>
- Courbon, G. M., Palme, P. R., Mann, L., Richter, A., Imming, P., & Rubinstein, J. L. (2023). Mechanism of mycobacterial ATP synthase inhibition by squaramides and second generation diarylquinolines. *The EMBO Journal*, 42(15), e113687. <https://doi.org/10.15252/embj.2023113687>
- De Angelis, S., Medda, E., Rotondi, D., Masocco, M., Minardi, V., Contoli, B., Possenti, V., Sorbo, A., D'Amato, M., Turco, A. C., Pastorelli, A. A., Stacchini, P., Cas, R. D., Bagnasco, M., Bonofiglio, D., Gasperi, M., Meringolo, D., Mian, C., Moleti, M., ... Olivieri, A. (2024). Fifteen Years of Iodine Prophylaxis in Italy: Results of a Nationwide Surveillance (Period 2015–2019). *The Journal of Clinical Endocrinology & Metabolism*, 109(2), e495–e507. <https://doi.org/10.1210/clinem/dgad593>
- Faleye, O. S., Boya, B. R., Lee, J.-H., Choi, I., & Lee, J. (2024). Halogenated Antimicrobial Agents to Combat Drug-Resistant Pathogens. *Pharmacological Reviews*, 76(1), 90–141. <https://doi.org/10.1124/pharmrev.123.000863>
- Gadde, P., Rodrigues, P., & Kamble, A. V. (n.d.). A Comparative Qualitative Analysis of Ozonised Water and Povidine Iodine as a Pre-Procedural Rinse in Chronic Periodontitis—A Randomized Controlled Clinical Trial.
- Gergeta, D., Badnjevic, M., Karleusa, L., Maglica, Z., Spalj, S., & Gobin, I. (2024). Effect of Chlorhexidine Digluconate on Oral Bacteria Adhesion to Surfaces of Orthodontic Appliance Alloys. *Applied Sciences*, 14(5), Article 5. <https://doi.org/10.3390/app14052145>
- Harefa, A. F. S. J., Kamelia, E., Santoso, B., & Suwondo, A. (2022). Potential of Lauric Acid, Miristic Acid and Combination Gel as Inhibiting the Growth of *Porphyromonas Gingivalis* Bacteria in Gingivitis.
- Huang, X., Li, Y., Zhang, J., & Feng, Q. (2024). Linking Periodontitis with Inflammatory Bowel Disease through the Oral–Gut Axis: The Potential Role of *Porphyromonas gingivalis*. *Biomedicines*, 12(3), Article 3. <https://doi.org/10.3390/biomedicines12030685>
- Jeong, G.-J., Khan, F., Tabassum, N., & Kim, Y.-M. (2024). Alteration of oral microbial biofilms by sweeteners. *Biofilm*, 7, 100171. <https://doi.org/10.1016/j.bioflm.2023.100171>
- Kumar, S., Sujir, N., Saha, A., Ahmed, J., & Bhushan, P. (2023). Unusual localized gingival redness: A case report. *Frontiers in Oral Health*, 4, 1292332. <https://doi.org/10.3389/froh.2023.1292332>

- Langgartner, D., Koenen, M., Kupfer, S., Glogger, L., Kurz, L., Perez-Rivas, L. G., Theodoropoulou, M., Noll-Hussong, M., Vettorazzi, S., Tuckermann, J., & Reber, S. O. (2023). Intact GR dimerization is critical for restraining plasma ACTH levels during chronic psychosocial stress. *Neurobiology of Stress*, 24, 100541. <https://doi.org/10.1016/j.ynstr.2023.100541>
- Lesmanawati, F. E., Budi, A. S., & Zarasade, L. (2023). Evaluation of the antiseptic efficacy of 4% chlorhexidine gluconate and 10% povidone iodine on Methicillin-Resistant Staphylococcus Aureus-infected wounds in White Rat (*Rattus Norvegicus*). *Eastern Journal of Medicine*, 28(3), 378–387. <https://doi.org/10.5505/ejm.2023.25901>
- Ni, C., Bao, D., Yan, F., & Chen, B. (2023). Correlation between serum α -Klotho levels and different stages of periodontitis. *BMC Oral Health*, 23(1), 369. <https://doi.org/10.1186/s12903-023-03099-4>
- Nosrati, H., Heydari, M., Tootiaei, Z., Ganjbar, S., & Khodaei, M. (2023). Delivery of antibacterial agents for wound healing applications using polysaccharide-based scaffolds. *Journal of Drug Delivery Science and Technology*, 84, 104516. <https://doi.org/10.1016/j.jddst.2023.104516>
- Prasetya, R. C., Fatimatuzzahro, N., Ermawati, T., Kristina, S., & Prabaningrum, R. R. H. (2024). Antibacterial Activity of Robusta Coffee (*Coffea Canephora*) Husk Extract Against *Enterococcus Faecalis* and *Porphyromonas Gingivalis*: In Vitro Study. *Trends in Sciences*, 21(3), Article 3. <https://doi.org/10.48048/tis.2024.7303>
- Rachmawati, E., Berlian, R. F., Hendiani, I., Najmi, N., & Syawqie, A. (2023). The Role of Entamoeba Gingivalis in Periodontal Disease: A Literature Study. *Jurnal EduHealth*, 14(02), Article 02. <https://ejournal.seaninstitute.or.id/index.php/health/article/view/2254>
- Rahmatika, A. N., Aspriyanto, D., & Nahzi, M. Y. I. (2024). Antibacterial Effectiveness of Rambai (*Sonneratia Caseolaris*) Leaves Extract Against *Streptococcus Mutans*. *Dentino: Jurnal Kedokteran Gigi*, 9(1), Article 1. <https://doi.org/10.20527/dentino.v9i1.18859>
- Rams, T. E., Sautter, J. D., & Shin, S. S. (2023). Molecular Iodine Mouthrinse Antimicrobial Activity Against Periodontopathic Bacteria. *The Journal of Contemporary Dental Practice*, 23(12), 1183–1189. <https://doi.org/10.5005/jp-journals-10024-3447>
- Shahoumi, L. A., Saleh, M. H. A., & Meghil, M. M. (2023). Virulence Factors of the Periodontal Pathogens: Tools to Evade the Host Immune Response and Promote Carcinogenesis. *Microorganisms*, 11(1), Article 1. <https://doi.org/10.3390/microorganisms11010115>
- Shreenidhi, S., & Rajasekar, A. (2024). Clinical Efficacy of Different Concentrations of Povidone Iodine in the Management of Peri-Implant Mucositis. *Journal of Long-Term Effects of Medical Implants*, 34(2). <https://doi.org/10.1615/JLongTermEffMedImplants.2023047348>
- Suhadi, A. P., Ristanto, R. H., Sigit, D. V., & Supriyatin, S. (2023). Assessment of biological literacy for high school students. *Biosfer: Jurnal Pendidikan Biologi*, 16(1), Article 1. <https://doi.org/10.21009/biosferjpb.24765>
- Sukhabogi, J. R., Doshi, D., Kumar, H. S. S., Bhargeva, S. S., & Kumar, K. S. (2023). Relationship between psychological distress with self-rated oral health and dental caries status among dental patients. *Clinical Epidemiology and Global Health*, 23, 101395. <https://doi.org/10.1016/j.cegh.2023.101395>
- Tsuchida, S., & Nakayama, T. (2023). Recent clinical treatment and basic research on the alveolar bone. *Biomedicines*, 11(3), 843.
- Waller, C., Marzinek, J. K., McBurnie, E., Bond, P. J., Williamson, P. T. F., & Khalid, S. (2023). Impact on *S. aureus* and *E. Coli* Membranes of Treatment with Chlorhexidine and Alcohol Solutions: Insights from Molecular Simulations and Nuclear Magnetic Resonance. *Journal of Molecular Biology*, 435(11), 167953. <https://doi.org/10.1016/j.jmb.2023.167953>
- Xu, J., Liu, W., Zhou, J., Kong, Y., Gong, M., Almajarsh, M., Zhao, X., & Wang, X. (2023). Preparation of lignin-based personal multifunctional protective mask interlayer with antibacterial, anti-UV and iodine trapping effects and exploration of its iodine trapping mechanism. *Industrial Crops and Products*, 203, 117175. <https://doi.org/10.1016/j.indcrop.2023.117175>
- Yavagal, P. C., Velangi, C. S., Lakshminarayan, N., & Nadar, B. G. (2023). Antimicrobial Efficacy of Irrigation with 4.8% Bromelain Extract against *Porphyromonas gingivalis* in the Periodontal Pockets: A Randomized Controlled Trial. *Journal of Indian Association of Public Health Dentistry*, 21(2), 157. https://doi.org/10.4103/jiaphd.jiaphd_224_21
- Zhang, M., Meng, N., Duo, H., Yang, Y., Dong, Q., & Gu, J. (2023). Efficacy of mouthwash on reducing salivary SARS-CoV-2 viral load and clinical symptoms: A systematic review and meta-analysis. *BMC Infectious Diseases*, 23(1), 678. <https://doi.org/10.1186/s12879-023-08669-z>
- Zhong, C., Wu, Y., Lin, H., & Liu, R. (2023). Advances in the antimicrobial treatment of osteomyelitis. *Composites Part B: Engineering*, 249, 110428. <https://doi.org/10.1016/j.compositesb.2022.110428>