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ANTIBACTERIAL EFFECTIVENESS OF LIME PEEL (*Citrus hystrix*) EXTRACT GEL ON *Porphyromonas gingivalis* BACTERIES

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ABSTRACT

Background: *Periodontitis is an inflammation of the tooth-supporting tissues caused by microorganisms, especially Porphyromonas gingivalis. Porphyromonas gingivalis has resistance to many antibiotics. Kuit lime peel has potential as an antibacterial with the most compound content is triterpenoid.* ***Objective:*** *To measure and analyze the effectiveness of antibacterial gel of kuit lime peel extract (Citrus hystrix) on the growth of Porphyromonas gingivalis bacteria.* ***Methods:*** *This study is a laboratory experimental study with post test with control group design, using seven treatment groups, namely 5%, 10%, 20% kecapi leaf extract, and metronidazole positive control with 7 repetitions of each treatment. Antibacterial effectiveness uses the disc diffusion method which is seen from the diameter of the inhibition zone formed on Mueller Hinton Agar media.* ***Results:*** *Based on the results of Kruskal-Wallis and Post hoc Mann Whitney tests, there were significant differences between concentration groups of 5%, 10%, 20%, and metronidazole.* ***Conclusion:*** *Lime peel extract gel (Citrus Hystrix) concentrations of 5%, 10%, and 20% have antibacterial potential against Porphyromonas gingivalis bacteria.*

Keywords**:** *kuit lime peel extract, antibactery, porphyromonas gingivalis*

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INTRODUCTION

Oral health is an important aspect that has a significant effect on overall body health. Poor oral conditions can trigger various oral and dental diseases, including systemic diseases.[1] One of the major problems frequently encountered in Indonesia is periodontitis, a chronic inflammatory disease of the tooth-supporting tissues that causes destruction of the periodontal ligament and alveolar bone, as well as the formation of deep periodontal pockets.[2]

The prevalence of periodontitis in Indonesia is very high, with the 2018 Basic Health Research (Riskesdas) data showing a rate of 74.1%, well above the WHO-estimated global average of 10- 15%.[3] The province of South Kalimantan is among the high prevalence areas, which is around 59%.[4] The disease is mainly caused by specific bacterial infections, especially Porphyromonas gingivalis, which is an anaerobic bacterium that plays an important role in the initiation and progression of periodontitis.[5]

Treatment of severe periodontitis often involves the use of antibiotics as supportive therapy, one of which is metronidazole, which is effective against anaerobic bacteria such as Porphyromonas gingivalis.[6] However, the use of metronidazole can cause side effects such as bitter taste, dry mouth, and bacterial resistance, so a safer and more natural alternative is needed.[7]

Kuit lime peel (Citrus hystrix DC.), which is abundant in South Kalimantan, contains phytochemical compounds such as flavonoids and essential oils that have antibacterial potential against bacteria that cause periodontitis.[8] Utilization of lime peel extract in the form of topical gel can be an effective alternative therapy and minimal side effects, with the advantage of easy application and good local absorption.[9,10]

This study aims to prove the effectiveness of lime peel gel at concentrations of 5%, 10%, and 20% as an antibacterial agent against Porphyromonas gingivalis, in the hope of reducing the prevalence of periodontitis in Indonesia and providing a safe and effective gel formulation for periodontal therapy.

MATERIALS AND METHODS

This study was conducted using a pure experimental method (true experimental), namely using a posttest-only design with control group design. This research has been approved by the Health Research Ethics Commission of FKG ULM with Ethical Clearance Letter No.007/KEPKG- FKGULM/EC/II/2025 This study used lime peel extract gel (Citrus hystrix) in this study using concentrations of 5%, 10%, 20% and metronidazole gel as a positive control.

Determination of Kuit Lime (*Citrus hystrix*)

Kuit limes (Citrus hystrix) were obtained from Astambul Sub-district, Banjar Regency, South Kalimantan. Determination test of limau kuit was conducted at the Basic Laboratory of FMIPA, Lambung Mangkurat University, Banjarbaru.

Kuit Lime Peel Extraction (*Citrus hystrix*)

The kuit lime peel used in this study was obtained from Astambul District, Banjar Regency, South Kalimantan. The peels were taken from old, dark green, relatively large sized, and good physical appearance kuit limes. A total of 5 kg of kuit limes were weighed and washed under running water to remove dirt. Next, peeling is done to separate the skin from the pulp. The kuit lime skin was then dried by aerating without direct sunlight, followed by oven drying at a certain temperature for 12 hours. After drying, the skin is pulverized using a blender to form simplisia. The kuit lime peel powder was then soaked in 96% ethanol in a closed container for 5x24 hours, protected from light and stirred several times, with solvent replacement every day. After the soaking process was complete, filtering was carried out using filter paper, and the residue was washed again with 96% ethanol, then stored in a place protected from light for 2 days. The extraction results were then evaporated using a rotary evaporator at 40°C and continued evaporation in a waterbath until 20.84 grams of ethanol extract of kuit lime peel with a concentration of 100% was obtained.

Ethanol Free Test of Kuit Lime Peel Extract

The ethanol-free test is carried out to determine whether or not ethanol is still contained in the extract so that a pure extract is obtained without any contamination. This is because ethanol has antibacterial properties so that if the extract still contains ethanol, then the extract will be free of ethanol then it can cause false positive results on the sample. Conduct ethanol-free test by inputting 1 ml of thick extract into a test tube, adding potassium dichromate then heated and added distilled water. Then testing is done using a spectrophotometer to see the absorbance value. After that, it is compared with the ethanol standard that has been made before.

Gel Formulation

In this study, gel preparations were made with a concentration variation of 5%, 10%, and 20%. Method of preparation: the extract was dissolved into a portion of water and then heated while stirring. Then added little by little Karbopol while continuing to stir and not to clot. Glycerin was added and Methyl Paraben and distilled water were added. Stirring was done until a gel was formed. After forming, the gel was stored in a dark and cool place for 1 night (10-15°C).

Bacterial Test Preparation

Suspensi bakteri yang telah dibiakkan di media *Mueller Hinton Agar* (MHA) kemudian diambil menggunakan ose steril dan dimasukkan ke dalam tabung reaksi yang berisi 1 ml *Brain Heart Infusion Broth* (BHIB) steril, kemudian diinkubasi dalam keadaan anaerob pada suhu 37ºC selama 24 jam. Langkah berikutnya menghomogenkan suspensi tersebut dengan menggunakan *vortex* selama 30 detik dan sesuaikan kekeruhannya menurut standart 0,5 *Mac Farland* memiliki jumlah bakteri setara dengan ($1,5 \times 10^8$) dengan cara melihatnya secara visual. Kekeruhannya masih belum sama, maka dilakukan pengenceran lagi pada media BHIB atau menambah bakteri hingga didapatkan kekeruhan yang sama.

Preparation of *Mueller Hinton Agar* (MHA) Media

This is done by mixing Mueller Hinton Agar (MHA) powder and distilled water according to the manufacturer's rules, then boiling on a hotplate. After boiling, the agar solution is sterilized using an autoclave. The sterilized agar solution was put into a Petri dish.

Antibacterial Test

Testing the antibacterial effectiveness of kuit lime peel extract gel (Citrus hystrix) using the well diffusion method. The first step was to apply the bacterial suspension using a sterile cotton swab. Making wells on agar media. Inserting lime peel extract gel (Citrus hystrix) with a concentration of
5%, 10%, 20%, and metronidazole into the wells that have been made before, then incubated at 37°C for 24 hours. After incubation, measure the inhibition zone formed around the pits using a digital caliper.

Processing and Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) 27. Data that have been obtained from each treatment were then tabulated and tested for normality using Shapiro- wilk. The statistical test results of the data on the number of inhibition zones of the lime peel extract gel (Citrus hystrix) in the normality test showed a significant value of $p > 0.05$, which means that the data was normally distributed. Furthermore, the homogeneity test using Levene's test showed a significant value of $p > 0.05$, meaning that the data variance was homogeneous. The analysis continued with the One Way Anova test with the Bonferroni Post hoc method because the data was homogeneous.

RESULTS

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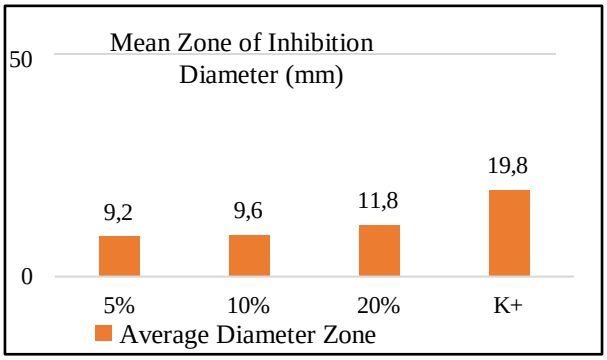

Figure 1. Bar Diagram of the Average Diameter of Inhibition Zone (mm) of Each Treatment Group Against the Growth of Porphyromonas gingivalis

Konsentrasi Gel Ekstrak Kulit Limau Kuit (Citrus hystrix)				**Kontrol**
Perlakuan	5%	10%	20%	(+) *metronidazole* 0,75%
5%		1.00	0,000*	0,000*
10%	1.00		0,001*	0,000*
20%	0,000*	0,001*		0,000*
Kontrol (+)	0,000*	0,000*	0,000*	

Figure 2. Results of Post Hoc Bonferroni Test of Zone of Inhibition of Kuit Lime Peel Extract Gel (Citrus hystrix) on the Growth of Porphyromonas gingivalis Bacteria

The results of One Way Anova test with Post Hoc Bonferroni method in Table 5. 2 shows that there is a significant difference between 5% concentration against 20% concentration and positive control, 10% concentration against 20% concentration and positive control, 20% concentration against positive control with the growth of Porphyromonas gingivalis bacteria, but does not show a significant difference between 5% concentration and 10% concentration so it can be concluded that the treatment group of kuit lime peel extract gel at each concentration has antibacterial effectiveness against Porphyromonas gingivalis, but at each concentration of kuit lime peel extract gel is not more effective than the positive control, namely metronidazole 0.75%.

DISCUSSION

Research on the antibacterial effectiveness of lime peel extract gel (Citrus hystrix.) concentrations of 5%, 10%, and 20% in inhibiting the growth of Porphyromonas gingivalis bacteria has potential and effectiveness as an antibacterial.[9] According to Yetto, et al (2022), the strength of inhibition is declared weak if it has a diameter ≤ 5 mm, moderate inhibition with a diameter of 6-10 mm, strong inhibition with a diameter of 11-20 mm, and very strong inhibition if the diameter is obtained ≥ 21 mm.[11] Based on this classification, the results show that the concentration of lime peel extract (Citrus hystrix.) has an antibacterial effect on the growth of Porphyromonas gingivalis bacteria with a moderate category at a concentration of 5% and 10% and a strong category at a concentration of 20% and a positive control of metronidazole 0.75%.[9]

The statistical test results show that there is a significant difference in the data obtained, which indicates that there is antibacterial effectiveness in the 5%, 10% and 20% concentration of kuit lime peel extract gel against Porphyromonas gingivalis. Research by Erinda, et al (2022) supports this statement in his research which tests the antibacterial effectiveness of lime peel extract (Citrus hystrix) against Porphyromonas gingivalis bacteria using the dilution method with concentrations of 5%, 10% 20%, 40%, 60%, 80% and 100% showing that the 5% concentration already has effectiveness in inhibiting Porphyromonas gingivalis bacteria.[9,12]

The results of the extract effectiveness test in this study were influenced by the increasing concentration of kuit lime peel extract, this is supported by research conducted by Ariyani et al, which shows that with increasing concentration of kuit lime peel extract, the number of microorganisms on the hands decreases. The greater the concentration, the greater the active substance contained in it, thus causing the inhibition of bacterial growth to also be greater.[8,12]

The antibacterial effectiveness of lime peel extract is influenced by the content of secondary metabolite compounds. The cell wall of gram- negative bacteria such as Porphyromonas gingivalis consists of multi-layered peptidoglycan so that compounds such as alkaloids, saponins, flavonoids, steroids and tannins are needed. Compounds such as triterpenoids, alkaloids, saponins, flavonoids, steroids, and tannins have different mechanisms of action against bacteria. This difference in mechanism contributes to the difference in antibacterial effectiveness of lime peel extract. The antibacterial mechanism in several ways, namely changing the permeability of the

cytoplasmic membrane which results in the cell wall coming out of the food material, and damage to the metabolic system in the cell as a result of inhibiting the work of intracellular enzymes and then denaturation of cell proteins, cell wall damage, resulting in lysis.[13,14] Each metabolic compound has a different mechanism in inhibiting bacteria. Triterpenoid compounds are the most metabolic compounds in kuit lime peel extract, which amounted to 899.13 mg/ml.[9]

Triterpenoids are compounds contained in lime peel that are antibacterial in nature which has a mechanism by causing a decrease in bacterial cell membrane permeability caused by triterpenoid compounds that will react with porins (transmembrane proteins) on the outer membrane of the bacterial cell wall, forming strong polymer bonds resulting in damage to porins which are the entrance and exit of compounds thereby reducing the permeability of the bacterial cell membrane.[13] Research by Tilarso et al, stated that the mechanism of alkaloids as one of the antibacterial compounds contained in lime peel is by disrupting the building blocks of bacterial peptidoglycan cells, thus preventing the formation of intact cell walls and causing the death of bacteria.[15]

Saponin is an antibacterial compound in kuit lime peel that has the ability as an antibacterial that causes damage to the bacterial cell membrane by destabilizing the membrane by diffusion through the cytoplasmic membrane.[9] Saponins work by increasing the permeability of the cell membrane, which causes hemolysis of the cell. When interacting with bacterial cells, saponins cause the bacteria to rupture or lysis.[16]

Flavonoid compounds as one of the ingredients in lime peel extract have the ability as antifungal by inhibiting the growth of pathogenic fungal conidia because flavonoids are lipophilic which can damage microbial membranes. According to Kartika et al, flavonoid compounds have genestein compounds that function as inhibitors of fungal cell division or proliferation by penetrating the fungal cell wall to the cell membrane. This is in line with the results of research conducted by Fatma et al. Flavonoids have a mechanism of action by inhibiting the permeability of fungal cell membranes and flavonoids will denature cell proteins and shrink cell walls, causing fungal cell walls to lysis because flavonoids form protein complexes with cell membrane proteins.[17]

Steroid is a compound found in kuit lime peel extract. The mechanism of action of saponins as antibacterial compounds is to reduce surface tension resulting in increased cell permeability or leakage and resulting in intracellular compounds will come out.[14] The mechanism of action of steroids in the study of Sadiah et al, as an antibacterial is related to lipid membranes and their sensitivity to steroids can cause liposomes to leak and membrane integrity to decrease and the morphology of the cell membrane changes so that cells become brittle and lysis.[18]

Tannin compounds as antifungal have been proven in several plants, one of which is the extract of kuit lime peel. According to research by Erinda et al, the mechanism of tannins as antibacterial is through H + ions that bind to bacterial cell proteins so that protein denaturation occurs due to a decrease in pH. Acidic conditions will inactivate bacterial enzymes resulting in disruption of cell metabolism until bacterial cell death.[9,18]

Metronidazole is an antibiotic and antiprotozoa drug made from the chemical compound 2-methyl-5-nitroimidazole. It belongs to the nitroimidazole group, which works by disrupting the DNA of microorganisms, making it effective in tackling a variety of bacterial and protozoan infections.[19] Metronidazole is one of the broad-spectrum antiprotozoa that is effective against many protozoa and even against anaerobic pathogenic bacteria, antibiotics that are bactericidal or kill bacteria and provide good clinical results in Amoebiasis therapy. The mechanism of metronidazole is by inhibiting bacterial DNA synthesis and damaging DNA through oxidation which causes DNA chain breaks and causes bacteria to die. Meanwhile, lime peel extract (Citrus hystrix) contains triterpenoids, alkaloids, saponins, flavonoids, steroids, and tannins that have antibacterial activity.[9,20]

Based on the results of this study, all treatment groups of lime peel extract gel (Citrus hystrix) had a smaller average diameter of inhibition zone than the control group. This is due to the difference in mechanism of action and antimicrobial potential between the two. Metronidazole has a specific mechanism that directly inhibits bacterial DNA synthesis, while the compounds in the kuit lime peel extract gel work through a more general mechanism.[20]

In addition, the concentration of active compounds in lime peel extract may vary and may not reach the levels required for a strong antibacterial effect such as metronidazole. Therefore, in the context of treating serious bacterial infections, metronidazole is often relied upon more heavily due to its proven effectiveness. Alternatively, other studies have shown that kuit lime peel extracts (Porphyromonas gingivalis) have effectiveness in inhibiting the growth of Porphyromonas gingivalis bacteria, which is the cause of periodontitis. This shows the potential of using other plant extracts as natural antibacterial agents.[7,19,21,22]

The development of herbal medicines in gel dosage forms is gaining popularity for several reasons. Gels have good absorption on the skin, do not inhibit the physiological functions of the skin such as respiration, and are easily washed off with water.[7,23] In addition, gels do not clog pores, are soft, and non-sticky, thus increasing user comfort. Several studies have examined the effectiveness of gel preparations from specific plant extracts. For example, breadfruit leaf extract was formulated in gel form to utilize its antioxidant properties.[24] Similarly, Moringa leaf extract, which is known to have anti-inflammatory potential, has been developed into a gel preparation for topical application. However, it is important to remember that while herbal remedies have many advantages, their use must remain appropriate and controlled. Consultation with a healthcare professional before starting herbal remedies is highly recommended to ensure their safety and effectiveness.[25]

CONCLUSION

Gel preparations of lime peel extract (Citrus hystrix) at concentrations of 5%, 10%, and 20% showed antibacterial effectiveness against the growth of Porphyromonas gingivalis. Concentrations of 5% and 10% have a moderate effectiveness category, while the 20% concentration has a strong category. However, the effectiveness of the three concentrations has not been able to match the effectiveness of metronidazole 0.75% as a positive control which has a strong category against the growth of these bacteria.

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