



# International Journal of PharmaO<sub>2</sub>

Journal Home Page: <http://www.ijpo.in/>

(IJPO: A Peer-reviewed Bi-monthly online journal)

## Research Article

### Antibacterial Activity of Papaya Leaves (*Carica Papaya L.*) and Guava Leaves (*Psidium Guajava L.*) Extract Combination towards *Escherichia Coli* and *Staphylococcus Aureus*

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#### ARTICLE INFO

##### Article history:

Received: 08/01/2022;

Revised: 08/01/2022

Accepted: 10/12/2022;

Available online:

15/01/2022.

##### Key Words:

*Carica papaya L.*,  
*Psidiumguajava L.*,  
*Escherichia coli*,  
*Stapylococcus aureus*,  
antibacterial

#### Please cite this article as:

Slamet W. et al. Antibacterial Activity of Papaya Leaves (*Carica papaya L.*) and Guava Leaves (*Psidium Guajava L.*) Extract Combination towards *Escherichia Coli* and *Staphylococcus Aureus* 3(6), 0267- 0274.

#### ABSTRACT

Papaya leaves (*Carica papaya L.*) were traditionally used by society in treating skin diseases such as acne and diarrhea. Papaya leaves (*PsidiumguajavaL.*) contained active compounds such as carotain alkaloids, antraquinone, saponins, steroids, tannins, and triterpenoids. Guava leaves had the ability to cure acute and chronic diarrhea. Guava leaves contained secondary metabolites such as flavonoids, alkaloids, polyphenols, and tannins. This study aimed to determine the antibacterial activity of a combination of papaya leaves and guava leaves extract against *Escherichia coli* and *Staphylococcus aureus*. The concentration of the extract combination used was 20%, 15%, 10%, and 5% with the antibiotic ciprofloxacin as a positive control and aquadest as a negative control. The results showed that the combination of papaya leaves and guava leaves extract (1:3) was effective in killing bacteria *Escherichia coli* and *Staphylococcus aureus* at a concentration of 20% with an average diameter of 12.50 mm and 12.41 mm. ANOVA test result with confidence level of 95% obtained p value = 0,000 (p<0,05) to conclude that there was a significant influence between the variation of combination and concentration of papaya leaves and guava leaves extract against *Escherichia coli bacteria* and *Staphylococcus aureus*. This study concluded that combination of papaya leaves and guava leaves extract (1:3) with concentration of 20% had an antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*.

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## INTRODUCTION

Indonesia is a tropical country which has high biodiversity. Therefore, the Indonesian people

begin to use natural ingredients to treat the health problems. Infectious diseases are the main cause of high morbidity and mortality,

especially in developing countries such as Indonesia. Bacteria can cause infection including *Escherichia coli* and *Staphylococcus aureus*. *Escherichia coli* and *Staphylococcus aureus* are bacteria causing infections in the human digestive tract such as diarrhea (Radji, 2010).

Diarrhea is a condition in which a person defecates with abnormal frequency and the concentration of looser or liquid stools, which usually comes up at least three times in 24 hours accompanied by pain in the lower abdomen (Dewi, 2017).

nowadays, diarrhea disease is still a public health problem in Indonesia. Based on the WHO report, deaths from diarrhea in Indonesia have decreased, but morbidity due to diarrhea remains high, especially in developing countries (Kemenkes RI, 2011).

Antibiotics are drugs used to prevent and treat bacterial infections. Inappropriate use of antibiotics in addition to being an economic waste is also clinically dangerous, as bacterial resistance to antibiotics. Resistance appears when bacteria experience immunity in response to antibiotics that are initially sensitive to treatment (Kemenkes RI, 2017). The method used to avoid the occurrence of resistance to antibiotics is to use other alternatives by utilizing plants which are efficacious as drugs.

Papaya leaves (*Carica Papaya L*) are traditionally used by the community in treating skin diseases such as acne and overcoming diarrhea diseases (Tuntun, 2016). Empirically, papaya is also widely used as a diuretic (roots and leaves), and to cure diseases caused by bile, as well as dyspepsia and other digestive disorders (Rahayu, 2016).

Guava leaves (*Psidium guajava L.*) are widely available in Indonesia as a medicine plant which is efficacious to cure various diseases such as acute and chronic diarrhea, dysentery, irregular menstruation, vaginal discharge, sore gums (Dalimartha, 2000).

The papaya leaves can inhibit *Escherichia coli* bacteria at concentrations of 25%, 50%, 75% and 100% (Hartini and Mursyida, 2019). Additionally, papaya leaves also have antibacterial activity against *Escherichia coli*

bacteria at concentrations of 30% to 100% (Tuntun, 2016). Moreover, papaya at a concentration of 10% with guava leaf extract are able to inhibit the growth of *Escherichia coli* bacteria (Dewi, 2017). Finally, the combination of ethanol extract of ceremai leaves and papaya leaves can inhibit *Escherichia coli* bacteria at concentrations of 20%, 30%, 40%, 50% and 60% (Rahayu, 2019).

Based on the description above and considering the use of papaya leaves and guava leaves to treat diarrhea, the authors are interested in testing the antibacterial activity of a combination of papaya leaf extract (*Carica papaya L.*) and guava leaf extract (*Psidium guajava L.*) against *Escherichia coli* and *Staphylococcus aureus* that causes diarrhea by the disc method.

## MATERIALS AND METHODS

### Materials

The tools in this study included petri dishes, sticks, sterile cotton, sterile gauze, needle loops, incubator, autoclave, tweezers, paper discs, test tubes and shelves, spirit lamp, oven, electric scales, 100 ml beaker glass, erlenmeyer 100 ml, measuring pipette 1 ml; 2 ml; 5 ml; 10 ml, balp, caliper, blender, sterile filter paper, sterile gauze, scissors, and blank disc..

Meanwhile the materials used were papaya leaves (*Carica papaya L.*) and guava leaves (*Psidium Guajava L.*), pure cultures of *Escherichia coli* and *Staphylococcus aureus* media Nutrient Agar (NA), 0.9% NaCl solution, sterile distilled water, 96% ethanol, the standard antibiotic ciprofloxacin.

### Methods

#### Making Extraction

The combination of papaya leaf extract and guava leaf was made in a ratio of 1:1, 1:3 and 3:1 by maceration. Then 500 grams of a combination of papaya leaf simplicia powder and guava leaves were put into a container, then soaked in 500 ml of 96% ethanol solution, for 5 days. After 5 days, the sample was filtered and then evaporated using a rotary evaporator, in order to obtain a thick extract of a combination of papaya leaves and guava leaves.

### Rejuvenating Bacteria

Each of *Escherichia coli* and *Staphylococcus aureus* bacteria derived from their pure cultures, each taken as much as 1 ose and then grown or inoculated by scratching on an inclined Nutrient Agar (NA) medium, then incubated for 24 hours.

### Making the Bacteria Suspension

The *Escherichia coli* and *Staphylococcus aureus* were first cultured on Nutrient Agar (NA) media and incubated at 37°C for 24 hours. Bacterial cultures were taken as much as 1-2 oses and suspended in a 0.9% NaCl solution until the turbidity was obtained according to the Mc Farland standard.

### Making NA Media (Nutrient Agar)

A total of 25 grams of nutrient agar was weighed and then put into an Erlenmeyer then dissolved by adding 1,250 mL of distilled water, then heated to boiling on a hot plate while homogenized using a stir bar then the media was sterilized by autoclaving at 121°C for 15 minutes.

### The Test of Antibacterial Activity

The test of antibacterial activity was carried out by agar diffusion method, using a paper disc with a diameter of 6 mm. The heated NA media was put into a petri dish and then homogenized and allowed to solidify. After the media solidified, the bacterial suspension was scratched using a loop on the surface of the media containing various concentrations of 20%, 15%, 10%, and 5%. Insert a 6 mm diameter paper disc that had been dripped with a combination extract solution.

The papaya leaves and guava leaves in a ratio of 1:1, 1:3, and 3:1, ciprofloxacin antibiotic disc as a positive control and a blank disc with distilled water as a negative control on the media. The filled media was incubated at 37°C, then observed and measured the inhibition zone formed in the next 24 hours. Observe the clear zone formed and measure the diameter of the inhibition zone using a caliper. This treatment was repeated 3 times.

### Data Analysis

The data from the test results of the combination of papaya leaf extract and guava leaf extract towards *Escherichia coli* and *Staphylococcus aureus* bacteria were analyzed using the one-way Analysis of Variance (ANOVA) statistical test with a 95% confidence level to determine whether there was a significant difference between the combined group data in the extract concentration group. Then the activity was followed by Post-Hoc Least Significant Difference (LSD).

### RESULTS AND DISCUSSION

In this study, the agar diffusion method is used. This method is done by placing the disc that has been soaked in the antimicrobial liquid to be tested. From the results of the study is obtained for the combination of papaya leaf extract and guava leaf on *Escherichia coli* bacteria, into the presence of antimicrobial activity which is characterized by the formation of a clear zone around the disc with an average diameter of 1:1 combination of 20% concentration of 12.16 mm, 15 mm. % is 11.25 mm, 10% is 10.25 mm, and at 5% concentration is 9.41 mm. At a combination of 1:3 the average diameter of 20% concentration is 12.5 mm, 15% is 11.75 mm, 10% is 10.75 mm, and at 5% concentration is 10 mm. At a combination of 3:1 with an average diameter of 20% concentration of 11.83 mm, 15% of 10.58 mm, 10% of 10 mm, and at 5% concentration of 9 mm.

For the combination of papaya leaf extract and guava leaves on *Staphylococcus aureus* bacteria, the presence of antimicrobial activity is indicated by the formation of a clear zone around the disc with an average diameter of 1:1 combination, 20% concentration of 12 mm, 15% of 11.25 mm, 10% by 10.25 mm, and at a concentration of 5% by 9 mm. At a 1:3 combination the average diameter of 20% concentration is 12.41 mm, 15% is 11.83 mm, 10% was 11 mm, and at 5% concentration was 10 mm. At a combination of 3:1 with an average diameter of 20% concentration of 11.41 mm, 15% of 11.00 mm, 10% of 10.31 mm, and at 5% concentration of 8.41 mm. The concentration used greatly affects the bacterial inhibition zone,

as the higher the concentration, the greater the inhibition zone formed or the greater the growth of bacteria which can be inhibited.

In this study, sterile distilled water is used as a negative control and ciprofloxacin antibiotic at a dose of 5 g as a positive control, the results obtained against *Escherichia coli* bacteria with an average diameter of 38.75 mm, and towards *Staphylococcus aureus* bacteria of 35.91 mm. From the results of the study, it can be stated that the antibiotic ciprofloxacin is sensitive to *Escherichia coli* and *Staphylococcus aureus* bacteria.

The use of this antibiotic is selected because the therapy used to treat digestive system disorders caused by *Escherichia coli* and *Staphylococcus aureus* bacteria is one of them using the antibiotic ciprofloxacin. Therefore the antibiotic ciprofloxacin is chosen as a positive control in this study. The use of negative control using sterile distilled water shows that the control does not indicate any inhibition zones formed, this condition comes up because aquadest is a neutral compound that does not contain toxins or substances which can inhibit and kill bacterial growth.

**Table 1: Results of Observation of Inhibitory Zone Diameter Combination of Papaya Leaf Extract and Guava Leaves towards *Escherichia coli* Bacteria**

No	Concentration	The average diameter of inhibition zone			The average inhibition zone $\pm$ SD (mm)	P
		The repetition of the test				
		I	II	III		
1	Combination of 1:1 5%	9,75	9,5	9	9.4167 $\pm$ .38188	
		10,00	10,25	10,55		
		11,00	11,25	11,5		
		12,25	12,5	11,75		
2	Combination of 1:3	10	10	10	10.0000 $\pm$ .00000	0,000
		10,75	10,5	11		
		12,00	11,5	11,75		
		12,5	12,75	12,25		
3	Combination of 3:1	9,5	9,25	8,25	9.0000 $\pm$ .66144	
		10,25	9,75	10		
		11	10	10,75		
		11,75	12,25	11,15		
4	Control	38,75	39,25	38,25	38.7500 $\pm$ .50000	
		0	0	0		
5	5%	10	10	10	10.0000 $\pm$ .00000	
6	10%	10,75	10,5	11	10.7500 $\pm$ .25000	
7	15%	12,00	11,5	11,75	11.7500 $\pm$ .25000	
8	20%	12,5	12,75	12,25	12.5000 $\pm$ .25000	
9	5%	9,5	9,25	8,25	9.0000 $\pm$ .66144	
10	10%	10,25	9,75	10	10.0000 $\pm$ .25000	
11	15%	11	10	10,75	10.5833 $\pm$ .52042	
12	20%	11,75	12,25	11,15	11.8333 $\pm$ .38188	
13	+	38,75	39,25	38,25	38.7500 $\pm$ .50000	
14	-	0	0	0	0,0000 $\pm$ ,000	

**Table 2: The Result of Observation of Inhibitory Zone Diameter Combination of Papaya Leaf Extract and Guava Leaves towards *Staphylococcus aureus* Bacteria**

No	Concentration	The average diameter of inhibition zone			The average inhibition zone $\pm$ SD (mm)	P
		The repetition of the test				
		I	II	III		
1	Combination of 1:1 5%	9,75	9,5	9	9.000 $\pm$ .50000	
2	10%	10,00	10,25	10,55	10.2500 $\pm$ .25000	
3	15%	11,00	11,25	11,5	11.2500 $\pm$ .25000	
4	20%	12,25	12,5	11,75	12.0000 $\pm$ .50000	
5	Combination of 1:3 5%	10	10	10	10.0000 $\pm$ .25000	
6	10%	10,75	10,5	11	11.0000 $\pm$ .25000	
7	15%	12,00	11,5	11,75	11.8333 $\pm$ .38188	0,000
8	20%	12,5	12,75	12,25	12.4167 $\pm$ .38188	
9	Combination of 3:1 5%	9,5	9,25	8,25	8.4167 $\pm$ .38188	
10	10%	10,25	9,75	10	10.2500 $\pm$ .25000	
11	15%	11	10	10,75	11.0000 $\pm$ .25000	
12	20%	11,75	12,25	11,15	11.4167 $\pm$ .52042	
13	Control +	38,75	39,25	38,25	35.9167 $\pm$ .87797	
14	-	0	0	0	0,0000 $\pm$ ,000	

According to Elgayar *et al* (2000) states that plant extracts can be grouped based on the diameter of inhibition produced into 3 categories, such as into (> 11 mm), medium (> 6 - < 11 mm), and low (< 6 mm).

From the data obtained, the combination of papaya leaf extract and guava leaf can be classified into plants having moderate inhibition ability and can be applied to the people as first aid or prevention of diarrhea diseases, and can be used as natural antibiotics to avoid resistance of chemical antibiotics caused by diarrhea.

The combination of papaya leaf extract and guava leaf has antibacterial activity towards *Escherichia coli* and *Staphylococcus aureus* which, when they are combined will increase their activities compared to the single substance. In addition, the antibacterial activity is seen to be greater towards *Escherichia coli* bacteria than *Staphylococcus aureus* bacteria. This is due to

the polar compounds contained in both plants. Polar compounds penetrate the cell walls of Gram-negative bacteria more easily than Gram-positive bacteria. It comes up because Gram-positive cell walls contain more peptidoglycan while Gram-negative cells contain more lipopolysaccharides (Pratiwi, 2008).

The best antibacterial activity of the combination of papaya leaf extract and guava leaf extract can be seen at a ratio of 1:3 at a concentration of 20% this is due to the secondary metabolite compounds as antibacterial contained in the combination more than the other combinations. Guava leaf powder looks more abundant than papaya leaf powder; compounds which act as antibacterial in guava leaves include flavonoids, alkaloids, polyphenols, and tannins.

The results of the normality test using Shapiro Wilk shows that the inhibitory power is

normally distributed with a significance ratio of  $> 0.05$  in *Escherichia coli* and *Staphylococcus aureus*, which has meaning that the concentration and comparison are normally distributed to the inhibitory power.

In the homogeneity test, the data on inhibition, concentration, and comparison of test samples has a significance value of  $> 0.05$ , thus it can be concluded that the variants of the three combinations of extracts compared are the same or homogeneous. Inhibitory data on the comparison variation is normally distributed and has homogeneous results, then continued with ANOVA analysis showing a significance value of  $0.000 < 0.005$ , which has meaning that there is a significant difference between the concentration and combination of papaya leaf extract and guava leaf extract.

The results of the LSD test data on *Escherichia coli* bacteria shows that the combination of guava leaf extract and papaya leaf extract at a combination of 1:1 and 1:3 at concentrations of 5%, 10%, 15% and 20% is significantly different because in this combination and concentration the P value  $< 0.05$  which has meaning that there is a significant difference between the combination and concentration and the combination of 3:1 at a concentration of 10% and 15% is not significantly different, the P value is  $0.170 > 0.05$ , which has meaning that the concentration of 10% is comparable to the concentration of 15% which has equivalent antibacterial activity.

The results of the LSD test data on *Staphylococcus aureus* bacteria showed a 1:1 combination at a concentration of 15% and 20% do not significantly differ P value  $0.113 > 0.05$ . At a combination of 1:3 the concentration of 10% and 15% is not significantly different, the P value of  $0.063 > 0.05$  and at the concentration of 15% and 20% there is no significant difference in the P value of  $0.173 > 0.05$ . At a combination of 3:1 the concentrations of 10% and 15% are not significantly different, the P value  $0.103 > 0.05$ . At concentrations of 15% and 20% there is no significant difference P value  $0.343 > 0.05$ . The combination and concentration of one extract and another also show significant differences with P value  $>$

$0.05$ , which has meaning that there is a significant difference between the combination and concentration. This shows that the combination and the test extract do not have the same effect as the positive control and do not have the same effect between the combination and the concentration of the extract in inhibiting *Staphylococcus aureus* bacteria.

## CONCLUSION

The conclusions obtained from this study are:

At the 1:3 combination at a concentration of 20% papaya leaf extract and guava leaf extract has the greatest inhibitory power with an average diameter of the inhibition zone of 12.50 mm towards *Escherichia coli* bacteria.

At the 1:3 combination, 20% concentration of papaya leaf extract and guava leaf extract has the greatest inhibitory power with an average inhibition zone diameter of 12.41 mm towards *Staphylococcus aureus* bacteria.

## CONFLICT OF INTEREST

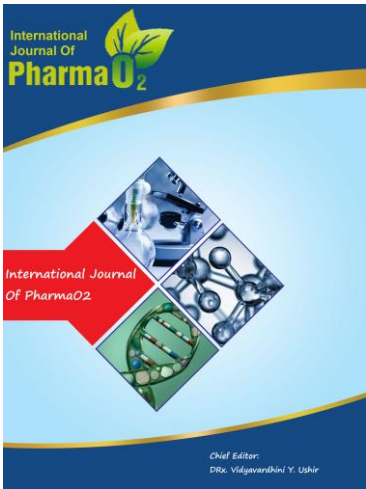
The author declares no conflict of interest.

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