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Antidiarrheal Effectiveness Test of Ketapang Leaf Infusion (Terminalia *catappa* L.) Against Male Mice (*musculus*)

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Keyword: Ketapang Leaves; Terminalia Catappa; Diarrhea; Mice; Infusion; Antidiarrheal;

Abstract
Introduction: *Diarrhea is a common health problem that can be serious if not treated immediately. Ketapang leaves (Terminalia catappa* L.*) contain active compounds such as tannins and alkaloids which are known to have antibacterial activity and have the potential as an antidiarrheal drug.* ***Objective:*** *This study aims to evaluate the effectiveness of ketapang leaf infusion in treating diarrhea and to determine the most optimal dose in male mice (Mus musculus).* ***Method:*** *The experimental study was conducted using the infusion method on 15 male mice divided into five treatment groups, namely negative control (Na CMC), positive control (loperamide), and three test groups with ketapang leaf infusion at concentrations of 25%, 50%, and 75%. Diarrhea was induced using oleum ricini, and the number of stools was monitored 180 minutes after treatment. Analysis was performed using an independent T-test.* ***Result and Discussion:*** *The results showed that 50% and 75% ketapang leaf infusions provided the highest stool reduction effect compared to the other groups.* ***Conclusion:*** *In conclusion, ketapang leaf infusion has potential as an antidiarrheal agent, with concentrations of 50% and 75% as the most effective doses in this study.*

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Introduction

The development of traditional medicine in Indonesia has a strong foundation of hereditary knowledge and has been recognized by the WHO for the purpose of health maintenance and treatment (Scott, Scott, Scott, & Scott, 2023); (Utami et al., 2024). For example, people use ketapang leaves to treat diarrhea, a disease that is still a major public health problem because it often triggers Extraordinary Events (KLB) (Asfianti, Sembiring, & Purba, 2020); (Maturahmah, Revisika, & Baharuddin, 2022).

This disease itself is caused by various bacteria such as Escherichia coli, Vibrio cholerae, Streptococcus viridans, and Salmonella. The leaves of ketapang (Terminalia catappa L.) are a medicinal plant that is easily recognizable by its characteristics: the dark green leaves will turn yellow to reddish before finally falling off (WICHAKSONO, 2021). Behind these discolorations, these leaves store a variety of beneficial chemical ingredients, which include flavonoids, alkaloids, tannins, saponins, quinones, and phenolic compounds. (Putri, Rasyidah, & Mayasari, 2023)

According to research by Nadeak (2019), ketapang leaf extract from Medan and Binjai has been proven to be able to inhibit the growth of Escherichia coli bacteria at various concentration levels. Interestingly, the highest inhibition activity varies depending on the origin of the sample; Ketapang leaf extract from Medan achieves peak effectiveness at 50% concentration, while Binjai extract shows the highest effectiveness at 100% concentration.

Based on a study by Putri et al. (2023), ketapang leaf extract has been shown to have antibacterial activity against Vibrio cholerae and Streptococcus viridans. This study found a positive relationship between extract concentration and inhibition; The higher the concentration given, the wider the clear zone produced. At the highest concentration (100%), this extract is able to form an average inhibition zone of 15.67 mm for V. cholerae and 16.8 mm for S. viridans, so it can be concluded that this extract is effective against both bacteria.

According to the research of Nurhalimah et al. (2015) at , beluntas leaf extract (Pluchea indica) showed significant antidiarrheal activity in mice infected with Salmonella typhimurium. This effect is effective at doses of 150 and 300 mg/kg bb, and at the highest dose (600 mg/kg bb), its efficacy is even equivalent to that of the drug loperamide. The chemical content that is thought to play a role in this effect are tannins (80329.58 ppm) and total phenols (5104.08 ppm) detected in the extract.

Senggani leaf infusion (Melastoma malabathricum L.) has been shown to have efficacy as an antidiarrheal (Minata, Ardianty, & Utomo, 2023). Specifically, a dose of 100 mg of senggani infusion showed effectiveness equivalent to that of the drug Loperamide, as it was able to stop the frequency of diarrhea (a 100% decrease) after 3 hours of observation. This effect is thought to come from the content of its active compounds such as tannins, flavonoids, and saponins (Aulia et al., 2024); (Syamsul, Amanda, & Lestari, 2020). These compounds are thought to function as antidiarrheals by improving the consistency of the stool back to its normal state (Mutmainah & Warditiani, 2022); (Suliska, Evrianto, & Herlinda, 2019); (Agustin & Wilsya, 2022); (Zhao et al., 2021)

Based on some of the above descriptions about previous research, ketapang leaves contain tannins and alkaloids as antibacterial, so researchers are interested in researching the effectiveness of ketapang leaves as an antidiarrheal against mice. The purpose of this study is to find out whether ketapang leaf extract has an antidiarrheal effect in mice. To find out at what concentration of ketapang leaf extract is effective as an antidiarrheal.

Method

This research is an experimental study conducted in July 2025 at the Integrated Laboratory of the Academy of Pharmacy Bina Pharmacy, Palu. The subjects of the study were 20 male mice (Mus musculus) aged 2–3 months and weighing 20–30 grams, with 15 animals randomly divided into 5 treatment groups, and 5 as reserves.
The treatment group consists of:

1. Negative control (Na CMC)
2. Positive control (loperamid)
3. Almond leaf extract 75%
4. Palm oil leaf extract 50%
5. Ketapang Leaf Extract 25%

Ketapang leaf extract is made by infusion method in a water bath at 90°C for 15 minutes, then filtered and diluted according to the concentration. The test suspension uses 0.5% Na CMC. The diarrhea test was carried out by administering oleum ricini, then the volume of feces was observed for 180 minutes with an interval of 30 minutes. The effect of antidiarrheal is measured based on a decrease in stool volume. The data was analyzed using the Independent T-Test test through Microsoft Excel to assess the significance between groups.

Results and Discussion

1. Results

From the results of the research that has been carried out, namely antidiarrheal in mice using ketapang leaf extract, the results were obtained:

Table 1
Results of the study in mice

MEDICINE	TREATMENT TO -	BB (g) ANIMAL	DOSE OLEUM RICINI (ml)	DOSE DRUG (ml)	STOOL BEGINNING	THE NUMBER OF STOOL SPOTS IN THE MINUTE - 30'	60'	90'	180'
Na.CMC	1	20	0.66	0.66	5	4	5	4	3
	2	22	073	0.73	4	4	5	4	3
	3	22	0.73	0.73	4	5	4	3	3
Loperamide	1	29	0.48	0.48	4	4	3	2	1
	2	21	0.35	0.35	4	4	3	1	-
	3	25	0.41	0.41	3	4	2	1	-
Extract 25%	1	29	0.96	0.96	4	3	4	2	1
	2	24	0.8	0.8	4	4	5	4	3
	3	20	0.66	0.66	3	5	5	4	2
Extract 50%	1	32	1.06	1.06	5	4	3	3	1
	2	27	0.9	0.9	6	5	4	2	-
	3	24	0.8	0.8	4	4	3	2	1
Extract 75%	1	36	1.2	1.2	5	5	4	1	-
	2	29	0.96	0.96	4	4	2	1	1
	3	27	0.9	0.9	5	4	3	1	-

In this study, after 60 minutes of orally injected *oleum ricini*, feces in mice increased. Mice that experience increased feces are mice that can be treated.

Table 2
Average Fecal Count

GROUP	AVERAGE AMOUNT OF STOOL			
	30'	60'	90'	180'
CONTROL (-)	4	5	4	3
CONTROLS (+)	4	3	1	1
Extract 25%	4	5	3	2
Extract 50%	4	3	2	1
Extract 75%	4	3	1	1

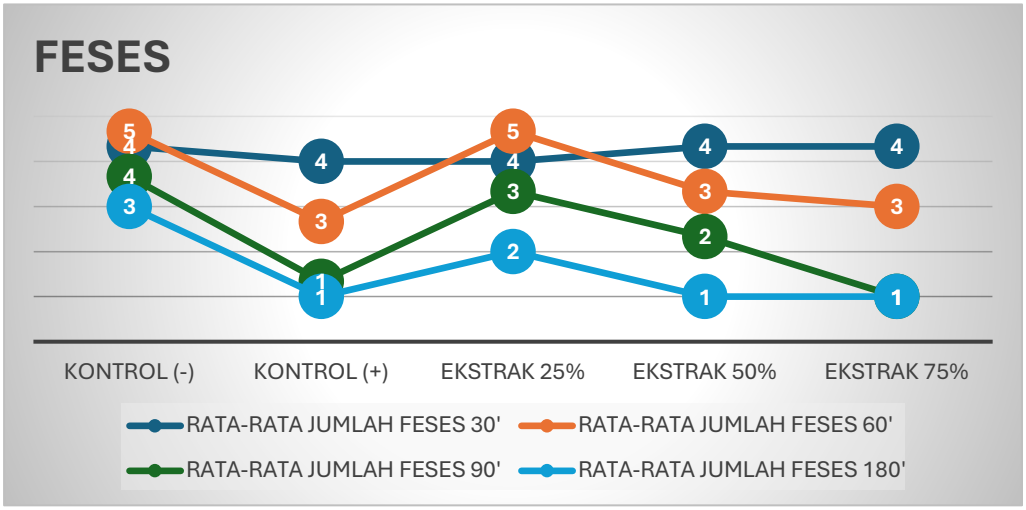

Figure 1. Average Fecal Count Graph

Information:
Control- : Na.CMC
Controls+ : Loperamid
Extract 25% : Ketapang Leaves 25%
Extract 50% : Ketapang Leaves 50%
Extract 75% : Ketapang Leaves 75%

Based on the graph of the average number of feces at the four observation times, it can be seen that the treatment group with ketapang leaf extract showed a decrease in the amount of feces over time, especially at concentrations of 50% and 75%. These results are close to the effectiveness of loperamide as a positive control. This decrease indicates that ketapang leaf extract has antidiarrheal effects, likely caused by active compounds such as tannins, flavonoids, or saponins that work to reduce intestinal motility and fluid secretion.

Extracts with a concentration of 25% only provide minimal stool reduction, so the antidiarrheal effect is relatively weak. At a concentration of 50%, there is a more pronounced decrease in the number of feces, indicating moderate antidiarrheal activity. Meanwhile, the administration of 75% extract resulted in a significant decrease in the amount of feces and was comparable to the positive control group, meaning the extract at this concentration had high effectiveness as an antidiarrheal agent. Thus, the higher the concentration of ketapang leaf extract, the greater its potential in reducing diarrhea symptoms.

Normality Test

Table 3
Normality Test Results

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Kontrol Negatif Sebelum	.385	3	.	.750	3	.000
Kontrol Negatif Sesudah	.	3	.	.	3	.
Kontrol Positif Sebelum	.385	3	.	.750	3	.000
Kontrol Positif Sesudah	.385	3	.	.750	3	.000
Ekstrak 25% Sebelum	.385	3	.	.750	3	.000
Ekstrak 25% Sesudah	.385	3	.	.750	3	.000
Ekstrak 50% Sebelum	.175	3	.	1.000	3	1.000
Ekstrak 50% Sesudah	.385	3	.	.750	3	.000
Ekstrak 75% Sebelum	.385	3	.	.750	3	.000
Ekstrak 75% Sesudah	.385	3	.	.750	3	.000
Kontrol Positif & 50%	.385	3	.	.750	3	.000
Kontrol Positif & 75%	.385	3	.	.750	3	.000

a. Lilliefors Significance Correction

Based on the Shapiro-Wilk *normality test*, the data obtained were not normally distributed ($p < 0.05$) in almost all treatment groups. Therefore, the analysis was continued using non-parametric tests. The test results showed a significance value of 0.01, which means that there was a significant difference between treatment groups on the average amount of feces.

The results of further tests showed that the 50% and 75% ketapang leaf extract groups significantly reduced the amount of feces when compared to the negative control group. This effect is similar to that of a positive control (loperamid), which indicates that ketapang leaf extract has potential antidiarrheal activity, especially at concentrations of 50% and 75%.

Independent T-Test

Positive Control Against Ketapang Leaf Extract 50%

Table 4

Data Processing Results Using Independent T-Test 50% Extract

Group Statistics

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Feses_Sesudah	Kontrol Positif	3	2.67	.577	.333
	Ekstrak 50%	3	3.33	.577	.333

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Feses Sesudah	Equal variances assumed	.000	1.000	-1.414	4	.230	-.667	.471	-1.975	.642
	Equal variances not assumed			-1.414	4.000	.230	-.667	.471	-1.975	.642

Based on the results of the analysis using the Independent Samples T-Test, it was shown that there was no significant difference between the positive control group (loperamid) and the 50% ketapang leaf extract treatment group on the amount of feces after treatment ($p = 0.230$, $p > 0.05$). This indicates that the administration of 50% ketapang leaf extract has an effectiveness close to loperamid in reducing diarrhea symptoms.

Positive Control Against Ketapang Leaf Extract 75%

Table 5

Data Processing Results Using Independent T-Test Extract 75%

Group Statistics

	Kelompok	N	Mean	Std. Deviation	Std. Error Mean
Feses_Sesudah	Kontrol Positif	3	2.67	.577	.333
	Ekstrak 75%	3	2.67	.577	.333

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Feses Sesudah	Equal variances assumed	.000	1.000	.000	4	1.000	.000	.471	-1.309	1.309
	Equal variances not assumed			.000	4.000	1.000	.000	.471	-1.309	1.309

Based on the results of the analysis of the Independent Samples T-Test, a significance value ($p = 1{,}000$) was obtained, which showed that there was no significant difference between the positive control group (loperamid) and the 75% ketapang leaf extract group to the average fecal count. With the same average (2.67), this indicates that 75% of ketapang leaf extract has antidiarrheal capabilities comparable to loperamid, so it has the potential to be developed as an alternative to natural antidiarrheal drugs.

2. Discussion

A decrease in the amount of feces indicates an antidiarrheal effect of the treatment given. In the negative control group, the treatment caused diarrhea symptoms to persist, as seen from the high amount of feces until the end of observation. In contrast, the positive control given loperamid showed a significant decrease, proving its effectiveness as a standard antidiarrheal drug.

Administration of ketapang leaf extract showed results that varied depending on the concentration. The 25% extract does not cause an antidiarrheal effect, because the concentration of active compounds in it is not enough to provide a real pharmacological effect. The low content of flavonoids, tannins, and saponins has not been able to optimally improve the condition of the intestinal mucosa, decrease motility, or inhibit the secretion of excess fluid in the intestine.

In the 50% and 75% extract groups, a consistent and significant decrease in the amount of feces occurs, approaching the effectiveness of loperamid. This shows that the content of bioactive compounds is already in the optimal amount to provide a therapeutic effect. Flavonoids are anti-inflammatory and antioxidant, tannins precipitate proteins in the intestinal mucosa and reduce fluid secretion, while saponins decrease intestinal motility and strengthen the epithelial barrier. The three compounds work synergistically to overcome diarrhea.

Although the mechanism of action of ketapang leaf extract is different from loperamid (which acts on peripheral opioid receptors to inhibit motility), both exhibit similar pharmacodynamic effects, namely decreasing the frequency of bowel movements and reducing fluid secretion in the gastrointestinal tract. Thus, 50% and 75% extracts can be considered as promising herbal alternatives in the treatment of diarrhea.

Conclusion

Ketapang leaf extract has an antidiarrheal effect which is shown by a decrease in the amount of feces in mice after treatment. The concentration of ketapang leaf extract that was most effective in reducing the amount of feces was 50% and 75%, which showed that the effect was close to the positive control group (loperamide).

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