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RESEARCH ARTICLE

Evaluation of antidiarrheal effect of combination of Salam Leaves (*Syzygiumpolyanthum*) and Jackfruit Leaves (*Artocarpus heterophyllus Lam.*) infusum in rats induced by castor oil

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Abstract

Backround: Diarrhoea is a condition characterised by watery, loose stools that occurs more than three times daily. In Indonesian traditional medicine, salam leaves and jackfruit leaves have been used as herbal treatments for many conditions, including as antidiarrheal medicines. **Aims:** The aim of this experimental study was to evaluate the antidiarrheal effect of a combination of Salam leaves and jackfruit leaves infusum induced by castor oil in rats. **Method:** The rats were divided into nine groups, where the negative control group was given CMC 1 %, the positive control group was given tannins, and five test groups were given the infusum with five comparisons of each dose administered orally. Castor oil was used as a stimulant of diarrhoea. **Results:** The results show that with all combinations of salam leaves: jackfruit leaves have antidiarrheal effects with decreased frequency of defecation, faeces consistency, and faeces weight at ratios of 1:1, 1:2, 1:3, 2:1, and 3:1 compared to the negative control ($p < 0.05$). Phytochemical test of the infusum indicated positive tannins. The antidiarrheal effect of both infusums might be due to the presence of tannins, which have anti-secretory effect in the intestinal lumen. **Conclusions:** The treatment with combination of salam leaves and jackfruit leaves infusum in rats induced by Castor oil has an antidiarrheal effect. The best result is a mixture of salam infusum: jackfruit infusum with 3:1 ratio.

Introduction

Diarrhoea is a major health problem, especially in low-income countries, which includes Indonesia. In several provinces in Indonesia, the prevalence of diarrhoea is more than 7.0% (Riskesdas, 2018). Diarrhoea is a bowel movement of fluid that occurs more than three times a day or in frequency more often than that of normal people. One of the processes in the body that causes diarrhoea is a change in the motility of the gastrointestinal tract (Pandango *et al.*, 2018).

Chemical drugs, such as loperamide, can cause side effects, such as abdominal pain, nausea, vomiting, dry mouth, drowsiness, and dizziness. The existence of these side effects causes people to prefer efficacious medicinal plants as alternative medicine (Nurhalimah *et al.*, 2015).

Ethanol extract of Salam leaves (*S.polyanthum*) has an anti-diarrhoea effect in white mice (Mus Musculus) that have been induced by castor oil (Ambari, 2019). The chemical content contained in salam leaves (*S. polyanthum*) is tannin, which is known to be effective as an astringent, which can relieve diarrhoea by shrinking the intestinal mucous membrane (Sundari, 2010).

Jackfruit leaves (*A. heterophyllus* Lam.) is a traditional medicine that has been used empirically by the

community to treat diarrhoea. Traditionally, these leaves are used by boiling for traditional medicine (Anas *et al*., 2012). From the antidiarrheal activity of the ethanol extract of jackfruit leaves (Artocarpus heterophyllus Lam.) in mice, it was found that the antidiarrheal activity of both extracts was better than the standard antidiarrheal drug of loperamide (Anas *et al.*, 2012).

The aim of this experimental study was to evaluate the antidiarrheal effect of a combination of Salam leaves, and jackfruit leaves infusum induced by castor oil in rats. The parameters that were measured were the time of diarrhoea/onset of diarrhoea, frequency of diarrhoea, and consistency and number/weight of faeces.

Method

This experimental laboratory research was designed using a randomised post-test controlled design method. The research was conducted in June 2019 at Pharmacology Laboratory of Muhammadiyah Health Institute, Indonesia, using adult male rats (*Rattus norvegicus)* with ages between two to four months, with weights between 150-200 g, and good physical health conditions. The rats used were divided into seven treatment groups by random sampling. The amount of replication was determined by using Freeder's formula, and it found 27 research subjects with three rats as a negative control group, three rats as a positive control group, and the other seven rats as a treatment group. Diarrhoea activity data retrieval was done by placing the rats in individual containers for observation.

Prior to implementation, this research proposal had been approved by the Health Ethics Committee of the Faculty of Pharmacy, Ahmad Dahlan University, Jogjakarta, Indonesia, due to the use of rats as experimental animals. This research was conducted in three stages, namely the pre-treatment stage, treatment stage, and data retrieval stage. At the pre-treatment stage, a salam and jackfruit leaf infusum was made by mixing the 87.5 grams of fresh leaves powder with 300 mL of distillate water on a measuring cup then heated and held at a temperature of 90°C over a pot containing water for 15 minutes or until the water volume reached 100 mL, after which it was filtered using flannel.

Before treatment, the rats were acclimatised for two weeks with laboratory conditions for self-habituation during the study. At the treatment stage, the animals were divided into nine groups at random, Group I, II, III, IV, V, VI, VII, VIII, and IX. Group I was a Group with Castor oil alone; Group II (positive control) was a Group of rats given 1 ml/kg bw of tannin; then after one hour, they were given 1 mL of castor oil orally; Group III and IV were groups of rats treated with 87.5% salam and jackfruits leaves infusum, and after one hour, they were given 1 mL of Castor oil orally; Group V-IX were groups of rats treated with mixtures of salam leaf infusum and jackfruit leaf infusum (87.5%, 1:1, 1:2, 1:3, 2:1 and 3:1), then after one hour, they were given 1 mL of Castor oil orally. The data retrieval stage about diarrheal activities was done by observation, which included time of diarrhoea, frequency of diarrhoea, consistency and number/weight of faeces, and duration of diarrhoea. The response of each rat was observed at the 30^{th}, 60^{th}, 90^{th}, 120^{th}, 150^{th}, 180^{th}, 210^{th}, 240^{th}, 300^{th}, 360^{th} minutes after it was given the Castor oil. One-way ANOVA was used to analyse the results; $p < 0.05$ was considered statistically significant at the 95 per cent confidence interval.

Results

Chemical group test

Results of different qualitative chemical tests on Salam leaves (*S.polyanthum*) and Jackfruit leaves (Artocarpus heterophyllus Lam.) with $FeCl_3$ 5% and H_2SO_4 5% reagents showed the presence of tannin.

Antidiarrheal effect of salam and jack fruit leaves infusum was tested using nine groups of rats, in which each group consisted of three rats. Group II, the negative control group were given 1% CMC. Group I, as the positive control group, used tannin. The treatment Groups III, IV, V, VI, VII were given mixtures of salam and jackfruit infusum (1:1, 1:2, 1:3, 2:1 and 3:1), and the treatment Groups VII and IX were given salam infusum only and jackfruit infusum only, respectively. An hour later, each rat was given the Castor oil as much as 1 mL/rat.

The diarrheal activities of the rats in each group can be seen in Table I, in which consistency is converted into the following scores: 0) normal faeces; 1) soft faeces; 2) slimy/watery mass form of faeces; 3) not slimy/watery mass form of faeces.

All data parameters were normal and homogenous ($p > 0.05$). Based on the ANOVA test, the significance values between groups in diarrhoea parameters were $p < 0.05$ (Table II). This means that there were significant differences between groups.

To know which groups had significant differences, the next test done was the Post Hoc LSD test. From the results of the test analysis, significant differences were found in almost all of the parameters, except at Groups III and IX in weight parameters. The best result based on the *p*-value was Group VII (see Table III).

Table I: Rats diarrheal activities

Group	Rat	Total Frequency	Total consistency	Consistency average	Total weight (gram)
I (+)	1	4	10	1	2.25
	2	8	6	0.6	2.00
	3	7	7	0.7	1.19
II (-)	1	31	19	1.9	6.62
	2	26	21	2.1	7.57
	3	18	11	1.1	6.66
III (1:1)	1	16	16	1.6	4.83
	2	12	12	1.2	6.14
	3	15	15	1.5	7.12
IV (1:2)	1	13	8	0.8	4.40
	2	10	12	1.2	4.94
	3	5	0	0	5.79
V (1:3)	1	11	12	1.2	5.22
	2	10	9	0.9	4.43
	3	8	7	0.7	4.10
VI (2:1)	1	13	7	0.7	4.10
	2	9	8	0.8	4.32
	3	10	13	1.3	3.20
VII (3:1)	1	10	9	0.9	2.88
	2	9	10	1	2.25
	3	7	7	0.7	2.00
VIII (salam)	1	9	14	1.4	1.19
	2	10	9	0.9	6.62
	3	7	8	0.8	7.57
IX (j.fruit)	1	15	11	1.1	6.66
	2	9	15	1.5	4.83
	3	11	18	1.8	6.14

(I) Group of rats given Tannins as comparison and then 1 mL of Castor oil orally; (II) Group of rats given CMC 1% orally as a control and then 1 mL of Castor oil orally; (III) Group of rats given infusum of salam and jackfruit mixture (1:1) and then given 1 mL of Castor oil orally; (IV) Group of rats given infusum of salam and jackfruit mixture (1:2) and then given 1 mL of Castor oil orally; (V) Group of rats given infusum of salam and jackfruit mixture (1:3) and then given 1 mL of Castor oil orally; (VI) Group of rats given infusum of salam and jackfruit mixture (2:1) and then given 1 mL of Castor oil orally; (VII) Group of rats given infusum of salam and jackfruit mixture (3:1) and then given 1 mL of Castor oil orally; (VIII) Group of rats given infusum of salam only and then given 1 mL of Castor oil orally; (IX) Group of rats given infusum of jackfruit only and then given 1 mL of Castor oil orally.

Table II: One way ANOVA test result

Diarrhoea Parameter	*p*-value
Frequency of defecation	0.001
Faeces consistency	0.06
Faeces weight	0.001

Discussion

In this study, there were significant differences between Groups I and II, where the negative control group was given 1% CMC and Castor oil and the positive control group was given tannin before being given castor oil. The positive control group was significantly different from the negative control group in the weight of the stool defecation frequency and faeces consistency. This is consistent with the pharmacological theory, in which diarrhoea results from an imbalance between the absorptive and secretory mechanisms in the intestinal tract, accompanied by hurry, resulting in an excess loss of fluid in the faeces (Horton, 1978).

In some diarrhoeas, the secretory component is predominant, while other diarrhoeas were characterised by hypermotility. It is logical because the autacoids and prostaglandins are involved in producing diarrhoea in humans. Other factors have been suggested to describe castor oil's diarrheal effect: Intestinal Na+ K+ ATPase inhibition reduces normal fluid absorption (Gaginella & Bass, 1978), adenylate cyclase activation or mucosal cAMP-mediated active secretion (Capasso *et al.*, 1994), prostaglandin production stimulation, and platelet-activating factor stimulation (Pintoy *et al.*, 1992).

Table III: Mean differences and *p* values based on ANOVA *post hoc LSD* test

Group	Frequency *p*-value	Mean differences frequency	Consistency *p*-value	mean differences frequency	Weight *p*-value	Mean difference weight
- vs +	0.0001	18.666	0.005	0.933	0.0001	5.136
- vs 1:1 (III)	0.0001	10.666	0.374	0.266	0.098	0.920
- vs 1:2 IV)	0.001	15.666	0.002	1.033	0.002	1.906
-vs 1:3 (V)	0.0001	15.333	0.017	0.766	0.0001	2.366
-vs 2:1 (VI)	0.0001	14.333	0.017	0.766	0.0001	3.076
-vs 3:1 (VII)	0.0001	16.333	0.011	0.833	0.0001	4.286
-vs salam (VIII)	0.0001	16.333	0.035	0.666	0.001	1.980
-vs j.fruit (IX)	0.0001	13.333	0.436	0.233	0.220	0.970

Importantly, it has been proposed that nitric oxide leads to castor oil's diarrheal effect (Capasso *et al.*, 1994). Castor oil, on the other hand, is well known to trigger diarrhoea due to its most active ingredient, ricinoleic acid, which triggers a hypersecretory reaction(Meite *et al*., 2009). The liberation of ricinolic acid from Castor oil results in irritation and inflammation of the intestinal mucosa, leading to the

release of prostaglandins, which stimulate motility and secretion (Labu *et al*., 2015).

Tannins have been proven to make the intestinal mucosa more resistant and decrease secretions; furthermore, they suppress the diarrhoea induced by Castor Oil (Hanwa *et al.*, 2007). Tannins present in the plant infusum (salam leaves and jackfruit leaves) are reported to inhibit the release of autacoids and prostaglandins, thereby inhibiting motility and secretion induced by Castor oil. All the treatment group results give significant differences, indicating that all of the groups (salam leaves, jackfruit leaves, or mixtures of salam leaves and jackfruit leaves) infusums had antidiarrheal effects in reducing faeces weight, defecation frequency, and faeces consistency. Hence, tannins as an active compound may be responsible for the antidiarrheal activity. The best result was in Group VII (salam: jackfruit with 3:1 ratio). This means that the optimum dose of inhibition of diarrheal activity from all treatment groups is a mixture of salam leaves and jackfruit leaves infusum with a 3:1 ratio.

Conclusion

The treatment with a combination of salam leaves and jackfruit leaves infusum in rats induced by Castor oil has an antidiarrheal effect. The best result is a mixture of salam infusum: jackfruit infusum with a 3:1 ratio.

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