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Ethanol Extract of Pomelo Peel to Prevent Dental Caries in Extracted Teeth *In-Vitro*

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Abstract

Dental caries is caused by the bacteria *Streptococcus mutans*. It is said that *S. mutans* can be reduced by the action of toothbrushing with mouthwashes. However, chemical mouthwashes bring adverse effect on the teeth such as tooth staining, microbiota ecology changes, and mucosa lesions. Natural mouthwashes have become the alternative solution. For instance, the ability of ethanol extract from Pomelo peel to inhibit the growth of *S. mutans* bacteria can be used to prevent dental caries. This study aims to determine the effectiveness of ethanol extract of Pomelo peel in preventing dental caries in extracted teeth in vitro. The research design was quasi-experimental with a number of samples is 30. Six treatments were carried out, each treatment consisted of five samples consisting of bacterial culture, ethanol extract of Pomelo peel 20%, 50%, 75%, negative control, and positive control plus teeth and substrate. Observations were recorded and analyzed using Univariate Multi-Way Analysis of Variance (ANOVA). The results of the study showed that the occurrence of dental caries after receiving ethanol extract treatment from Pomelo peel is at least in the 75% concentration group, namely 0 teeth (0%), at the 25% concentration, all teeth experienced caries (100%), and in the 50% concentration group, dental caries occurred 67%. Statistically, grapefruit peel extract with a concentration of 75% significantly inhibits the process of tooth decay in conditions of white spots, black spots and holes. In conclusion, 75% concentration of Pomelo peel ethanol extract is effective in preventing dental caries in extracted teeth in-vitro.

Keywords: Caries Teeth, Citrus Maxima, In Vitro Extracted Teeth, Pomelo Peel Extract, *S. Mutans*

1. Introduction

Diseases of hard tooth tissue, also known as enamel, dentin, and cementum are caused by the activity of microorganisms contained in a fermented carbohydrate called dental caries. Dental caries is caused by the bacteria named *Streptococcus mutans* (Ozdemir, 2013). The combination of *S. mutans* with other factors such as substrate, host, and time causes the acceleration of dental caries. The process of dental caries commences with white spots, black spots, or lines and subsequently continues to create holes in the teeth (Warreth, 2023). The prevalence of dental caries in the world is quite high, between 49% - 83% and in Indonesia, dental caries is the most common

dental problem cases in Indonesia, namely 45.3%. Dental caries is most common in the age group 55-64 years (96.8%) followed by those aged 65 (95%), 45-54 (94.5%), and 35-44 (92.2%) (Kementerian Kesehatan RI, 2018). The occurrence of dental caries can be inhibited mechanically, chemically, or both, namely by reducing the attachment, proliferation, and aggregation of *S. mutans* bacteria. The plaque removal action through toothbrushing is recognized as the solution to prevent caries. Twice-daily toothbrushing at night and in the morning can remove the leftover residues during meals. The residues can provide the ideal substrate for *S. mutans* to create demineralizing acids. It is generally known and agreed that night toothbrushing is a must in daily routine to do. The study by (Sahoo et al., 2022) shows that the study of dental nursing students who were divided into groups and instructed to follow tooth brushing in pre-breakfast and post-breakfast with rinsing and without rinsing revealed the statement that the action of tooth brushing after breakfast with rinsing and without rinsing shows significant reduction of *S. mutans* colony-forming unit (CFU) in 38% and 29%. The habit of toothbrushing was evaluated in 5 years old children regarding daily tooth brushing and its significant effect on caries shows the number of relative risk for caries is significant with $p < 0.05$. This information shows that less than twice toothbrushing commenced in the child stage can bring the potential caries (Boustedt et al., 2020). However, the mechanical action of toothbrushing is not sufficient to prevent the occurrence of dental caries. Therefore, a combination with mouthwash is needed. The study shows that the active ingredients in the mouthwashes are cetyl pyridinium chloride, essential oils, chlorhexidine, triclosan, fluorides, delmopinol, and other substances (Tartaglia et al., 2019). The short duration use of less than 6 months of mouthwash can bring adverse effects such as local morphological (oral mucosa and dental-crown staining, mucosal lesions) and the functional effect comprises taste modifications and abnormal oral sensation. Besides, tooth staining was reported as the most listed adverse effect (Poppolo Deus & Ouanounou, 2022). The exposure of oral biofilms to mouthwash is correlated to adverse reactions such as residual structure, pathogenicity enhancement, and microbiota ecology changes (Takenaka et al., 2022). Long-term use of chemical mouthwash can cause various side effects such as extrinsic staining of the teeth as proven by (Erturk-Avunduk et al., 2021) who investigated the commercial mouthwashes effect on the discoloration of the tooth using a spectrophotometer. The color change was evaluated and shows that the commercial mouthwashes show unacceptable discoloration. Therefore, natural antibacterial ingredients are necessary, as those have fewer side effects from their use.

Pomelo (*Citrus maxima*) is a natural ingredient known for its antibacterial effects. The antibacterial effect of pomelo lies largely in the peel. The initial research showed that the ethanol extract of pomelo peel is positive for containing flavonoids of 102.92 ± 1.96 mg/100g QE, tannins of $6,867.61 \pm 167.95$ mg/100g TAE, phenols of $4,865.65 \pm 106.83$ mg/100g GAE. The results of the 25% concentration inhibition test are 6.7517, 50% resulted in 7.2583, and 75% resulted in 7.7550. The results of statistical analysis by Anova show a significant effect ($\text{sig} < 0.05$) on the diameter of the inhibition zone in *S. mutans* bacteria. Other research also found that pomelo contains phenols, tannins, flavonoids, and vitamin C. Pomelo peel contains antibacterial compounds. However, few studies explore the effectiveness of pomelo peel extract in preventing dental caries in extracted teeth. The objective of this research is to determine the effectiveness of ethanol of pomelo peel extract in preventing dental caries of the extracted tooth. The study was conducted by a test of the inhibitory power of ethanol extract of pomelo peel on the growth of *Streptococcus mutans* bacteria.

2. Method

This research uses a quasi-experimental research design in the form of a post-test-only control group design.

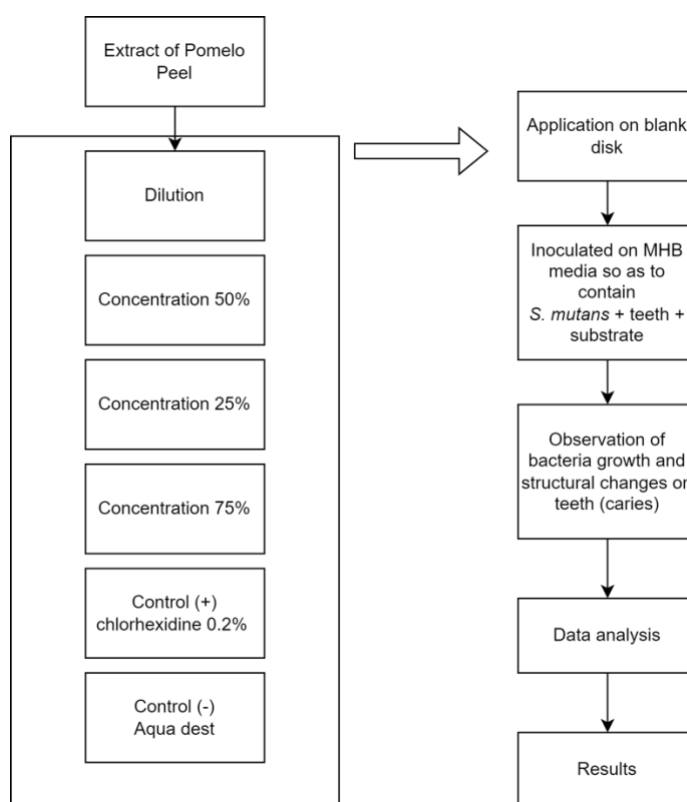


Figure 1: Steps of Extracting Pomelo Peel

The research procedure in this study was that teeth that had been coated with substrate and irradiated with bacterial suspension were placed on each blank disc containing saturated Mueller Hinton Blood (MHB) in a petri dish. Next, extracts of 25%, 50%, and 75% concentration were added to each medium, chlorhexidine as a positive control and distilled water as a negative control, then incubated at a temperature of 37°C during the observation period on days 0, 7, 28, and 42nd, 56th and 70th. Observation results were recorded. The data obtained was entered into a master table and then processed using SPSS 25 program. The results of data processing are presented in the form of tables, narratives, and/or images. Data on the effect activity of Pomelo peel ethanol extract were analyzed using Univariate Multi-way Analysis of Variance (ANOVA). This study was carried out under the Ethical Approval No. LB.02.03/EA/KEPK/0264/2022.

3. Results

3.1 Observation of Research Subject

The results of the observation of the research subject regarding the inhibitory power of Pomelo peel ethanol extract with concentrations of 25%, 50%, and 75% on the growth of *S. mutans* in-vitro are shown in Table 1.

Table 1: Average Value of Inhibition Zone Diameter of Pomelo Peel Ethanol Extract

Treatment	Inhibitory Diameter (mm)
Concentration 25%	0.000 c
Concentration 50%	6.688 b
Concentration 75%	7.316 b
Positive control	10.098 a
Negative control	0.000 c

Note: The average value followed by the same letter in the same column indicates that the difference is not significant at the 5% level Duncan test.

Table 1 shows that a concentration of 75% Pomelo peel ethanol extract produces an inhibitory zone diameter that is higher than other concentrations, namely 7,316 mm. However, an extract concentration of 75% resulted in a smaller inhibition zone diameter compared to the positive control. Meanwhile, the lowest is at a concentration of 25% and negative control. The average value of the inhibitory zone diameter of Pomelo peel extract with different concentration variants 2 shows that Pomelo peel extract has the highest antibacterial activity at a concentration of 75%.

The frequency of caries in extracted teeth is based on the inhibitory power of ethanol extract of Pomelo peel with concentrations of 25%, 50%, and 75% on the growth of *S. mutans* in-vitro as shown in Table 2.

Table 2: Treatment in The Teeth

Treatment	Looping	Healthy teeth (0)		White spotted teeth (1)		Black spotted teeth (2)		Cavities (3)		Caries	
		f	%	f	%	f	%	f	%	f	%
Concentration 25%	6	0	0	6	100	6	100	5	83	6	100
Concentration 50%	6	0	0	6	67	4	67	4	67	4	67
Concentration 75%	6	6	100	0	0	0	0	0	0	0	0
Positive control	6	6	100	0	0	0	0	0	0	0	0
Negative control	6	0	0	6	100	6	100	6	100	6	100
Total	30										

Table 2 shows that the occurrence of dental caries after receiving treatment with ethanol extract of grapefruit peel was at least in the 75% concentration group, namely 0 teeth (0%), at the 25% concentration all teeth experienced caries (100%), in the 50% concentration group caries occurred. teeth 67%. Compared with the control group, the positive control had 0 teeth (0%) and the negative control had all teeth caries (100%).

3.2 Statistics Results

The results of the Anova test for the inhibitory power of grapefruit peel (*Citrus maxima*) ethanol extract with concentrations of 25%, 50% and 75% on the growth of *S. mutans* are shown in Table 3.

Table 3: ANOVA Test Results on The Zone of Inhibitory Diameter *S. mutans*

Inhibitory Zone	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	504.298	4	126.074	260.547	.000
Within Groups	12.097	25	.484		
Total	516.395	29			

Table 3 shows that the concentration of Pomelo peel extract has a significant effect ($\text{sig} < 0.005$) on the zone of inhibitory diameter against *S. mutans* bacteria.

The results of the analysis of the formation of dental caries can be seen in the ANOVA test results as presented in Table 4.

Table 4: ANOVA Test on Caries Occurrence

		Sum of Squares	df	Mean Square	F	Sig.
White spot	Between Groups	400.000	4	100.000	1.000	.003
	Within Groups	2000.000	20	100.000		
	Total	2400.000	24			
Black spot	Between Groups	3855.600	4	963.900	.590	.004
	Within Groups	32700.400	20	1635.020		
	Total	36556.000	24			
Cavity	Between Groups	3311.200	4	827.800	10.901	.000
	Within Groups	1518.800	20	75.940		
	Total	4830.000	24			

Table 4 shows that the concentration treatment of Pomelo peel has a significant effect on the formation of white spots, and black spots on the teeth and the formation of cavities.

4. Discussion

The initial research of this study investigated the compounds of Pomelo peel such as flavonoids, phenols, and tannins. Flavonoid levels were 102.92 ± 1.96 mg/100 g QE, phenols were $4,865.65 \pm 106.83$ mg/100g and tannins were $6,867.61 \pm 167.95$ mg/100g TAE. Subsequently, the inhibitory power analysis of Pomelo peel was performed, and investigated the effectiveness of dental caries prevention was by applying the ethanol extract of Pomelo peel at concentrations of 25%, 50%, 75%, positive control (chlorhexidine 0.2%) and negative control (aqua dest) on the activity of the caries-causing *S. mutans* bacteria to the extracted teeth in vitro. The results in Table 1 show that a concentration of 75%, produces an inhibitory zone diameter that is higher than other concentrations specifically in 7.316 mm. However, an extract concentration of 75% resulted in a smaller inhibition zone diameter compared to the positive control. The lowest was at a concentration of 25% and negative control. The higher the concentration produces a larger inhibitory zone diameter as in Table 1. The results of the ANOVA test (Table 4) show the concentration of the ethanol peel extract of Pomelo has a significant effect ($\text{sig} < 0.005$) on the diameter of the inhibition zone for *S. mutans* bacteria. This is because the ethanol extract of Pomelo peel contains flavonoids, phenols, and tannins. Flavonoid compounds function to exhibit antimicrobial properties, several phenolic groups such as flavonoids, tannins, and other phenolic compounds function as a defense tool for plants against pathogenic microorganisms so that they can act as antibacterial/antimicrobial compounds (Tamsin et al., 2023; Tungmunnithum et al., 2018).

The results of this study also show that an extract concentration of 75% produces a smaller diameter of the inhibition zone compared to the positive control. This is because the positive control used was mouthwash containing 0.2% chlorhexidine. Chlorhexidine is not an antibiotic, not a herbal ingredient but an antiseptic and antibacterial agent. Chlorhexidine belongs to the biguanide antimicrobial group, which has a broad spectrum and works by damaging the integrity of the cell wall and cytoplasm of microorganisms (Ampawong & Aramwit, 2017; Cieplik et al., 2019; Hoang et al., 2021; Vitt et al., 2015).

The results of research on the effectiveness of Pomelo peel ethanol extract in preventing dental caries in extracted teeth in vitro show that the occurrence of dental caries after applied Pomelo peel ethanol extract treatment is at least in the 75% concentration group, namely 0 teeth (0%), concentration 25% of all teeth experienced caries (100%), in the 50% concentration group 67% of dental caries occurred. Compared with the control group, the positive controls experienced dental caries (0%) and the negative controls had all teeth experiencing caries (100%) as shown in Table 2. The results of the ANOVA test show that the concentration of Pomelo peel treatment has a significant effect on the formation of white spots, and black spots on teeth, and the formation of cavities. This is due to the inhibitory power of ethanol extract from Pomelo peel on the activity of the *S. mutans* bacteria which

causes dental caries. This is in accordance with the opinion (Ozdemir, 2013) that dental caries is a disease of the hard tissue of the teeth, namely enamel, dentin, and cementum, which is caused by the activity of microorganisms contained in fermented carbohydrates. Dental caries is caused by the activity of bacteria present in fermented carbohydrates. One of the bacteria that causes dental caries is *S. mutans* (Dianawati et al., 2020; Lemos et al., 2019). The ability of Pomelo peel extract to inhibit the growth of *S. mutans* bacteria can be used to prevent dental caries. The results of this study are in accordance with (Shehata et al., 2021) who stated that Pomelo peel extract contains various phytochemical compounds that function as antibacterial. Pomelo peel extract contains various phytochemical compounds including tannins, terpenoids, flavonoids, saponins, alkaloids, cardiac glycosides, phenol, and ascorbic acid (Lee et al., 2022). Phytochemical compounds known to have antibacterial properties are saponins, flavonoids, tannins, and phenols. Saponin is a class of terpenoid compounds that can inhibit the growth or kill bacteria by interfering with the process of cell wall formation, where the cell wall is not formed or is formed imperfectly (Huang et al., 2022; Rahayu et al., 2019). Flavonoids can create damage to the bacterial cell walls, microsomes, and lysosomes which lead to the interaction of flavonoids and bacterial DNA (Hidanah et al., 2022; Rifa'i et al., 2023). The lipophilic properties of flavonoids cause these compounds to damage bacterial cell membranes. Then, apart from that, the antibacterial activity of tannin compounds is related to its ability to inactivate microbial adhesins, enzymes, and transport proteins on cell membranes (Ngajow et al., 2013; Nirwana et al., 2018). Furthermore, other compounds, namely phenol, can kill bacterial cells, namely by denaturing bacterial cell proteins (Purwantiningsih et al., 2014).

This study has investigated the inhibitory power of Pomelo peel (*Citrus maxima*) ethanol extract on the growth of *S. mutans* and the effectiveness of preventing dental caries in teeth that have been extracted in vitro. The concentration of Pomelo peel extract showed a significant effect on the diameter of the inhibitory zone of *S. mutans* bacteria. A concentration of 75% grapefruit peel ethanol extract produced the highest inhibitory zone diameter compared to concentrations of 25%, and 50%. Giving orange peel extract is 75% effective in preventing dental caries in vitro.

Author Contributions:

Conceptualization, IMBA.; Methodology, IMBA.; Software, IGSK.; Validation, IMBA.; Formal Analysis, IGSK, ING.; Investigation, IMBA.; Resources, ING.; Data Curation, IMBA.; Writing – Original Draft Preparation, IMBA.; Writing – Review & Editing, IMBA.; Visualization, IMBA.; Supervision, IMBA.; Project Administration, ING.; Funding Acquisition, IMBA.

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Conflicts of Interest: The authors declare no conflict of interest.

Informed Consent Statement/Ethics approval:

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Poltekkes Kemenkes Denpasar No. LB.02.03/EA/KEPK/0264/2022.

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