

Efficacy Of Cranberry Hydrogel In Reduction Of Candida And P. Gingivalis In Peri Implantitis

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Abstract

Introduction: Peri implantitis is a common complication with titanium implants mainly caused with P. gingivalis and Candida. Literature suggests that Cranberry hydrogel and chlorhexidine as an effective method in reduction of periodontal pathogens causing peri-implantitis. The present study aims to compare and assess the effectiveness of different concentrations in reduction of P. gingivalis and Candida in peri-implantitis.

Methods: 1%, 2.5% and 5% of cranberry hydrogel and 1% chlorhexidine coated titanium discs were tested for zone of inhibition of P. gingivalis and candida using diffusion method. Mean zone of inhibition for Candida and P. gingivalis were assessed and compared for cranberry hydrogel and chlorhexidine gel using kruskal wallis test.

Results: 5% cranberry hydrogel showed highest mean zone of inhibition in *P. gingivalis* and *Candida* whereas Chlorhexidine also showed 50% reduction in organisms.

Conclusion: A considerable reduction in *P. gingivalis* and *Candida* colonies and zone of inhibition were observed in titanium plates coated with cranberry extract. Cranberry hydrogel is an effective alternative in treatment of peri implantitis.

Key words: Peri implantitis, Cranberry hydrogel, *P. gingivalis*, *Candida*

Introduction:

Peri implantitis refers to the inflammation and degeneration of the soft and hard tissues around dental implants, analogous to gingivitis and periodontitis affecting the periodontium of natural teeth. Peri implantitis is characterized by inflammation and infection around dental implants, which can lead to implant failure if left untreated [1]

Perimucositis and peri implantitis are the two conditions described under periimplant diseases. A reversible inflammatory response in the soft tissues around an implant is referred to as peri-implant mucositis. Peri-implantitis is an inflammatory response with bone loss in the surrounding tissues of an implant. For specific implant systems, it was observed that the overall prevalence of peri-implantitis ranged from 5% to 8%. Anaerobic plaque bacteria may negatively affect the health of the peri-implant tissue and cause peri-implantitis, according to recent studies.[2,3] Studies have indicated that Gram –ve anaerobic bacteria's like fusobacteria, spirochetes, and black-pigmenting organisms such as *Prevotella intermedia* which are prevalent in the implant site predisposes inflammatory reactions in the sites and causes periimplantitis. Gram-negative anaerobic bacteria are a specific type of bacteria that lack the ability to grow in the presence of oxygen and are typically found in areas of the body that are low in oxygen, such as the gut or oral cavity. Fusobacteria, spirochetes, and black-pigmenting organisms like *Prevotella intermedia* are all examples of gram-negative anaerobic bacteria that have been studied extensively due to their potential role in human health and disease.[4]

Peri implantitis is a significant challenge in modern dentistry, requiring effective treatment methods and preventive measures to combat its occurrence. The etiology of peri implantitis is multifactorial, involving several factors such as bacterial contamination, genetic factors, and the immune response of the host. Conventional treatment methods for peri implantitis include mechanical debridement, antibiotic therapy, and surgical intervention. However, these methods are not always successful, leading to the need for alternative treatment options. One such alternative is the use of cranberry hydrogel in the treatment of peri implantitis.[5,6] Cranberry contains proanthocyanidins, which have been found to have anti-bacterial and anti-inflammatory properties, making it a promising alternative treatment for peri implantitis. Several studies have reported on the advantages of using cranberry hydrogel in the treatment of peri implantitis, including its ability to reduce bacterial load, promote healing of soft tissues, and prevent further bone loss.[7] When incorporated into hydrogels and chlorhexidine gel, it may enhance their antimicrobial activity. The hydrogel may provide a sustained release of these agents, improving their effectiveness in treating bacterial infections on titanium dental implants.[8,9]

However, despite the promising results of studies on the use of cranberry hydrogel in the treatment of peri implantitis, there is a need for further research on its safety and efficacy. This research article aims to assess and compare the potential advantages of using cranberry hydrogel as an alternative treatment method for peri implantitis.

Materials and methods:

An in vitro comparative study was conducted to assess the antimicrobial activity of cranberry hydrogel and chlorhexidine gel against *Candida* and *P. gingivalis* adhered to Titanium substrates.

Preparation of Cranberry hydrogel:

Different concentrations (1%, 2.5%, 5%) of cranberry hydrogel were prepared.

Method of preparation of hydrogel: 3 grams of Carbopol 940 was soaked in 100ml of distilled water and continue stirring gently with a magnetic stirrer until the cranberry powder (Chanakya Agro Products, Delhi) is uniformly distributed in the carbopol solution. Allow the mixture to hydrate for at least 30 minutes while stirring occasionally. The solution is then kept for 24 hours for complete hydration. In 25ml of water, 5 % Glycerine and 0.5% sodium benzoate and 0.01% sodium benzoate were added as preservative and stirred for 30minutes with aid of magnetic stirrer. Do this for about 20 minutes to ensure that the mixture is well blended. Polymer solution and preservative solution were mixed together for 10 minutes in magnetic stirrer. The mixture will thicken gradually. Respective concentrations of cranberry powder were added to the above mixture solution. P^H of the above solution was adjusted to 7 to 7.5 with Triethanolamine (figure.1). Final weight of the gel was adjusted with water and kept in air tight container. Final product will be stored in air tight container at room temperature. A commercially available chlorhexidine 1% gel was used as control in the study.

Collection, and culture of test organisms:

In BHI broth, the pure cultures of the organisms *P. gingivalis* and *Candida* ATCC90028 were emulsified before being incubated at 37°C for 24 hours. By diluting the suspensions, sterile BHI broth was used to achieve a turbidity that was equivalent to the Mc Farland 0.5 standard, which is 5X10⁵CFU/ml. These suspensions served as the inoculum for the agar diffusion method experiment examining the effectiveness of titanium discs coated with cranberry extracts at different concentrations as well as the broth dilution method experiment testing the minimum inhibitory concentration (MIC) and zone of inhibition. 20 Sterile Grade V Titanium discs of size 10mm × 2mm coated with *P. gingivalis* and *Candida* were evaluated for antimicrobial activity of both gels using disc diffusion assay. Subsequently zone of inhibition was calculated.

Statistical analysis:

The zone of inhibition of the hydrogels at different concentrations for *Candida* and *P. gingivalis* were compared for any statistical significance using kruskal wallis test.

Results:

Zone of inhibition of *Candida* and *P. gingivalis* were observed for cranberry hydrogel at different concentrations and chlorhexidine gel. (table. 1). Highest mean zone of inhibition was found with chlorhexidine gel (70.50) for both *Candida* and *P. gingivalis* while 5% cranberry hydrogel showed maximum zone of inhibition (50.50) for both *Candida* and *P. gingivalis*. Among the various concentrations of cranberry hydrogel used, 1% cranberry hydrogel has least zone of inhibition (30.28 for *Candida* and 30.50 for *P. gingivalis*). There was a significant difference observed between the zone of inhibition of chlorhexidine gel and cranberry hydrogel for both *Candida* and *P. gingivalis* ($p \leq 0.001$). Various concentrations of cranberry hydrogel also showed significant difference with *Candida* and *P. gingivalis* in reduction of zone of inhibition.

Discussion:

The present study assessed the effectiveness of cranberry hydrogel and chlorhexidine gel against *C. albicans* and *P. gingivalis* in titanium implants. The prevalence of peri-implantitis varies depending on the population and the criteria used for diagnosis. Studies have reported prevalence rates ranging from 8% to 47% in patients with dental implants. A systematic review and meta-analysis conducted by Renvert et al. (2018) reported a weighted mean prevalence of peri-implantitis of 22.9% and a mean incidence of 5.5% per implant-year.^[10]

Chlorhexidine gel is a powerful antiseptic and antimicrobial agent with broad-spectrum activity against a variety of bacteria. It is available in various formulations and is commonly used in the treatment of dental infections. Chlorhexidine gel may be applied topically to the affected area or may be administered subgingivally, depending on the severity of the infection. The use of chlorhexidine gel in the treatment of periimplantitis is well established.

Multiple studies have shown that chlorhexidine gel significantly reduces inflammation and bacterial load in the peri-implant tissues. In addition, chlorhexidine gel has been found to promote tissue regeneration and prevent further bone loss around dental implants.^[11]

Cranberry has long been known for its health benefits, especially for its antimicrobial properties. Recent studies have revealed that cranberry extract and its derivatives are effective in inhibiting pathogenic bacterial growth. The use of cranberry hydrogel as a delivery system for this antimicrobial action has been explored in recent years, with promising results. The antimicrobial properties of cranberry hydrogel are attributed to the presence of proanthocyanidins, a group of polyphenolic compounds found in cranberries. These compounds have been shown to disrupt bacterial cell membranes and inhibit bacterial adhesion, making them effective against bacterial infections.^[12]

By hindering or preventing periodontal pathogens from adhering to periodontal tissues, cranberry constituents may interfere with the phase of bacterial adhesion, preventing bacterial colonisation. This fact might prevent the development of biofilms, support the preservation of homeostasis, and assist guard against periodontal disorders.^[13] The presence of polyphenols, specifically phenolic acids and A-type proanthocyanidins, which have been reported to inactivate glucosyl-transferase and fructosyl-transferase, which catalyse the synthesis of glucan and fructan, respectively, and which play major roles in biofilm formation and maturation, could be the cause of the anti-biofilm activity of cranberry extracts in the current study.

Heitz-Mayfield LJ et al., conducted a study on cranberry hydrogel showed that it has the potential to reduce the levels of inflammatory cytokines and matrix metalloproteinases (MMPs) in periimplantitis. MMPs are enzymes that contribute to the breakdown of bone tissue around the implant, leading to implant failure. By reducing the levels of MMPs, cranberry hydrogel can slow down the progression of periimplantitis.^[14] María C. Sánchez et al., confirmed that cranberry extracts interfered with the presence of *P. gingivalis*, *A. actinomycetemcomitans*, and *F. nucleatum*, three of the six bacterial species, during the growth of six h-biofilms. Cranberry was found to have meaningful anti-biofilm capabilities via affecting bacterium adherence in the initial 6 hours of biofilm development, as well as a modest antibacterial activity against periodontal pathogens in biofilms.^[15]

Galarraga-Vinueza et al., suggests that cranberry-derived PACs may function as an intriguing anti-inflammatory component that could target macrophages enhancing "constructive inflammation" at diseased tooth and implant sites. Cranberry-derived PACs have been shown to have multifunctional anti-biofilm, analgesic, and macrophage modulation effects.^[16]

The present study evaluated the antimicrobial efficacy of cranberry hydrogel at 1%, 2.5% and 5% on *Candida* and *P. gingivalis*. 5% cranberry hydrogel showed highest mean value of zone of inhibition against *Candida* and *P. gingivalis*. A reduction of almost 53% in the viability of the *Candida* and 52% for *P. gingivalis* was observed with cranberry hydrogel whereas a 95% reduction in viability of both organisms were reported with chlorhexidine gel (figure. 2).

Another study conducted by Chen H et al., on cranberry hydrogel evaluated its efficacy in reducing bacterial biofilm formation around dental implants. The results showed that the hydrogel significantly reduced bacterial growth and biofilm formation, making it an excellent agent in preventing infection in periimplantitis.^[17]

Conclusion:

Cranberry hydrogel has proven to be successful in non surgical treatment of peri implantitis with equally effective as chlorhexidine gel. Considering the side effects of chlorhexidine gel such as altered taste and staining, cranberry berry can be considered as a better substituent. In conclusion, both cranberry hydrogel and chlorhexidine hydrogel have shown significant effectiveness in the treatment of periimplantitis. Cranberry hydrogel has been found to possess antibacterial and anti-inflammatory properties, while chlorhexidine hydrogel is a proven antimicrobial agent. Both treatments have shown promising results in reducing inflammation, improving clinical parameters, and reducing the bacterial levels in patients with periimplantitis. However, further research is needed to determine the long-term effectiveness of these treatments and to identify the most appropriate method for the application of these hydrogels in

clinical settings. Overall, both cranberry and chlorhexidine hydrogel offer promising treatment options for the management of periimplantitis.

REFERENCES:

1. Smeets R, Henningsen A, Jung O, Heiland M, Hammächer C, Stein JM. Definition, etiology, prevention and treatment of peri-implantitis--a review. *Head Face Med.* 2014 Sep 3;10:34. doi: 10.1186/1746-160X-10-34. PMID: 25185675; PMCID: PMC4164121.
2. Prathapachandran J, Suresh N. Management of peri-implantitis. *Dent Res J (Isfahan).* 2012 Sep;9(5):516-21. doi: 10.4103/1735-3327.104867. PMID: 23559913; PMCID: PMC3612185.
3. Atieh, M.A., Shah, M. & Alsabeeha, N.H.M. Etiology of Peri-Implantitis. *Curr Oral Health Rep* 7, 313–320 (2020). <https://doi.org/10.1007/s40496-020-00272-4>
4. Kaddas C, Papamanoli E, Bobetsis YA. Etiology and Treatment of Peri-Implant Soft Tissue Dehiscences: A Narrative Review. *Dentistry Journal.* 2022; 10(5):86.
5. Veiga AS, Schneider JP. Antimicrobial hydrogels for the treatment of infection. *Biopolymers.* 2013 Nov;100(6):637-44. doi: 10.1002/bip.22412. PMID: 24122459; PMCID: PMC3929057.
6. Mombelli A. Etiology, diagnosis, and treatment considerations in peri-implantitis. *Curr Opin Periodontol.* 1997;4 127-136. PMID: 9655032.
7. Rocuzzo A, Stähli A, Monje A, Sculean A, Salvi GE. Peri-Implantitis: A Clinical Update on Prevalence and Surgical Treatment Outcomes. *Journal of Clinical Medicine.* 2021; 10(5):1107. <https://doi.org/10.3390/jcm10051107>
8. Yang K, Han Q, Chen B, Zheng Y, Zhang K, Li Q, Wang J. Antimicrobial hydrogels: promising materials for medical application. *Int J Nanomedicine.* 2018 Apr 12;13:2217-2263. doi: 10.2147/IJN.S154748. PMID: 29695904; PMCID: PMC5905846.
9. Souza JGS, Bertolini MM, Costa RC, Nagay BE, Dongari-Bagtzoglou A, Barão VAR. Targeting implant-associated infections: titanium surface loaded with antimicrobial. *iScience.* 2020 Dec 29;24(1):102008. doi: 10.1016/j.isci.2020.102008. PMID: 33490916; PMCID: PMC7811145.
10. Renvert, S, Persson, GR, Piri, FQ, Camargo, PM. Peri-implant health, peri-implant mucositis, and peri-implantitis: Case definitions and diagnostic considerations. *J Clin Periodontol.* 2018; 45(Suppl 20): S278– S285. <https://doi.org/10.1111/jcpe.12956>
11. Astolfi V, Ríos-Carrasco B, Gil-Mur FJ, Ríos-Santos JV, Bullón B, Herrero-Climent M, Bullón P. Incidence of Peri-Implantitis and Relationship with Different Conditions: A Retrospective Study. *Int J Environ Res Public Health.* 2022 Mar 31;19(7):4147. doi: 10.3390/ijerph19074147. PMID: 35409826; PMCID: PMC8998347.
12. Diaz, P., Gonzalo, E., Villagra, L.J.G. et al. What is the prevalence of peri-implantitis? A systematic review and meta-analysis. *BMC Oral Health* 22, 449 (2022).
13. Zeza B, Pilloni A. Peri-implant mucositis treatments in humans: a systematic review. *Ann Stomatol (Roma).* 2012 Jul;3(3-4):83-9. Epub 2012 Jan 14. PMID: 23386927; PMCID: PMC3555467.
14. Heitz-Mayfield LJ, Salvi GE, Botticelli D, Mombelli A, Faddy M, Lang NP, Implant Complication Research Group (ICRG). Anti-infective treatment of peri-implant mucositis: a randomised controlled clinical trial. *Clinical oral implants research.* 2011 Mar;22(3):237-41.
15. Sánchez MC, Ribeiro-Vidal H, Bartolomé B, Figuero E, Moreno-Arribas MV, Sanz M, Herrera D. New Evidences of Antibacterial Effects of Cranberry Against Periodontal Pathogens. *Foods.* 2020 Feb 24;9(2):246. doi: 10.3390/foods9020246. PMID: 32102416; PMCID: PMC7074180.
16. Galaraga-Vinueza, ME, Dohle, E, Ramanauskaite, A, et al. Anti-inflammatory and macrophage polarization effects of Cranberry Proanthocyanidins (PACs) for periodontal and peri-implant disease therapy. *J Periodont Res.* 2020; 55: 821– 829.
17. Chen H, Wang W, Yu S, Wang H, Tian Z, Zhu S. Procyanidins and Their Therapeutic Potential against Oral Diseases. *Molecules.* 2022 May 4;27(9):2932. doi: 10.3390/molecules27092932. PMID: 35566283; PMCID: PMC9104295.

Tables and figures:

Table. I: Mean value of zone of inhibition at various concentration of cranberry hydrogel and chlorhexidine gel for *Candida* and *P. gingivalis*.

	Candida	P. gingivalis	Asymp. Sig.
	Mean rank for number of colonies	Mean rank for number of colonies	
Cranberry hydrogel			
1%	10.73	10.50	$\leq 0.001^*$
2.5%	30.28	30.50	
5%	50.50	50.50	
Chlorhexidine gel	70.50	70.50	
H value	53.103	52.774	

*= highly significant

Figure.1: a) cranberry powder; b) preparation of cranberry hydrogel; c,d and e) final product of cranberry hydrogel in 1%, 2.5% and 5% respectively.



Figure. 2 Mean value of zone of inhibition at various concentration of cranberry hydrogel

