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Anti-Inflammatory Activity of *Artocarpus altilis* (Parkinson) Fosberg in Wistar Male Rats

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Abstract

Inflammation is a local reaction in vascular tissue characterized by several symptoms, *e.g.,* swelling, redness, and pain. Indonesia is one of the countries with high biodiversity, including traditional medicinal plants. *Artocarpus altilis* is one the plants that is widely used to treat inflammation. There is limited information on biological activity of *A. altilis.* This study was performed to evaluate anti-inflammatory properties of *A. altilis* detached and attached leaves in Wistar male rats. *A. altilis* was extracted using soxhlet method at 67.4 ^{0}C with methanol solvent. Inflammation was induced by the administration of carrageenan to the rats paw. Subsequently, the extract of *A. altilis were* orally administered. The edema were measured using plethysmometer for 6 hours. We found that there were differences in anti-inflammatory activity between detached and attached leaves. The inhibition of edema in attached leaves were 50% and 53.33% for the concentration of 50 mg and 100 mg, respectively. The greater inhibiton was observed in the detached leaves, with 73.33% and 76.67% inhibition, for the concentration of 50 mg and 100 mg, respectively. Nevertheless, the inhibition percentage was still below diclofenac sodium as a positive control (83.33%). In conclusion, *A. altilis* leaves extracts showed good anti-inflammatory properties and has the potential for development of anti-inflammatory drug.

Keywords: *Artocarpus altilis*, carageenan, inflammation, edema

Introduction

Inflammation is a local response to celullar injury, characterized by capilary dilatation, swelling, redness, and pain. The treatment includes the administration of anti-inflammatory drugs. Nevertheless, many side effects were associated with the use of these drugs, such as gastrointestinal ulcer, bleeding, kidney failure, *etc*.[1-3]

The increasing use of herbal medicine and phytonutrients has been observed during the last decade. The use of medicinal plant is preferred by many individuals since it may have fewer side effects compared to the conventional treatment. It is estimated that up to four billion people worldwide rely on herbal medicinal products.[4,5]

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Table 1. Characteristics of *A. Altilis* Leaves

Leaves	Ash (%)	Water Soluble Compounds (%)	Ethanol Soluble Compounds (%)
Attached	26.00	32.94	8.92
Detached	27.36	35.94	12.44

Indonesia is one of the country with highest biodiversity, including traditional medicinal plants.[6] *A. altilis* is one of the Indonesian traditional medicinal plants that is used to treat inflammation. Previous study showed that detached and attached leaves had significant differences in defence response.[7] Two types of leaves might have different metabolites which can influence its biological activities. Nevertheless, there is limited information on biological activity of the variety of *A. altilis* leaves. This study was performed to evaluate anti-inflammatory properties of *A. altilis* in Wistar male rats.

Methods

Materials

The materials used in this study included the leaves of *A. altilis* (Park.) Fosberg which were obtained from the Cipamokolan, Bandung, West Java, Indonesia, methanol, distilled water, carrageenan, diclofenac sodium, and several phytochemical screening reagents, *e.g.,* ammonia, chloroform, hydrochloride, gelatin solution, amyl alcohol, ether, vanilla, H2SO4p, KOH, Mayer, Dragendorff and Lieberman-Burchard reagent.

Tools

The tools used in this study included rotary evaporator, waterbath, soxhlet, petri dish, volumetric pipette, erlenmeyer flask, measuring cup, syringe, stirring rod, plethysmometer, analytical balance, porcelain dishes, oven, desiccators, wood clamps, tube racks, drip plates, spatulas, and spirits burners

Preparation and extraction

Plant determinantion was conducted at the herbarium of School of Life Sciences, Bandung Institute of Technology. *A. altilis* leaves were cleaned, chopped and dried. Phytochemical screening was performed to determine the content of secondary metabolites, such as alkaloids, flavonoids, tannins, phenolics, triterpenoids, steroids, quinones, monoterpenes, sesquiterpenes, and saponins. Determination of ash content, water and ethanol soluble compunds were also performed. The leaves were extracted using soxhlet method with methanol solvent at 64.7 ^{0}C. Each filtrate was separated and evaporated using a rotary evaporator at 45 ^{0}C.

Table 2. Phytochemical Screening o*f A. Altilis* Leaves

Metabolites	**Attached Leaves**	**Detached Leaves**
Alkaloid	-	-
Flavonoid	+	+
Tannin	+	+
Phenolic	+	+
Monoterpene, sesquiterpene	+	+
Steroid	+	+
Triterpenoides	-	-
Quinone	+	+
Saponin	-	-

Table 3. Average of Edema Volume

Group	V_0	t_1	t_2	t_3	t_4	t_5	t_6
Negative control	0.035	0.051	0.061	0.061	0.063	0.065	0.065
Positive control	0.026	0.031	0.033	0.037	0.037	0.035	0.031
Attached 50 mg	0.028	0.035	0.04	0.043	0.043	0.043	0.043
Attached 100 mg	0.028	0.042	0.042	0.042	0.042	0.042	0.042
Detached 100 mg	0.025	0.032	0.033	0.033	0.035	0.035	0.032
Detached 50 mg	0.025	0.033	0.037	0.037	0.037	0.038	0.033

Anti-inflammatory activity assay

Experimental animals used in this study were Wistar strain male rats (180-250 g). Male rats were selected to avoid the influence of hormonal change in inflammatory responses. The animals were acclimatized for two weeks before the experiment. The animals were classified into 6 groups, each group consisting of 3 rats, *i.e.*, negative control, positive control, and 4 treatment group with different doses. The negative control group was given 3 ml/200 g body weight 2% PGA suspension orally, while the positive control group was given 0.9 mg/ 200 g body weight diclofenac sodium orally. The experimental doses were 50mg/kg and and 100mg/kg body weight, for both detached and attached leaves. Inflammation was induced by administering carrageenan on rats paw. The volume of edema was measured, before and after the treatment.

Results and Discussion

The results of plant determination showed that the plants used in this study was *A. altilis* (Parkinson) Fosberg. The yield of extracts were 11.12% and 13.05% for attached and detached leaves, respectively. Methanol was selected as the solvent since it has better polarity compared to other solvents. The temperature used in the extraction process was based on the boiling point of the solvent. The percentage of ash contents and water soluble compounds of both types of leaves were relatively similar. However, the ethanol soluble compounds was higher in detached leaves (12.44%) compared to attached leaves (8.92%). The results can be seen in the Table 1. Determination of ash content was conducted to determine the mineral and metal content from the initial process to the formation of extracts. Phytochemical screening showed that both types of leaves contained flavonoids, tannins, phenolics, monoterpenes, sesquiterpenes, steroids, and quinones (Table 2).

The anti-inflammatory activity assay showed that there was a decrease in the volume of edema in all groups, except negative control.

Table 4. Percentage of the Inhibition of Inflammation

Group	V0 (%)	T_1 (%)	t_2(%)	t_3(%)	t_4(%)	t_5(%)	t_6(%)
Negative control	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Positive control	0.00	68.75	73.08	57.69	60.71	70.00	83.33
Attached 50 mg	0.00	56.25	53.85	42.31	46.43	50.00	50.00
Attached 100 mg	0.00	12.50	46.15	46.15	50.00	53.33	53.33
Detached 100 mg	0.00	12.50	69.23	69.23	64.29	66.67	76.67
Detached 50 mg	0.00	50.00	53.85	53.85	57.14	56.67	73.33

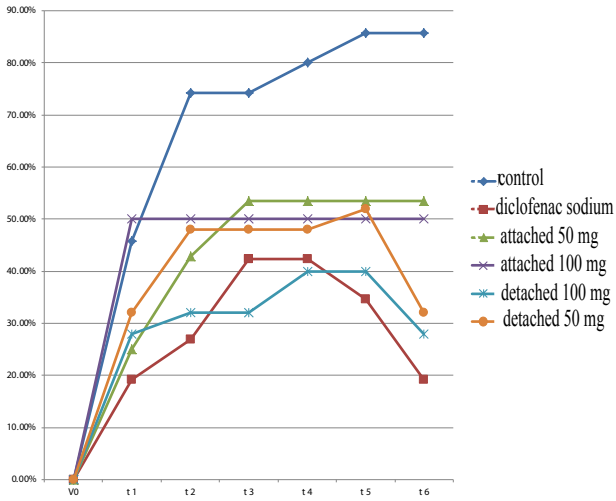

Figure 1. Percentage of Inflammation Over Observed Time

The smaller the average volume of edema, the better the anti-inflammatory effect of this particular compound. The largest inhibition of inflammation was observed in positive control group with 83.33% reduction of edema. There were differences in anti-inflammatory activity between detached and attached leaves. The inhibition of edema in attached leaves were 50% and 53.33% for the concentration of 50 mg and 100 mg, respectively. The greater inhibiton was observed in the detached leaves, with 73.33% and 76.67% inhibition, for the concentration of 50 mg and 100 mg, respectively. Among the treatment group, the extract of detached leaves 100 mg showed the best anti-inflammatory activity. Nevertheless, the percentage of the reduction was still higher than that of diclofenac sodium.

Differences in anti-inflammatory activity between detached and attached leaves might be due to differences in ethanol soluble compounds. Previous study showed that phenolic compounds might be responsible for anti-inflammatory activity of *A. altilis* plants. Further study is needed to confirm and elucidate the structure of the active anti-inflammatory compound in *A. altilis*.[8-13]

Conclusion

A. altilis leaves extracts showed good anti-inflammatory properties and has the potential for development of anti-inflammatory drug.

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Conflict of Interest

None declared.

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