

Analysis of the Potential of Betel Leaf (*Piper Betle L.*) and Cetylpyridinium Chloride (CPC) to Reduce the Number of Bacteria in the Oral Cavity

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ABSTRACT

Introduction: poor oral health can be caused by the growth of pathogenic bacteria. Mouthwash is a solution or liquid that can be used to eliminate pathogenic bacteria, thereby preventing halitosis and dental caries. Betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) have antibacterial inhibition that can reduce the number of bacteria. Differences in concentration and composition in betel leaf and CPC can affect the effectiveness in inhibiting bacterial growth in the oral cavity.

Purpose: to further analyze the potential of betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) to reduce the number of bacteria in the oral cavity.

Methods: based on the exclusion and inclusion criteria, a total of fifteen (15) journals were analyzed from the Google Scholar, Research Gate, PubMed's and NCBI. The journals that analyzed are regarding an article that discusses the potential of betel leaf and CPC to reduce the number of oral bacteria.

Results: research with gargling using betel leaf and CPC shows that betel leaf are as effective as mouthwash containing CPC in reducing the number of oral bacteria. However, there are studies that state that gargling with mouthwash containing CPC is significantly higher inhibition of bacterial growth compared mouthwash containing betel leaf extract.

Conclusion: this review reveals that betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) are equally effective in reducing the number of bacteria in the oral cavity.

KEYWORDS: Betel Leaf; CPC; Oral Bacteria.

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INTRODUCTION

Poor oral conditions can cause several diseases, therefore oral health is one of the important factors that can affect a person's quality of life. The World Health Organization (WHO) has conducted many policy promotions and education regarding the prevention of oral and dental diseases.^{1,2} Poor oral health can be caused by the growth of pathogenic bacteria. *Streptococcus mutans* is one of the most dominant bacteria and is a gram-positive bacteria that causes dental caries.^{3,4} Caries is a progressive oral disease and is the main cause of tooth loss.⁵ Based on the results of Basic Health Research (RISKESDAS) data in 2018, the prevalence of dental and oral diseases still reached 57.6%.⁶ Mechanical plaque control can be aided by the use of mouthwash to remove bacteria between teeth that are not reached by toothbrushes and dental floss.^{7,8}

Alcohol-free mouthwashes sold in the market contain Cetylpyridinium chloride (CPC). CPC is a quaternary ammonium compound that has a broad antimicrobial spectrum. CPC in mouthwash has anti-bacterial, anti-plaque abilities and can treat gingivitis after continuous use for 2 weeks. Research conducted by Toar et al. in 2012 has shown that CPC mouthwash has a significantly higher inhibition against *Streptococcus mutans* than alcohol-free mouthwash containing betel leaf extract.^{8,9} Betel leaf (*Piper Betle L.*) is often used as a traditional medicine to nourish and strengthen teeth. Betel leaf is very popular in Asia, and is often referred to as the "Golden Heart of Nature".^{8,10} The use of betel leaf as a treatment for oral diseases has been widely practiced because it contains chemical compounds including alkaloids, carbohydrates, amino acids, tannins and steroids.¹¹ The main

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component of essential oil consists of phenol and its derivative compounds namely betiephenol, sesquiterpene, hydroxy caviko, chavibetol, estragolel, eugenol, carvacol and cavicol.^{12,13,14} Research conducted by Hanum et al. in 2012 has shown that there is a significant difference between the plaque score of the results of gargling with 10% betel leaf decoction water compared to bottled water, but there is no significant difference between 10% betel leaf decoction water and mouthwash containing 0.05% CPC.¹⁵ Furthermore, research conducted by Yanti and Lilianti in 2016 showed that there was no significant difference in the mean difference in the number of bacteria between the betel leaf decoction gargle group and the mouthwash group containing CPC. These results indicate that betel leaf decoction water is as effective as mouthwash containing CPC in reducing the number of bacteria in the oral cavity.¹⁴ Based on this introduction, this study aims to further analyze the potential of betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) to reduce the number of bacteria in the oral cavity.

METHODS

This literature review was made by analyzing and evaluating scientific knowledge from various references. The references used are sourced from articles, journals, and websites accessed through databases: Google Scholar, Research Gate, PubMed's and NCBI. The search strategy was based on the keywords betel leaf, CPC, oral bacteria. The types of journals used in writing are research journals and literature reviews published from 2012-2022. The initial selection of research journals and literature reviews was carried out based on the title and abstract related to betel leaf and CPC, then the text was read in its entirety. Information related to the evaluated variables was then collected based on: author's name, year, type of article, and results with the theme of discussion regarding the potential of betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) to reduce the number of bacteria in the oral cavity.

RESULTS

The results found in the searched database are shown in the flowchart provided in figure 1. Sixty-seven references were found in the Google Scholar database, 33 references were found in the Research Gate database, 25 references were found in the PubMed database, and 7 references were found in the NCBI database. After conducting an analysis based on the inclusion criteria and reading the available abstracts, the titles and relevance of the abstracts were filtered so that 27 articles were selected. Total articles read as a whole were 15. Articles discussing the potential of CPC and betel leaf in general were 10. Articles regarding articles discussing the potency of CPC and betel leaf have similar levels of effectiveness against reducing bacterial counts by 2, articles discussing CPC has a higher potential to reduce bacterial counts than betel leaf by 1. The articles obtained were then analyzed to understand and draw conclusions from the various research articles. It was found that there were articles discussing the potential of betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) to reduce the number of bacteria in the oral cavity, so that the total number of articles relevant to the theme of the literature review was 3. The referenced journals were published between 2012 and 2022. This influence is still the pros and cons because of differences in the results of research that has been conducted by experts. Some research experts argue that gargling betel leaf decoction is as effective as gargling mouthwash containing CPC. Other researchers also stated that the inhibition of *Streptococcus mutans* growth of alcohol-free mouthwash preparations containing CPC is significantly higher than alcohol-free mouthwash containing betel leaf extract. This is a concern for health practitioners, in order to provide knowledge to the public regarding the various opinions of these experts. The main findings related to potential of betel leaf (*Piper Betle L.*) and Cetylpyridinium chloride (CPC) to Reduce the number of bacteria in the oral cavity can be seen in table 1.

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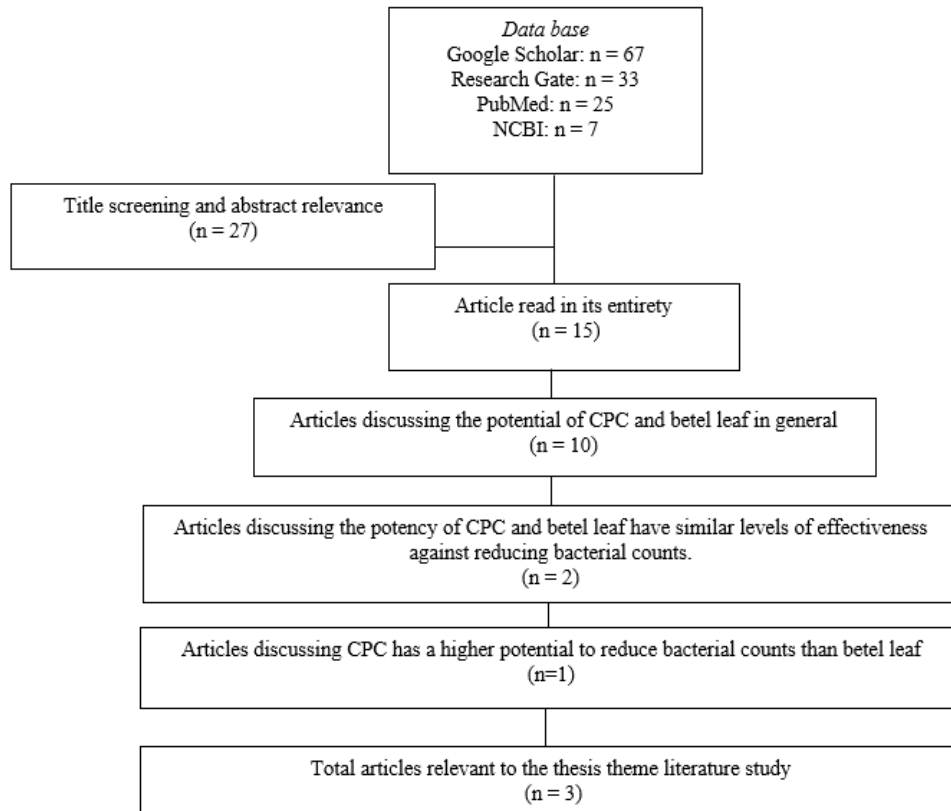


Figure 1. Publication flowcharts of all database

Table 1. Relevant Article Descriptions Based on Author, Year, Type of Article, and Results

Author	Year	Type of Article	Result
Yanti GN, Lilianti E	2016	Research Report	Statistical test results showed that there was no significant difference in the mean difference in the number of bacteria between before treatment and after treatment in the betel leaf decoction gargle group $105.67 \times 10^3 \pm 6.94 \times 10^3$ CFU/ml and the mouthwash group containing CPC $101.20 \times 10^3 \pm 6.01 \times 10^3$ CFU/ml ($p > 0.05$). It can be concluded that gargling betel leaf decoction is as effective as gargling mouthwash containing CPC.
Hanum Ismalayani, Syanariah M	NA, 2012	Research Report	In the study, it was found that there was a significant difference between the plaque scores of mouth rinses with betel leaf decoction compared to bottled water, but there was no significant difference between betel leaf decoction and mouthwash containing CPC. These results show that betel leaf cooking water is as effective as mouthwash containing CPC in reducing the number of bacteria. This may be because betel and CPC have antibacterial power that can cause a decrease in the number of bacteria.
Toar AI, Posangi J, Wowor V	2012	Research Report	From the results of the study, it can be concluded that the inhibition of <i>Streptococcus mutans</i> growth of alcohol-free mouthwash preparations containing CPC is significantly higher than alcohol-free mouthwash containing betel leaf extract.

DISCUSSION

Various methods have been used to reduce the number of bacteria and restore normal salivary pH as early as possible.

One of these methods is the use of mouthwash.¹⁶ Mouthwash is a solution or liquid for cleaning the oral cavity that can support the effectiveness of plaque control by removing

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bacteria between teeth that are not reached by toothbrushes and dental floss.^{8,17} Mouthwash is useful for cleaning the mouth from debris, antibacterial agents, preventing and reducing plaque accumulation and reducing the activity of microorganisms that cause halitosis so as to improve oral health.¹⁸ Gargling is one way to mechanically control plaque, in addition to brushing teeth and using dental floss. The use of mouthwash in maintaining oral health has been widely used.¹⁹

One plant that has antibacterial activity is betel leaf. Betel leaf is a traditional medicinal plant that is closely related to oral health. The use of betel as a mouthwash has a strong basis due to the content of essential oil which is a natural phenol component that functions as a strong antiseptic.²⁰

Cetylpyridinium chloride (CPC) is one of the mouthwashes that has the ability to control the amount of plaque and gingivitis.⁸ CPC compounds are commonly used as therapy for superficial infections of the oral cavity and esophagus. Cetylpyridinium chloride is a compound that is monocationic bactericidal and has the property of being soluble in water, alcohol, chloroform, benzene and ether.⁹ CPC is an antimicrobial agent that affects gram-positive and gram-negative bacteria, viruses, fungi and algae. The effective concentration of CPC against microbes is in the range of 0.05% to 0.1%. At concentrations above 0.1%, CPC will be toxic to humans and have no therapeutic effect. Meanwhile, at concentrations below 0.05% CPC becomes less effective as an antimicrobial agent. The best concentration of CPC as an antimicrobial is 0.07%. Most of the CPC sold in the market is available in this concentration.²¹

Yanti and Lilianti in 2016 conducted a study to determine the effectiveness of gargling with green betel leaf decoction compared to mouthwash containing CPC on the number of oral bacteria. The results of the statistical test showed that there was no significant difference in the mean difference in the number of bacteria between before and after treatment in the betel leaf decoction group $105.67 \times 10^3 \pm 6.94 \times 10^3$ CFU/ml and the mouthwash group containing CPC $101.20 \times 10^3 \pm 6.01 \times 10^3$ CFU/ml ($p > 0.05$).¹⁴ These results are in accordance with the research of Hanum et al. in 2012 on the effect of betel leaf cooking water on plaque growth. The results of the study found that there was no significant difference between betel leaf cooking water and mouthwash containing CPC. The results of this study indicate that betel leaf cooking water is as effective as mouthwash containing CPC in reducing the number of bacteria.¹⁵

Another study conducted by Wilis and Andriani in 2017 on the effectiveness of gargling betel leaf decoction compared to saga leaf decoction on changes in the degree of acidity of saliva in children obtained results, namely, it is more effective to gargle with betel leaf decoction on changes in the degree of acidity of salivary pH. The use of betel leaves as mouthwash also has a bactericidal and bacteriostatic effect on oral bacteria such as *Streptococcus mutans*, so that acid

production by bacteria can be prevented.²² In addition, research conducted by Armianty and Kirana also found that betel leaf extract with a concentration of 20% had an antibacterial effect on *Enterococcus faecalis* bacteria.²³

Research conducted by Mardiani and Mediastini in 2013, found that betel leaf decoction has an antibacterial effect on *Staphylococcus aureus* bacteria incubated at 37°C for 18-24 hours.²⁴ Furthermore, Haniastusi and Asih also reported that exposure to 10% red betel leaf decoction was able to reduce acid production from *Streptococcus sobrinus*. The number of *Streptococcus sobrinus* colonies after being incubated at 37°C for 24 hours with 10% red betel leaf decoction showed that the number of *Streptococcus sobrinus* colonies was less.²⁵

Different from previous studies, Toar et al. in 2012 conducted a study on the comparison of the inhibition of mouthwash containing CPC with betel leaf mouthwash against the growth of *Streptococcus mutans*. The study was using the Kirby Baurer disc diffusion method accompanied by distilled water as a negative control. The average results of the inhibition zone size of each test material CPC, betel leaf and distilled water are 34.69 mm (SD \pm 3.10) 11.57 mm (SD \pm 3.51), and 0 mm, respectively. Kruskal-Wallis test results showed the mean ranking of the CPC test material was higher than that of betel leaf and distilled water ($P < 0.05$). These data indicate the greatest inhibition of *Streptococcus mutans* by mouthwashes containing CPC compared to mouthwashes containing betel leaf extract and distilled water.⁸

The results of the study can be concluded that the inhibition of *Streptococcus mutans* growth from alcohol-free mouthwash preparations containing Cetylpyridinium chloride is higher than alcohol-free mouthwash containing betel leaf extract. This is in line with Akande et al. who conducted research on three different mouthwash brands on the number of oral bacteria. In this study, it was found that mouthwash containing CPC was able to significantly reduce the number of oral bacteria compared to mouthwashes containing phenol compounds and essential oils.⁸

In vitro research by Schaeffer et al. showed that mouthwash containing 0.075% alcohol-free CPC can inhibit 99.9% more *Streptococcus mutans* bacteria. In vivo research by Sreenivasan et al. showed that mouthwash containing 0.05% CPC can inhibit 90% more bacteria in dental plaque. The results obtained in this study are in accordance with the two research results above, which show the antibacterial activity of CPC with a wide inhibition zone, exceeding the inhibition zone of mouthwash containing betel leaf extract. The data is in accordance with the theory that CPC has the ability to increase the permeability of bacterial cell walls, reduce cell metabolism, reduce bacterial attachment to the tooth surface and inhibit cell growth.⁸

The differences in the results of the research conducted by Toar et al. were caused by various factors,

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including the composition, form of active ingredients, and the content of antibacterial ingredients. The composition of mouthwash containing CPC includes fluoride while the composition of betel leaf mouthwash does not contain fluoride. The fluoride contained in mouthwash causes CPC to have a greater inhibitory power than mouthwash containing betel leaf extract. The concentration of fluoride contained in mouthwash containing CPC is not listed, therefore it cannot be confirmed the antibacterial role of fluoride in this mouthwash. Toar et al. mentioned the shortcomings in their research, namely that the CPC trial material used was a mouthwash in a patented dosage form available on the market. This causes the levels and content contained in the mouthwash and betel leaf mouthwash cannot be controlled.⁸

Some of the above studies used different forms of active ingredients, composition and concentrations in the betel leaf mouthwash and CPC mouthwash used. The difference in CPC concentration and the presence of other antibacterial ingredients such as fluoride in the content of mouthwash sold in the market can affect the results of the study. The effective concentration of CPC in fighting microbes is in the range of 0.05% to 0.1%, while betel leaf decoction water is effective in reducing the amount of bacterial growth at a concentration of 10%. Gargling with mouthwash containing CPC and betel leaf has the same level of effectiveness in reducing the number of oral bacteria. The antibacterial properties of betel leaf and CPC can prevent bacterial growth in different ways.^{8, 14, 21}

CONCLUSIONS AND SUGGESTIONS

Cetylpyridinium chloride (CPC) and betel leaf (*Piper betle* L.) have been shown to have strong antibacterial potential. Based on the results of several studies on betel leaves and CPC, it can be concluded that both have the same effectiveness in reducing the number of oral bacteria. However, there are studies that state that CPC is more effective in reducing the number of oral bacteria compared to betel leaf. This happens because there are differences in the concentration and composition of the active ingredients of the mouthwash used.

It is hoped that other studies will be carried out, so that further information can be obtained about the potential of betel leaf (*Piper betle* L.) and Cetylpyridinium chloride (CPC) as a mouthwash by paying more attention to the concentration and composition of the active ingredients contained in the mouthwash to be used and conducting other studies to find out if there are any side effects of using betel leaf and CPC on oral health.

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