

## Antidiarrheal Effectiveness Test of Noni Leaf Infusion (*Morinda citrifolia* L.) Against Male White Mice (*Mus musculus*) Induced by *Oleum ricini*

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### ABSTRACT

Diarrhea is a disease of the digestive system which is defined as defecation more than three times a day which is characterized by changes in the shape and consistency of the stool. The results of the Indonesian Nutritional Status survey (2020) stated that the prevalence of diarrhea was 9.8%. One of the plants that has antidiarrheal properties is noni leaves (*Morinda citrifolia* L.) with the compounds contained in noni leaves being flavonoids. This study aims to determine the effective dose of noni leaf infusion as antidiarrhea in male white mice (*Mus musculus*) induced by *oleum ricini*. The research design used was laboratory experimental using male white mice (*Mus musculus*) as test animals by dividing the negative control, positive control, noni leaf infusion treatment groups with infusion doses of 100, 200, and 400 mg/KgBW. Results of observations of the antidiarrheal effectiveness of noni leaf infusion at the most effective dose was a dose of 400 mg/KgBW with the initial parameters of diarrhea the average frequency of diarrhea was five times with the average weight of feces is 0.53 grams and the average duration of diarrhea is 90.25 minutes. The data obtained were analyzed by ANOVA at a confidence level of 95%. Noni leaf infusion (*Morinda citrifolia* L.) has effectiveness as an antidiarrhea in male white mice (*Mus musculus*) induced by *oleum ricini* with the dose 400 mg/KgBW.

#### Keywords:

Antidiarrhea, Noni leaves (*Morinda citrifolia* L.), *Oleum ricinii*

### INTRODUCTION (11 PT)

According to WHO, diarrhea is one of the diseases that is still a problem in Indonesia. In several developing countries, especially Southeast Asia and Africa, the percentage of deaths due to diarrhea is still relatively high, namely 78%, with two billion cases of diarrhea in adults and 1.9 million cases in toddlers every year. And the prevalence of diarrhea in Indonesia is 9.8% in 2020. Diarrhea is one of the diseases that is still a problem in Indonesia (Ministry of Health., 2022). The Sample Registration System states that diarrhea was one of the main causes of death in 2015 at 2.5% and in 2016 at 4.2% (Usman et al., 2019). Basic health research (2018) states that the prevalence of diarrhea for teenagers is 8%, for toddlers it is 12.8% and for babies it is 10.6% (Riskasdes., 2018).

Generally, in Indonesia, diarrhea is caused by problems with food hygiene, the environment and infection with microorganisms. This is a problem in Indonesia as a developing country where morbidity and mortality rates are still high (Manek et al., 2018). Currently, people still often think that the cause of diarrhea is catching a cold or eating wrong things. There are still many people who think that diarrhea is a mild disease, so it is often fatal when treated. This occurs due to delays in treatment and initial treatment that has not been carried out properly, causing dehydration and making the situation worse, even death. And for the community, especially in areas that are far from the reach of facilities such as pharmacies, people experience problems in obtaining medicines. (Ambari., 2018).

Most synthetic antidiarrheal drugs can cause undesirable side effects, so it is hoped that alternative drugs from natural ingredients that are safer can be obtained (Suliska et al., 2019). Apart from having fewer side effects and being more economical, the back to nature lifestyle is being popular again now so that people can reuse various natural ingredients, including for treatment (Manek et al., 2018). One of the herbal plants that can be used as an antidiarrheal candidate is noni leaves. Noni leaves (*Morinda citrifolia*

L.) contain morindin oil, glutamic acid, thiamine, beta carotene, xeronine, proxeronine, anthraquinone, and scopoletin which are active antimicrobial compounds (Muthia et al., 2019). Apart from that, the compounds contained in noni leaves based on the results of phytochemical screening are flavonoids, saponins, steroids, alkaloids, glutamic acid (Simatupang et al., 2017). Previous research stated that noni leaf extract containing flavonoids could stop diarrhea induced by *oleum ricini*. Flavonoids work by inhibiting intestinal motility so that fluid and electrolyte secretion can be reduced (Thahir et al., 2017).

## METHOD

### Research sites and Ethics

This research was conducted at the Pharmacology Laboratory at Dr Soebandi University, Jember. The results of the researcher's ethical suitability statement in the ethical certificate number 22/KEPK/UDS/I/2024 stated that the researcher was ethically fit. Plant determination was carried out at the Biology Learning Laboratory at Ahmad Dahlan University, Yogyakarta. The results of plant determination with letter number 013/Lab.Bio/B/I/2024 show that in this study the part used was noni leaves (*Morinda citrifolia* L.)

### Tools & Materials

The tools used in the research include analyte scales, filter paper, 1ml syringe, glassware (measuring cup), sonde, tray, stopwatch. Meanwhile, the ingredients used in the research were noni leaves, loperamide (tablets), CMC-Na, distilled water and *oleum ricini*.

### Sample preparation

#### 1. Sample Preparation

The samples of noni leaves (*Morinda citrifolia* L.) used were leaves from old plants obtained from the Tegal Besar Palace housing complex, Kaliwates District, Jember Regency. The leaves that have been washed clean are then chopped and dried for approximately 7 days and ground using a blender.

#### 2. Preparation of 0.5% Na CMC Solution

A 0.5% Na CMC solution is made by weighing 0.5 grams of Na CMC powder into 50 ml of hot distilled water, then leaving it for approximately 15 minutes until it forms like a gel, then stirring until it becomes a homogeneous mass. Then put it in a measuring flask and add distilled water to 100 ml.

#### 3. Preparation of Loperamide HCl Stock Solution

Grind 10 tablets of 2 mg loperamide HCl in a mortar. Then dissolved in 10 ml Na CMC 0.5%, then shaken until homogeneous.

#### 4. Making Noni Leaf Infusion Stock Solution

The concentration of noni leaf infusion (*Morinda citrifolia* L.) made is 10%. With doses of 100 mg/KgBB, 200 mg/KgBB and 400 mg/KgBB. Weigh 100 grams of simplicia powder then put it into the infusion pan and add 1000 ml of distilled water. Boil for 15 minutes calculated when the temperature reaches 90°C then evaporate over a water bath until it becomes thick.

### Preparation of Research Animals

The mice were adapted for approximately 1 week before treatment. The mice were first fasted for 1-8 hours but still given water. Then the mice were randomly divided into 5 treatment groups with details of the negative control group being given CMC-Na, the positive control group being given loperamide HCl, and the group being treated with noni leaf infusion at doses of 100 mg/KgBW, 200 mg/KgBW, and 400 mg/KgBW. All mice were given 0.5 ml of Ricini oleum induction orally and waited until they had diarrhea. After diarrhea, each mouse was given treatment according to the treatment group and observations were made every 30 minutes for 3 hours with parameters namely frequency of diarrhea, weight of feces, consistency of feces, and duration of diarrhea.

## RESULTS AND DISCUSSION

This research begins with making an infusion where the infusion is a filtering process using a water solvent at a temperature of 90°C for 15-20 minutes. The infusion is prepared by immersing the sample in a vessel. Making infusions is the simplest way to make herbal preparations from soft ingredients such as leaves and flowers. The advantages of the infusion method are that it is short and fast to make, the tools and materials used are easy to obtain and not too much, it is a simple method that uses water as a filter. The disadvantage of the infusion method is that the results cannot be stored and used after 24 hours because the water solvent used is unstable and easily contaminated with fungus and mold (Suwarni et al., 2016).

Making noni leaf infusion is done by taking fresh noni leaves and processing them until they become dry simplicia powder, weighing 10 grams. Then the process of making the infusion was carried out using 100 ml of distilled water at a temperature of 90°C for 15 minutes starting when the temperature reached 90°C and the infusion was obtained, which was then evaporated over a water bath to obtain a thick extract. The yield obtained was 23% as shown in Figure 1.

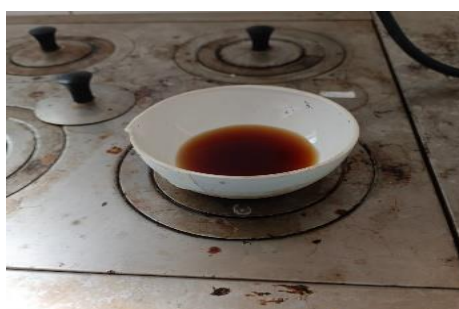


Figure 1. Results of noni leaf infusion

Oleum ricini or castor oil was used as an inducer in this study with the active substance contained in ricinoleic acid which functions as a laxative. Oleum ricini can cause colic and lack of fluids, and can cause electrolyte disorders in the body. The diarrhea inducer Oleum Ricini can be used in research using experimental animals (Meliala et al., 2022).

Loperamide HCl was used as a comparison. Loperamide HCl is used because it has the same chemical formula as the opiate pethidine which can reduce peristalsis. The substances contained in loperamide HCl can normalize the balance of mucosal secretory resorption so that hypersecretory cells can be restored to normal. Loperamide HCl is used because it does not work on the central nervous system, and does not cause dependency side effects (Sembiring et al., 2021).

Based on the results of observations on male white mice (*Mus musculus*) that had been treated with noni leaf infusion (*Morinda citrifolia* L.) the parameters of diarrhea frequency, stool weight, stool consistency and duration of diarrhea can be seen as follows:

Table 1. Frequency of Diarrhea

Treatment	Diarrhea Frequency (times)				amount	average± SD
	1	2	3	4		
CMC Na 0,5%	15	16	18	19	68	17±1,82
Loperamide HCl 0,26 mg/KgBB	4	6	6	8	24	6±1,63
Noni leaves dose 100 mg/KgBB	13	12	16	15	56	14±1,82
Noni leaves dose 200 mg/KgBB	11	13	14	11	49	12,25±1,50
Noni leaves dose 400 mg/KgBB	5	4	6	5	20	5±0,81

Table 2. Stool Consistency

Treatment Group	Stool consistency at minute-					
	30	60	90	120	150	180
CMC Na	++	+++	+++	+++	++	+
	++	+++	+++	++	+++	++
	+++	+++	+++	+++	+++	+
	+++	+++	+++	+++	+++	++

Loperamide HCl	+++ ++ ++ +++	++ ++ ++ +++	+ + + ++	- - - +	- - - -	- - - -
Noni leaves dose 100 mg/KgBB	++ +++ +++ +++	+++ +++ +++ +++	++ ++ ++ +++	+ ++ + ++	- + + ++	- + + -
Noni leaves dose 200 mg/KgBB	+++ ++ +++ +++	++ +++ ++ +++	++ ++ ++ +++	+ + ++ +	- + + -	- - - -
Noni leaves dose 400 mg/KgBB	+++ ++ ++ +++	++ + ++ ++	+ - + -	+ - + -	- - - -	- - - -

Information:

+ = normal stool

++ = soft stools

+++ = watery / slimy feces

Table 3. Feces weight

Treatment	Feces Weight (grams)				Amount	Average± SD
	Replication					
	1	2	3	4		
CMC Na 0,5%	1,12	1,15	1,16	1,25	4,68	1,17±0,05
Loperamide HCl 0,26 mg/KgBB	0,48	0,52	0,54	0,60	2,14	0,53±0,05
Noni leaves dose 100 mg/KgBB	1,04	0,99	1,08	1,05	4,16	1,04±0,03
Noni leaves dose 200 mg/KgBB	0,98	1,02	1,05	0,92	3,97	0,99±0,56
Noni leaves dose 400 mg/KgBB	0,53	0,49	0,61	0,51	2,14	0,53±0,05

Table 4. Duration of Diarrhea

Treatment	Duration of Diarrhea (minutes)				Amount	Average ± SD
	Replication					
	1	2	3	4		
CMC Na 0,5%	176	170	165	168	679	169,75±4,64
Loperamide HCl 0,26 mg/KgBB	80	78	90	94	342	85,50±7,72
Noni leaves dose 100 mg/KgBB	145	160	162	155	622	155,50±7,59
Noni leaves dose 200 mg/KgBB	124	130	132	125	511	127,75±3,86
Noni leaves dose 400 mg/KgBB	97	75	96	83	351	90,25±7,27

The results of research conducted using oleum ricini induction provided results in the form of observing the frequency of diarrhea in the positive control group and the noni leaf infusion treatment group experienced a decrease in the frequency of diarrhea when compared to the negative control group, with the most effective dose of noni leaf infusion being at a dose of 400 mg/KgBW. with an average frequency of diarrhea of five times which indicates that at a dose of 400 mg/KgBW it has activity equivalent to loperamide HCL as an antidiarrhea and is not significantly different from the positive control loperamide HCl.

Stool consistency parameters are determined by looking at the shape or texture of the stool. Observations of stool consistency carried out visually can be seen in table 2. The results of the study show that in the negative control group the stool consistency was still soft when observed up to the 180th minute, this shows that in the negative control group diarrhea was still occurring continuously. The results of the research in the positive control group and the treatment group with noni leaf infusion showed changes in stool consistency which gradually became normal with a dose that had a consistency equivalent to the positive control of loperamide HCl at a dose of 400 mg/KgBW which indicated that the most effective infusion dose was dose 400 mg/KgBW.

Stool consistency can be categorized into three levels which can be symbolized by (+) with levels of normal consistency, soft stool consistency, and watery or slimy stool consistency (Purwaningdyah et al., 2015). The consistency of the stool is said to be slimy or watery if the water content of the stool exceeds 80% and there is a thick liquid resembling a gel. The consistency of the stool is said to be soft if the water content of the stool does not exceed 80% but has a texture that is still slightly watery. The consistency of feces is said to be normal if the weight and composition of the feces is 100% dregs, slightly hard and tends to be slightly oily (Widyaningsih et al., 2014).

The liquid consistency of feces indicates the excretion of excess electrolytes or water, this occurs due to increased motility of the large intestine resulting in abnormal fluid absorption and this is a characteristic of diarrhea (Pongoh et al., 2020). The mechanism of action of the flavonoid compounds contained in noni leaves is by inhibiting intestinal motility so that it can reduce the secretion of fluids and electrolytes so that the consistency of feces will affect the secretion of fluids and electrolytes. With the mechanism working to inhibit intestinal motility and reduced fluid secretion, the stool consistency will return to normal (Rambe et al., 2021).

Feces weight was observed visually and expressed in grams. In table 3, in the positive control group and noni leaf infusion treatment group, there was a decrease in the average weight of feces, this also depends on the frequency of diarrhea and the consistency of feces. In the treatment group with noni leaf infusion which had the same average feces as the positive control loperamide HCl was the treatment group with a dose of 400 mg/KgBB which was 0.53 grams which indicates that at a dose of 400 mg.KgBB it had antidiarrheal activity equivalent to loperamide HCl. Low stool weight is one of the parameters that indicates success in treating diarrhea (Mayasari., 2020). Fecal weight is the total weight of mouse feces calculated over the entire observation period for each treatment group (Muthia et al., 2019). The weight of the feces can be observed with the help of a tissue to make it easier to weigh the feces. The smaller the stool weight value, the diarrhea condition is getting better, and the reduced water or mucus content due to diarrhea will reduce the stool weight (Nugrahani et al., 2021).

The final observation was the duration of diarrhea which was carried out by calculating the time from the beginning of the diarrhea to the last time the diarrhea occurred. The results of research on the duration of diarrhea can be seen in table 4. The duration of diarrhea for mice in the infusion treatment group experienced an accelerated cessation of diarrhea with the fastest duration of diarrhea cessation occurring in the treatment group with a dose of 400 mg/KgBW with an average duration of 90.25 minutes. The best dose of noni leaf infusion based on the parameters of the duration of diarrhea is 400 mg/KgBW and is not significantly different from a positive control of loperamide HCl.

The flavonoid compounds contained in noni leaves began to provide antidiarrheal activity in male white mice in the second 30 minutes, which was marked by a change in stool consistency from slimy to soft and a reduction in the frequency of diarrhea. Noni leaf infusion caused the mice to stop diarrhea in the fourth 30 minutes at a dose of 400 mg/Kg BW which was different from a dose of 100 mg/KgBW and a dose of 200 mg/KgBW which still gave signs of diarrhea at the same minute but there was an improvement in stool consistency and a decrease in the number of frequency of diarrhea. This is because the higher the dose of the infusion, the more flavonoid compounds there are in the infusion and the greater its activity as an antidiarrheal. The accelerated cessation of diarrhea in mice induced by oleum ricini indicates that noni leaf infusion can have an anti-diarrheal effect by speeding up the duration of diarrhea and changing the stool consistency to normal due to the presence of flavonoid compounds. The mechanism of flavonoids in stopping diarrhea induced by oleum ricini is by inhibiting intestinal motility thereby reducing fluid and electrolyte secretion. The activity of other flavonoids, especially quercetin, is to inhibit the release of acetylcholine in the digestive tract. Inhibition of the release of nicotinic acetylcholine which mediates smooth muscle contraction and activation of muscarinic acetylcholine receptors which regulate gastrointestinal motility and smooth muscle contraction (Thahir et al., 2017).

## CONCLUSION

Noni leaf infusion has an antidiarrheal effect which is induced by ricin oleum based on the frequency of diarrhea, stool consistency, stool weight, and duration of diarrhea with the most optimum dose being a dose of 400 mg/kgBW. And it is necessary to test the toxicity of noni leaf infusion (*Morinda citrifolia* L.) so that its safety can be determined when used as an antidiarrheal.

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