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COMPARISON OF ANTIBACTERIAL ACTIVITY OF *Curcuma longa* AND *Curcuma zedoaria* RHIZOMES EXTRACTS AT A CONCENTRATION OF 12.5% AGAINST *Streptococcus mutans* (*PERBANDINGAN AKTIVITAS ANTIBAKTERI EKSTRAK RIMPANG Curcuma longa DAN Curcuma zedoaria KONSENTRASI 12,5% TERHADAP Streptococcus mutans*)

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ABSTRACT

Streptococcus mutans is a microorganism that important in dental caries. Herbs are known to have antibacterial activity against oral bacteria. The rhizomes of *Curcuma longa* and *Curcuma zedoaria* are two of the eight species of genus Curcuma that are most widely used as traditional herbal medicine in Indonesia. Both rhizomes have antibacterial activity against oral bacteria at a concentration of 12.5%. This study aimed to examine the inhibitory of *Curcuma longa* and *Curcuma zedoaria* rhizomes extracts against the growth of *Streptococcus mutants*. The study was in vitro study. Both rhizomes got from the Experimental Garden of Balittro Manoko Lembang, West Java, Indonesia. The maceration was employed to obtain the extracts with the final extracts of both rhizomes at a concentration of 12.5%. Antibacterial activity test was carried out by using the agar well diffusion method.

The positive control group was 0.2% Chlorhexidine and distilled water as a negative control group. The data obtained were then analyzed using the One Way ANOVA Test and Post Hoc Test. Results showed that chlorhexidine 0.2% had the largest mean diameter of the inhibition zone. *Curcuma longa* rhizome extract had a larger mean diameter of inhibition zone compared to *Curcuma zedoaria* rhizome extract. However, the difference in the mean values of the two rhizomes extracts was not statistically significant. Distilled water didn't have antibacterial activity. It can be concluded that both *Curcuma longa* and *Curcuma zedoaria* rhizomes extracts at a concentration of 12.5% have antibacterial activity against *Streptococcus mutans.*
Keywords: antibacterial; *Curcuma longa; Curcuma zedoaria*

ABSTRAK

Streptococcus mutans merupakan bakteri yang memainkan peran penting dalam karies gigi. Bahan-bahan herbal dilaporkan memiliki aktivitas antibakteri terhadap bakteri oral. Rimpang Curcuma longa dan Curcuma zedoaria merupakan dua dari delapan spesies dari genus Curcuma yang paling banyak dimanfaatkan sebagai obat tradisional di Indonesia. Kedua rimpang ini dilaporkan memiliki aktivitas antibakteri terhadap bakteri oral pada konsentrasi 12,5%. Tujuan dari penelitian ini adalah untuk mengetahui perbandingan pengaruh ekstrak rimpang Curcuma longa dan Curcuma zedoaria pada konsentrasi 12,5% terhadap diameter zona hambat pertumbuhan bakteri Streptococcus mutans. Penelitian ini dilakukan secara secara in vitro. Kedua rimpang diperoleh dari Kebun Percobaan Balittro Manoko Lembang, Jawa Barat. Pembuatan ekstrak dilakukan dengan metode maserasi dengan hasil akhir ekstrak kedua rimpang pada konsentrasi 12,5%. Uji aktivitas antibakteri dilakukan dengan metode difusi sumuran. Chlorhexidine 0,2% digunakan sebagai kelompok kontrol positif dan akuades digunakan sebagai kelompok kontrol negatif. Data yang diperoleh kemudian dianalisis dengan uji One Way Anova dan uji Post Hoc. Hasil penelitian ini adalah chlorhexidine 0,2% memiliki rerata diameter zona

hambat terbesar. Ekstrak rimpang Curcuma longa memiliki rerata diameter zona hambat yang lebih besar dibandingkan Curcuma zedoaria. Namun, perbedaan nilai rerata diameter zona hambat kedua rimpang tidak signifikan secara statistik. Akuades tidak memiliki aktivitas antibakteri. Kesimpulan penelitian ini adalah ekstrak rimpang Curcuma longa dan Curcuma zedoaria konsentrasi 12,5% memiliki aktivitas antibakteri terhadap bakteri Streptococcus mutans.
***Kata kunci**: antibakteri; Curcuma longa; Curcuma zedoaria*

INTRODUCTION

Caries is an infection of the teeth that causes progressive destruction of the tooth tissue. Caries is caused by the interaction between bacteria from dental plaque, fermentable carbohydrates, and dental tissue over time.[1] As caries deepens to reach the dentin. Bacteria can penetrate through the dentinal tubules into the pulp. Bacterial by-products have previously resulted in local chronic cell infiltration causing pulpitis.[2] *Streptococcus mutans* is a bacterium that plays an essential role in dental caries. *S. mutans* adhere to tooth surfaces by producing glycosyltransferase enzymes. It converts glucose into sticky polysaccharides called dextran, thus forming a glycocalyx. The ability to survive in an acidic environment by modulating glucose metabolism pathways and irreversible binding to teeth is a vital component of the pathogenesis of *S. mutans* which progressively causes dissolution of hydroxyapatite crystals in enamel and dentin, resulting in dental caries.[3,4]

Herbal ingredients are reported to have antibacterial activity against oral bacteria. Therefore, herbal ingredients have the potential to be used in the field of dentistry. The advantages of herbal antibacterial ingredients are that they are safe, readily available, inexpensive, and have low microbial resistance.[5] Curcuma is a genus of members of the *Zingiberaceae* family with high economic value and has been widely cultivated in Indonesia as a traditional medicinal plant to treat various diseases. The parts of plants that are generally used include rhizomes, leaves, and flowers. Subositi et al. reported that eight species of the genus Curcuma are most widely used as traditional medicinal plants

by various ethnic groups in Indonesia. These species include *Curcuma longa* and *Curcuma zedoaria*.[6] *Curcuma longa* is a species of Curcuma used for thousands of years as a spice and food coloring in Asia. In Indonesia, *C. longa* is the species most widely used as a traditional medicinal plant in the genus Curcuma. In dentistry, *C. longa* is reported to help reduce pain in the gums, prevent plaque formation and gingivitis, and as a dye for pit and fissure sealants.[6,7] *C. longa* is said to have antibacterial activity against *Pseudomonas sp., Staphylococcus aureus*, and *Enterococcus faecalis*.[8,9] Pangesti et al. reported that at a concentration of 12.5% C. longa rhizome extract, other herbal ingredients could inhibit the growth of *S. aureus* bacteria.[10] Other species of Curcuma that were reported to have the potential to be used as ingredients for dental products is *Curcuma zedoaria.* The rhizome of *C. zedoaria* has low cytotoxicity against LMF cell lines from the oral mucosa. It could lower blood sugar and relieve gingivitis.[11,12] *C. zedoaria* has antibacterial activity against *Pseudomonas aeruginosa, Streptococcus viridans,* and *Staphylococcus aureus*.[13,14] Puspita et al. said that the rhizome extract of *C. zedoaria* at a concentration of 12.5% could inhibit the growth of *S. viridans* bacteria.[14]

Research reports on the antibacterial activity of *C. longa* and C. *zedoaria* against *S. mutants* still show contradictory results. Batubara et al. conducted a study on the antibacterial activity of C. *longa* and *C. zedoaria* against *S. mutans* using the leaves.[15,16] The essential oil of these two ingredients showed that *C. longa* could inhibit the growth of *S. mutans* bacteria while *C. zedoaria* did not deter the growth of *S. mutans* bacteria.[15] On the other hand, the extracts of these two materials obtained from the residue of the distillation process showed that *C. longa* did not inhibit the growth of *S. mutans* bacteria while *C. zedoaria* could hinder the growth of *S. mutans* bacteria.[16] Another study by Putri et al. and Kumara et al. with disc diffusion test showed that *C. zedoaria* could inhibit the growth of *S. mutans*, while *C. longa* could not inhibit the growth of *S. mutans* bacteria.[17,18] The rhizomes of *C. longa* and *C. zedoaria* can be used as antibacterials in the medical field. Tooth. The differences occurred in the antibacterial activity of *C. longa and C. zedoaria* against S. mutans bacteria and the lack of research on this matter. The authors are interested in researching the comparison of the antibacterial activity of the rhizomes of *C. longa* and *C. zedoaria* in the concentration of 12.5% against *S. mutans* bacteria.

METHOD

This research was a laboratory quasi-experimental research conducted in vitro with a post-test-only control group design. This research was executed after being declared free from ethical review by the Medical and Health Research Ethics Committee (KEPKK) Faculty of Medicine, Sriwijaya University. The analysis was carried out from November to December 2020. Both rhizome species were obtained from the Experimental Garden of the Manoko Lembang Spice and Medicinal Research Institute (Balittro), West Bandung Regency, West Java. Extracts of *C. longa* and *C. zedoaria* rhizomes were made at the Biochemistry Laboratory of the Faculty of Medicine, Sriwijaya University, with the maceration method three times. The antibacterial activity test of two materials against *Streptococcus mutant* bacteria was carried out at the Microbiology Laboratory of the Palembang Health Laboratory. The tests used the well diffusion method where 0.2% Chlorhexidine was used as a positive control group, and aqua dest was used as a negative control group.

Preparation of Rhizome Extract of *C. longa* and *C. zedoaria* Concentration of 12.5%

Both species of rhizome obtained were washed with running water, then peeled and cut into small pieces. The pieces of each rhizome were then dried in the oven at 45ºC for two days. After drying, the stakes are mashed with a blender until they become powder. Powdered simplicia of each rhizome was then extracted using the maceration method using 96% ethanol as a solvent for three days. The extract mixed with solvent was then filtered with filter paper to separate the filtrate and debris. Maceration was carried out three times. Therefore, the waste resulting from maceration I and II filtering have soaked again in 96% ethanol for three days and then filtered again. Each filtrate produced from each maceration process was then evaporated at 40ºC for three days to evaporate the 96% ethanol content in the filtrate to obtain a 100% thick extract of each rhizome. Dilution of the wide section of each rhizome was carried out using 5% tween as a diluent. Tween 5% of 17.5 ml was mixed with 2.5 ml of thick extract for each rhizome to obtain a final volume of 20 ml of extract of both species of rhizome in a concentration of 12.5%.

Preparation of *Streptococcus mutans* Suspension

Streptococcus mutans strain ATCC 25175 was taken from pure culture using sterile ose, cultured on blood agar media, and then incubated for 24 hours at 37ºC

under anaerobic conditions. The bacterial suspension was added with 0.9% NaCl until it reached turbidity following the standard 0.5 McFarland bacterial concentration equivalent to 1.5x108 cfu/mL.

Preparation of Test Media

So that as much as 5 grams of blood were mixed with 125 ml of distilled water until homogeneous, then heated for 15 minutes with an electric stove and then allowed to cool. The media is then put into the incubator. After 15 minutes, the media was then poured into a sterilized petri dish.

Antibacterial Activity Test

A sterile cotton swab was dipped in the bacterial suspension and then applied to the surface of the media so that the blood was evenly distributed and waited for it to dry for five minutes. Then, the blood agar medium in the petri dish was made in four wells with a sterile cork borer. Each well was then labeled according to its treatment group on the outer surface of a petri dish labeled CL for 12.5% *C. longa* rhizome extract, CZ for *C. zedoaria* rhizome extract 12.5%, K(+) for *C.* zedoaria rhizome extract. Chlorhexidine 0.2% as a positive control, and K(-) for distilled water as a negative control. After that, 12.5% *C. longa* rhizome extract, 12.5% *C. zedoaria*, positive control, and negative control were dripped into the wells according to their respective descriptions. The test medium was then incubated at 37oC for 24 hours. Observation of antibacterial activity was carried out by measuring the bacterial growth inhibition zone formed with a caliper (Figure 1). The antibacterial activity test was repeated six times.

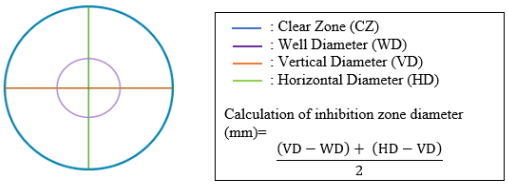

Figure 1. Diagram of bacterial growth inhibition zone measurement.

Data analysis

The measurement data obtained are then tested for an even and homogeneous distribution with the Shapiro-Wilk normality test and Levene homogeneity test. Furthermore, the One-way ANOVA test was carried out to determine whether or not there was a difference in the average inhibition zone of each treatment at the 95% confidence level. The Post Hoc Tukey HSD test was carried out to determine the significant difference in the area of inhibition between groups.

RESULT

Table 1 shows the mean value of the diameter growth inhibition zone of *S.*

mutans is significant in the 0.2% Chlorhexidine group (namely 14.0650 ± 1.24590 mm). The mean value of the diameter of the growth inhibition zone of *S. mutans* was the smallest in the distilled water group, which had no power. Antibacterial. Based on these data, the rhizome of *Curcuma longa* showed the highest mean diameter of the *S. mutans* growth inhibition zone among the two herbal ingredients tested, which was 11.3867 ± 0.93611 mm.

Table 1. Average diameter of the growth inhibition zone of *Streptococcus mutans*

Treatment Group	Mean ± SD (mm)
Chlorhexidine 0.2%	14.0650 ± 1.24590
Rhizome Extract C. *longa* 12.5%	11.3867 ± 0.93611
Rhizome Extract *C. zedoaria* 12.5%	10.3200 ± 1.01116
Aquadest	0.0000 ± 0.00000

The Shapiro-Wilk normality test of Levene's homogeneity test showed that the data obtained were normally distributed and homogeneous (p 0.05). The One-Way ANOVA test analysis showed a significant difference in the inhibition zone diameter mean value between all test groups against Streptococcus mutant bacteria ($p < 0.05$). The Post Hoc Tukey HSD test analysis results in Table 2 show no significant difference between the two groups of Curcuma rhizomes tested ($p > 0.05$). Meanwhile, both groups of rhizomes showed tremendous differences from each control group ($p < 0.05$).

Group	Chlorhexidine 0.2%	Rhizome Extract *C. longa* 12.5%	Rhizome Extract *C. zedoaria* 12.5%	Aquadest
Chlorhexidine 0.2%	-	0.000	0.000	0.000
Rhizome Extract C. *longa* 12.5%		-	0.225	0.000
Rhizome Extract C. *zedoaria* 12.5%			-	0.000
Aquadest				-

Table 2. Results of the Post Hoc Tukey HSD test analysis

Table 2 show the category diameter of bacterial growth inhibitory zone

Table 3. Category diameter of bacterial growth inhibitory zone

Category	Growth Inhibitory Zone
Inactive	< 9 mm
Partial Active	9-12 mm
Active	13-18 mm
Very active	> 18 mm

DISCUSSION

Comparative study of the antibacterial activity of *Curcuma longa* and *Curcuma zedoaria* rhizome extracts against *Streptococcus mutans* bacteria showed that *C. longa* rhizomes had a larger mean diameter of the inhibition zone for bacterial growth than *C. zedoaria*. It is maybe due to the quantitative difference in curcumin

content between the two ingredients. Dutta B reported that the curcumin content of the ethanol extract of *C. longa* rhizome was higher at 125 mg/100g than that of *C. zedoaria* rhizome, which was 88 mg/100g.[19]

Curcumin is an antibacterial due to the ability of curcumin to bind to the FtsZ protein. FtsZ is a protein for prokaryotic cells with the same function as tubulin for eukaryotic cells, namely cytoskeletal. It can inhibit the FtsZ protofilament group formation, causes inhibition of cytokinesis and bacterial proliferation. In addition, curcumin is known to bind to peptidoglycan in bacterial cell walls so that it can cause cell wall and membrane damage which then ends with bacterial cell lysis.[20] However, the difference in the mean diameter of the inhibition zone between *C. longa* and *C. zedoaria* against *S. mutans.* The results obtained in this study were not statistically significant.

The difference in the mean diameter of the inhibition zone of the *C. zedoaria* rhizome, which was not significant to the *C. longa* rhizome, was probably due to the high content of essential oil possessed by the *C. zedoaria* rhizome extract obtained. Angel G.R. et al. reported that the yield of essential oil obtained from the rhizome of *C. zedoaria* was the highest compared to the essential oil obtained from the rhizome of seven other Curcuma species used in the study.[21] The composition of the active compounds in the essential oil of the rhizome of C. zedoaria in GC analysis -MS includes Germacrene, -Curcumene, and Zingiberene. These compounds belong to the sesquiterpene group, which have hydrophobic properties that can disrupt cell integrity by reducing intracellular ATP reserves. In addition, essential oils can also be absorbed into cells and then experience precipitation and cause protein denaturation, which will eventually cause lysis of bacterial cell membranes. Rhizome used and its effect as an antibacterial against *S. mutans* bacteria.

The two groups of rhizomes used in this study showed that both ingredients effectively inhibited the growth of *S. mutans* bacteria compared to the negative control group. The ability of the two groups of rhizomes to form inhibition zones for bacterial growth is thought to occur due to the content of secondary metabolites in both ingredients. The secondary metabolite content analysis conducted by Dutta B on the ethanolic extracts of C. longa and C. zedoaria rhizomes showed that these two herbal ingredients contained alkaloids and flavonoids terpenoids phenols, tannins, and saponins. These compounds act as antibacterial, namely compounds that cause inhibition of cell wall formation,

compounds that cause changes in cell membrane permeability, and compounds that inhibit protein and nucleic acid synthesis.

Drying temperature and duration affect the diameter of the formed inhibition zone. Both rhizomes in this study were dried at 45^{o}C for two days. The choice of temperature and time is because the content of active polyphenolic compounds is reported to decrease with increasing drying temperature. It is due to the content of thermolabile polyphenols. When the temperature is too hot or exposed to heat for too long, it can cause irreversible chemical changes in the phenol content. for two positive days contains all six targeted secondary metabolites.[19]

The choice of ethanol solvent in this study was because the compounds targeted from the rhizome for extraction, such as phenols, tannins, flavonoids, and alkaloids, were polar, so it was necessary to use polar solvents as well. Purbowati et al. reported that ethanol solvent had the highest extractive ability compared to ethyl acetate and hexane in the roselle flower extraction process. The antibacterial activity of roselle flower extract with ethanol solvent was also better than that of hexane.[22] In addition, curcumin, the most significant component of curcuminoids, is insoluble in water but soluble in ethanol and acetone.[8] It should also be noted that the compound composition of the resulting extract can be different when the solvent used is also different. The different dielectric constants in each solvent can cause other interactions with phytochemical components that can affect the final composition of the compounds from the extract obtained.[11]

The structure and composition of the bacteria used in this study can also affect the results obtained. *Streptococcus mutans* is a Gram-positive bacterium. It is known to have teichoic acid in peptidoglycan in its cell wall. Gram-negative bacteria do not possess this teichoic acid. Teichoic acid is helpful for bacteria as transport of ions to enter or exit. Gram-positive bacteria are susceptible to inhibition caused by antibacterial compounds. It is lipoteichoic acid (including teichoic acid, which can bind to tannins).

The results obtained in this study indicate that the two materials used effectively inhibit the growth of the same bacteria, namely *S. mutans*. It is different from the effects of previous studies on *S. mutans* bacteria using the disc diffusion method and against other Gram-positive bacteria, namely Enterococcus faecalis using the well method.[17-18, 23-24]

The study results by Kumara et al. and Putri et al. with the disc diffusion test showed that the rhizome of *C. longa* could

not inhibit the growth of *S. mutans* bacteria. In contrast, the rhizome of *C. zedoaria* could inhibit the growth of *S. mutans*.[17-18.] Kumar reported that the rhizome *C. longa* at 20% inhibits the growth of *E. faecalis* bacteria. It was with an inhibition zone of 23 mm.[23]. Mozartha M et al. reported *C. zedoaria* rhizome extract 10%, 25%, and 50% could not inhibit the growth of *E. faecalis*. It was only at concentrations of 75% antibacterial activity.[24] Several factors can influence the difference in the diameter of the resulting bacterial growth inhibition zone. These factors include the antibacterial test method used, the extract drying method, the bacteria tested, and differences in rhizome content.[14,18]

The antibacterial test used in this study used the well diffusion method. In contrast, the previous research used the disc diffusion method using the rhizome of *C. longa* against *S. mutans* bacteria. It affected the diameter of the inhibition zone that was not formed. In addition, with the well method, the test material can diffuse directly with the growth medium to the bottom of the well so that the inhibition zone is more significant.[8] The drying method used in this study was using an oven for two days. Previous studies conducted drying of *C. longa* rhizomes in direct sunlight and did not show antibacterial activity. Drying in direct sunlight can reduce the active compounds contained in the rhizome, thereby affecting the ability of the rhizome to inhibit bacterial growth.[18] Wirasisya reported that oven-dried extract had higher total phenolic content and better antibacterial activity against *S. mutans*. It was compared to extracts dried in direct sunlight. It is presumably because drying in the sun takes a long time, so catabolic enzyme activity continues and causes secondary metabolite levels to decrease.[25]

Differences in the content of active compounds can also affect the ability of the rhizome to inhibit bacterial growth. Differences in the scope of active compounds can be influenced by several factors, including climate, plant sources, soil conditions where the rhizomes grow, and harvesting procedures. West Bandung Regency, West Java. While previous studies used rhizomes obtained from different growing places. It is thought to cause differences in the content of the active compounds possessed by the rhizome, affecting the diameter of the resulting inhibition zone. The average diameter of the inhibition zone of the two rhizome groups in this study was compelling compared to the negative control group but smaller than the positive control group, namely 0.2% Chlorhexidine. The inhibition zone average diameter of *C. longa* is 11.3867 mm, and *C. zedoaria* is 10.3200 mm. It means that both

rhizomes were included in the category of partially active antibacterial agents, while the average diameter of the inhibition zone owned by the positive control group was 14.0560. mm, which means CHX 0.2% is included in the category of active antibacterial agents (Table 3).[9] This indicates that *S. mutans* bacteria are sensitive to CHX 0.2%, but this bacterium is still partially exposed to the two rhizome extracts used.

The CHX molecule mechanism as an antibacterial has a role as a cation-charged molecule. It can bind electrostatically to the surface of bacteria which is negatively charged and causes damage to the outer layer of the cell wall and increases cell permeability so that intracellular leakage occurs.[26] CHX can inhibit enzyme metabolism processes: namely glucosyltransferase and phosphoenolpyruvate phosphotransferase. In addition, the lower average diameter of the inhibition zone of the two rhizomes compared to 0.2% CHX was also thought to be related to the concentration of the extract used, which was 12.5%. Pangemanan et al. reported a strong positive relationship between the engagement and the inhibition zone produced by C. longa against Staphylococcus aureus and Pseudomonas sp. The higher the concentration used, the higher, the more significant the inhibition zone had.[8]

This study still has limitations, including the absence of qualitative and quantitative phytochemical tests to understand more about what dominant compounds influence the antibacterial activity produced. To better understand the antibacterial activity, bacteria-killing time and antibacterial tests can be done with different methods. The effect of inhibiting bacterial growth is bactericidal or bacteriostatic and dependent on concentration and bacterial cell damage that appear.

CONCLUSION

The conclusion that can be drawn from this study is that both *Curcuma longa* and *Curcuma zedoaria* rhizome extracts at a concentration of 12.5% have antibacterial activity against *Streptococcus mutans* bacteria.

CONFLICT OF INTEREST

We declare that there is no conflict of interest in the scientific articles.

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