



Research Article

EVALUATION OF ANTIDIARRHEAL EFFECT OF *Artocarpus altilis* (PARK.) LEAVES IN MICE

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ABSTRACT

The current study was conducted to evaluate the anti-diarrheal activity of ethanol extract of *Artocarpus altilis* (Park.) leaf in mice. The antidiarrheal activity of ethanol extract of *A. altilis* leaf was performed using castor oil-induced diarrhea and intestinal transit methods. The extract was administered orally at doses of 100, 200, 400 mg/kg body weight (BW) one hour after induced by castor oil. Then, the mice were observed every 30 minutes for 6 hours to determine the onset of diarrhea, frequency of diarrhea, consistency, weight of stool and duration of diarrhea. Meanwhile, the distance travel of china ink was measured to determine gastrointestinal motility. Loperamide (0.52 mg/kg BW) was used as a positive control. The ethanol extract of *A. altilis* leaf reduced onset of diarrhea, frequency of diarrhea, consistency, weight of stool and duration of diarrhea when compared to negative control group ($P > 0.05$). The extract showed anti-diarrheal activity at a dose dependent manner. The extract at doses of 200 and 400 mg/kg BW showed higher activity in reducing the onset of diarrhea than loperamide as positive control ($P < 0.05$). However, anti-diarrheal activity evaluation using intestinal transit method showed that all doses of *A. altilis* extract reduced the gastrointestinal motility but only at the dose of 400 mg/kg BW revealed comparable effect with loperamide. The ethanol extract of *A. altilis* leaf possesses anti-diarrheal activity which supports its use in folk medicine.

Keywords: *Artocarpus altilis*, anti-diarrheal, castor oil-induced diarrhea, intestinal transit

INTRODUCTION

Diarrhea is a common gastrointestinal tract (GIT) dysfunction which characterized by the condition of increased in bowel movements and frequency defecation each day¹. It could be due to contaminated food, food allergy or infection. Diarrhea is still one of major health problem in developing countries. The morbidity and mortality rates caused by diarrhea is relatively high. Diarrheal disease remain the leading cause of death among children worldwide².

Medicinal plants have been used to treat various diseases in human civilization. Previous studies have reported that many herbs such as *Allamanda neriifolia*, *Crinum latifolium* and *Bruguiera cylindrica*, *Manihot esculenta* Crantz, *Morinda morindoides* and *Lantana camara* were able to treat diarrhea³⁻⁵. One of them is *Artocarpus altilis* (Park.) (Moraceae) which has been in folk medicine to treat various diseases. It is widely distributed in Indonesia, South America, Africa, India, Malaysia, Northern Australia and South Florida⁶. *Artocarpus communis* is synonym of *Artocarpus altilis*⁷. *Artocarpus altilis* is locally known as “sukun” in Indonesia. Indonesian people known this plant by its edible fruit. Phytochemical study of *A. altilis* led to the identification of saponins, tannins, steroids, flavonoids and polyphenols⁸. Tannins are well known secondary metabolite to have anti-diarrheal activity by narrowing the cells so that preventing the muscle secretion⁹.

Previous study has reported the anti-inflammatory activity of *A. altilis*¹⁰. The hypoglycemic activity of *Artocarpus altilis* has been reported by Adewole and Ojewole (2007)¹¹. This plant has found to have antioxidant, anthelmintic and antimicrobial activities¹²⁻¹⁴. Another species of *Artocarpus*, *Artocarpus heterophyllus* has

been reported to have anti-diarrheal activity by previous study¹⁵. However, the scientific study to evaluate the anti-diarrheal activity of *A. altilis* leaf has not been reported. The present study was conducted to investigate the anti-diarrheal effect of ethanol extract of *A. altilis* leaf using two different methods, these include castor oil-induced diarrhea and intestinal transit methods.

MATERIALS AND METHODS

Plant materials

The leaves of *A. altilis* were collected from Padang Bulan, Medan, Indonesia. The plant identification was confirmed by Herbarium Medanese (MEDA), Faculty of Math and Science, Universitas Sumatera Utara, Indonesia (1657/MEDA/2017).

Extraction procedure

The leaves materials were washed, dried and ground. Then 500 g of sample was soaked in 3.75 mL ethanol. After 5 days, the mixture was filtrated. The residue was again macerated with another 1.25 L ethanol for 2 days then filtrated. The filtrates were combined, and the solvent was removed using rotary evaporator to obtain extract of *A. altilis*¹⁶.

Animals

The use of mice was approved by the Animal Research Ethics Committees of Universitas Sumatera Utara (approval number 635/KEPH-FMIPA/2017). Twenty five animals used were mice weighing 20-30 g, then the animals were acclimatized in the experimental room for 7 days with room temperature and conditions 12 hours of light and 12 hours of darkness. The mice

were fed on a standard pellet diet and provided access to water ad libitum.

Castor oil-induced diarrhoea

The anti-diarrheal activity evaluation using castor oil to induce diarrhea was performed by a modified method by Meite, et al., (2009)¹⁷. The mice were divided into several groups, which include negative control, positive control and treatment groups. Prior to treatment all animals were fasted for 18 hours but consumed water ad libitum. Then, animals were induced by 0.5 mL of castor oil. One hour after induction, the treatment group received extract at doses of 100, 200 and 400 mg/kg body weight (BW) of ethanol extract of *A. altalis* leaves. Meanwhile the negative control group received 0.5 % Na CMC only and positive control group was administered with Loperamide HCl 0.52 mg/kg BW. The mice were placed in cages which have been layered with weighted paper. Observation was performed every 30 minutes for 6 hours. Several parameters were observed, including the onset of diarrhea, frequency of diarrhea, consistency, weight of stool and duration of diarrhea.

Intestinal Transit Method

The anti-motility activity of extract was investigated using transit intestinal methods as described previously by Gong, et al., (2017)¹⁸. The mice were divided into several groups, which include negative control, positive control and treatment groups. Prior to treatment all animals were fasted for 18 hours but consumed water ad libitum. Then, animals were induced by 0.5 mL of castor oil. One hour after induction, the treatment group received extract at doses of 100, 200 and 400 mg/kg body weight (BW) of ethanol extract of *A. altalis* leaves. Meanwhile the negative control group received 0.5 % Na CMC only and positive control group was administered with Loperamide HCl 0.52 mg/kg BW. After one hour, china ink 0.1 mL/10 g was administered orally to all animals. Then, one hour after administration of china ink, all animals were sacrificed by cervical dislocation method and their intestine were removed. Thereafter, the distance travelled by the china ink and the total intestine length (from the pylorus to the cecum) was measured to determine gastrointestinal motility. The peristaltic index was calculated by following formula:

$$\text{Peristaltic index} = \frac{\text{Distance travelled by china ink}}{\text{Length of small intestine}} \times 100 \%$$

Statistical analysis

The data were analysed using Statistical Package for Social Sciences (SPSS). The data presented as mean $\pm$ standard error of the mean (SEM) and analysed using a one-way analysis of variance (ANOVA) and followed by Tukey post hoc test. $P < 0.05$ was considered to be different significantly.

RESULTS AND DISCUSSION

Castor oil-Induced Diarrhea

There were several parameters observed to evaluate the anti-diarrheal activity of ethanol extract of *A. altalis* leaves. These include the onset of diarrhea, frequency of diarrhea, consistency, weight of stool and duration of diarrhea. Castor oil was used to induce diarrhea in mice. Ricinoleic acid, active metabolite of castor oil induces diarrhea by increasing peristaltic activity of intestinal mucosa and alters cell permeability to water and electrolyte¹⁸. The onset of diarrhea was determined by the first time loose after treatment with extract or loperamide or Na CMC only. Table 1 shows that all doses of extracts were able to delay the onset of diarrhea significantly as compared to negative control ($P > 0.05$). Surprisingly the effect of extract at the doses of 200 and 400 mg/kg BW revealed higher effect in delaying the onset of diarrhea than loperamide as positive control (Table 1). The *A. altalis* extract also reduced the frequency of diarrhea (4.4-5.6 times) when compared to negative control (7.6 times). However, only at the dose 400 mg/kg BW showed comparable effect as positive control ($P > 0.05$). The weight of stool were differentiated according to the consistency of stool. As shown in Table 1, the ethanol extract of *A. altalis* reduced the weight of stool at various consistency (solid, watery, mushy stool) in a dose dependent manner. In addition, the ethanol extract of *A. altalis* leaf at the doses of 200 and 400 mg/kg BW reduced the duration of diarrhea significantly and comparable with loperamide ($P > 0.05$). The duration of diarrhea was measured by determining the first time liquid stool until solid stool appeared. The result was in agreement with previous study which reported the ability of *A. heterophyllus* to reduce the frequency of diarrhea¹⁵. The ability of *Artocarpus altalis* to reduce the onset of diarrhea, frequency of diarrhea and duration of diarrhea might be due to the presence of tannin as reported in previous phytochemical study⁸. Tannins are able to narrow the cells so that preventing the muscle secretion⁹.

Gastrointestinal Motility Test

The effect of *A. altalis* on intestinal motility was evaluated by transit intestinal method. China ink was used as an indicator to measure the peristaltic activity of intestine. As shown in Figure 1 the ethanol extract *A. altalis* leaf reduced the motility activity of mice intestine after induced by castor oil. The statistical analysis revealed that *A. altalis* at the dose of 400 mg/kg BW demonstrated comparable effect with positive control in reducing peristaltic activity. Tannin and flavonoid might be major contributor to this effect, as previous study showed that tannins are able to induce denaturation of protein in intestinal mucosa by forming protein tannates. Furthermore, tannins may inhibit microbial toxin and others motility agents to contact with intestinal mucosa²⁰⁻²¹. Flavonoids has found to inhibit gastrointestinal motility and mucus secretion²².

Table 1: Effect of ethanol extract of *A. altalis* leaves on diarrhea induced by castor oil (Data $\pm$ SEM, n: 5)

No.	Treatment	Onset (minutes)	Frequency (times)	Solid stool (g)	Watery stool (g)	Mushy stool (g)	Duration (minutes)
1	Na CMC 0.5%	50.80 $\pm$ 3.441 ⁺	7.61 $\pm$ 0.245 ⁺	0.3 $\pm$ 0.005 ⁺	3.83 $\pm$ 0.010 ⁺	1.60 $\pm$ 0.015 ⁺	288.6 $\pm$ 8.565 ⁺
2	Loperamide 0.52 mg/kg BW	105.80 $\pm$ 6.756*	3.62 $\pm$ 0.245*	0.16 $\pm$ 0.004*	1.91 $\pm$ 0.002*	0.91 $\pm$ 0.015*	125.8 $\pm$ 0.970*
3	<i>A. altalis</i> extract 100 mg/kg BW	118.40 $\pm$ 3.203*	5.60 $\pm$ 0.200**	0.23 $\pm$ 0.003**	3.00 $\pm$ 0.004**	0.90 $\pm$ 0.032**	142.6 $\pm$ 4.214**
4	<i>A. altalis</i> extract 200 mg/kg BW	126 $\pm$ 4.062**	4.83 $\pm$ 0.200**	0.22 $\pm$ 0.003*	1.57 $\pm$ 0.005**	0.68 $\pm$ 0.012*	114.6 $\pm$ 4.020*
5	<i>A. altalis</i> extract 400 mg/kg BW	138.21 $\pm$ 4.790**	4.42 $\pm$ 0.245*	0.17 $\pm$ 0.002*	1.34 $\pm$ 0.004**	0.61 $\pm$ 0.015*	114.4 $\pm$ 3.108*

* $P < 0.05$ significant with 0.5% Na CMC, + $P < 0.05$ significant with loperamide 0.52 mg/kg body weight (BW)

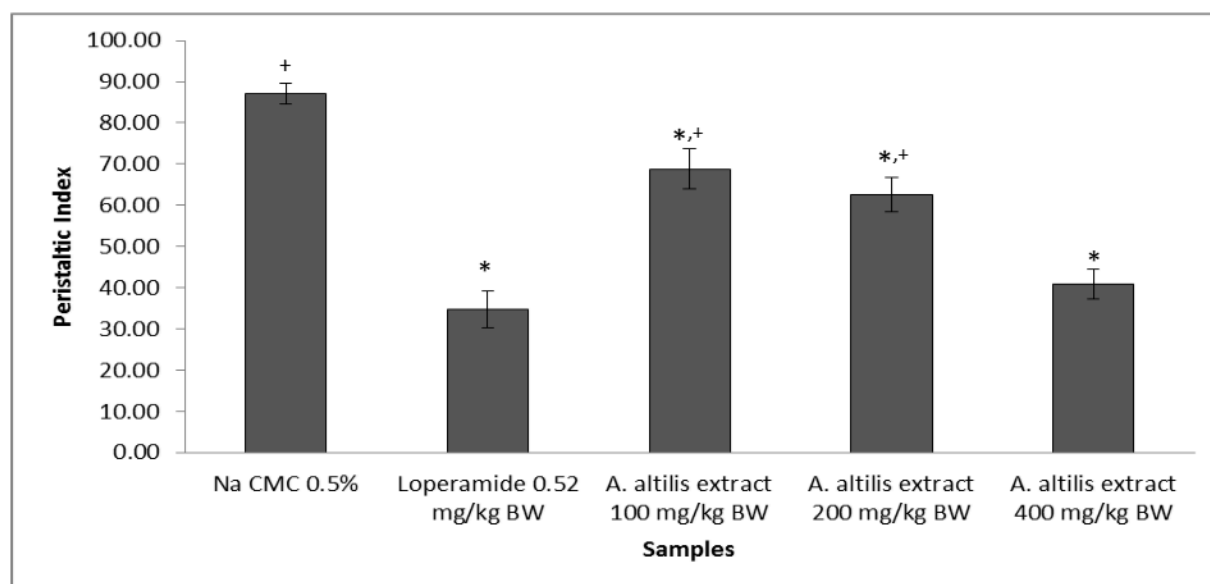


Fig. 1: Effect of ethanol extract *Artocarpus altilis* leaf on peristaltic index (Data: Mean ± SEM, * P < 0.05 significant with negative control, + P < 0.05 significant with positive control).

CONCLUSION

The ethanol extract of *Artocarpus altilis* leaf decreased the the onset of diarrhea, frequency of diarrhea, consistency, weight of stool and duration of diarrhea in mice after induced by castor. In addition, the extract was also reduced gastrointestinal motility which indicated by distance travelled by china ink as compared to total intestinal length. *Artocarpus altilis* has potential to be developed as new anti-diarrheal agent. However, further studies are required to elucidate its mechanisms to treat diarrhea.

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REFERENCES

- Schiller LR, Pardi DS, Sellin JH. Chronic diarrhea: diagnosis and management. Clin Gastroenterol Hepatol 2017; 15: 182–193.
- Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. Bull World Health Organ 2003;81:197-204.
- Ashrafuzzaman MD, Raju GS, Abeer MIU, et al. Antidiarrheal Activity of Three Medicinal Plants in Swiss Albino Mice. Int J Biomed 2016; 6(3): 233-236.
- Bahekar SE, Kale RS. Antidiarrheal activity of ethanolic extract of Manihot esculenta Crantz leaves in Wistar rats. J Ayurveda Integr Med 2015; 6(1): 35-40.
- Tadesse E, Engidawork E, Nedi T, et al. Evaluation of the anti-diarrheal activity of the aqueous stem extract of *Lantana camara* Linn (Verbenaceae) in mice. BMC Complement Altern Med 2017; 17: 190.
- Deivanai S, Bhore SJ. Breadfruit (*Artocarpus altilis* Fosb.)- An Underutilized and Neglected Fruit Plant Species. Middle-east J Sci Res 2010; 6(5): 1-13.
- Sikarwar MS, Hui BJ, Subramaniam K, et al. A Review on *Artocarpus altilis* (Parkinson) Fosberg (breadfruit). J App Pharm Sci 2014; 4 (08): 091-097.
- Sivagnanasundaram P, Karunanayake KOLC. Phytochemical screening and antimicrobial activity of *Artocarpus heterophyllus* and *Artocarpus altilis* leaf and stem bark extracts. Open Univ Sri Lanka J 2015; 9: 1-17.
- Mutschler, E. Drug action: Basic principles and therapeutic aspects. 6th ed. Germany: Medpharm Scientific Publisher. 1991
- Fakhrudin N, Hastuti S, Andriani A, et al. Study on the antiinflammatory activity of *Artocarpus altilis* leaves extract in mice. Int J Pharmacogn Phytochem Res 2015; 7(6): 1080-1085.
- Adewole SO, Ojewole JA. Hyperglycaemic effect of *Artocarpus communis* Forst (Moraceae) root bark aqueous extract in wistar rats. Cardiovasc J Afr 2007; 18(4): 221–227.
- Horng-Huey K, Wen-Chun L, Cheng-Wei T, et al. Prenylated flavonoids from *Artocarpus altilis*: antioxidant activities and inhibitory effects on melanin production. Phytochemistry 2013; 89: 78–88.
- Chinmay P, Monalisa M, Abhijeeta R, et al. Phytoconstituent screening and comparative assessment of antimicrobial potentiality of *Artocarpus altilis* fruit extracts. Int J Pharm Pharm Sci 2013; 5(3): 1.
- Carine MM, Maurice M, Marie-Laure L, et al. In vitro evaluation of the nematicidal value of *Artocarpus altilis* (Parkinson) var. seminiifera and non seminiifera and *Terminalia cattapa* L. against *Haemonchus contortus*. Adv Anim Biosci 2010; 1(02): 440-441.
- Munira S. Antioxidant and antidiarrhoeal activities of methanolic extract of *Artocarpus heterophyllus* seed. Int J Pharm Drug Anal 2014; 2(10):890-895.
- Indonesian Pharmacopoeia. 3rd ed. Jakarta: Departemen Kesehatan Republik Indonesia. 1979. p. 649.
- Meite S, N'guessan JD, Bahi C, et al. Antidiarrheal activity of the ethyl acetate extract of *Morinda morindoides* in rats. Trop J Pharm Res 2009; 8 (3): 201-207.
- Gong XP, Sun YY, Chen W, et al. Anti-diarrheal and anti-inflammatory activities of aqueous extract of the aerial part of *Rubia cordifolia*. BMC Complement Altern Med 2017; 17: 20.
- Ammon HV, Thomas PJ, Phillips SF. Effects of oleic and ricinoleic acids on net jejunal water and electrolyte movement: Perfusion studies in man. J Clin Invest 1974; 53: 374-379.
- Havagiray R, Ramesh C, Sadhna K. Study of antidiarrhoeal activity of *Calotropis gigantea* R.B.R. In experimental animals. J Pharm Pharm Sci 2004; 7: 70-75.
- Otshudi LA, Vercruysse A, Foriers A. Contribution to the ethnobotanical, phytochemical and pharmacological studies of traditionally used medicinal plant in the treatment of

- dysentery and diarrhoea in lomela area, Democratic Republic of Congo (DRC). *J Ethnopharmacol.* 2000; 71(3): 411-423.
22. Perez GS, Perez GC, Zavala MA. A Study of Antidiarrhoeal Properties of *Loeselia mexicana* on Mice and Rats. *Phytomedicine.* 2005;

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