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The Antipyretic Activity of Leaves Extract of *Ceiba pentandra* Better than *Gossypium arboreum*

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ABSTRACT

Background: The Indonesian people were used the leaves of silk cotton tree (*Gossypium arboreum* L.) and cotton tree (*Ceiba pentandra* Gaertn.) as an antipyretic, empirically. There is no scientific evidences on the antipyretic activity of these plants. **Objective:** The aim of this study is to determine the better antipyretic activity of the leaves extract of *G. arboreum* and *C. pentandra* in Swiss mice as an animal model. **Methods:** The steps of the study consisted of extraction, phytochemical screening, and antipyretic activity assay on Swiss mice which induced by 20% yeast suspension. **Results:** The results showed that the leaves extract of *G. arboreum* and *C. pentandra* have antipyretic activity. The effective dose of antipyretic activity for the leaves extract of *G. arboreum* and *C. pentandra* is 1120 mg/kg and 189 mg/kg, respectively. **Conclusion:** The antipyretic activity of *C. pentandra* leaves extract better than *G. arboreum* leaves.

INTRODUCTION

The hypothalamus regulates body temperature with a delicate balance between heat production and heat loss through the set-point control. Infection, tissue damage, inflammation, graft rejection, malignancy and other disease may elevate the set point to induce fever (Goodman and Gilman, 2001). Fever is a complex physiologic response which triggered by abnormalities in the brain, toxic substances that affect temperature regulation, bacterial infections, brain tumors, and dehydration. Elevation of the body temperature occurs when the concentration of prostaglandin E2 (PGE2) increases within parts of the brain. The mechanism of antipyretic drugs is inhibit the cyclooxygenase (COX) activity and consequently reducing the levels of PGE2. Synthetic antipyretic drugs have side effects (DiPiro *et al*., 2008). Therefore, it is worthed to searching herbal medicines that are equally efficacious and comparatively side effects free, as substitutes for synthetic drugs, such as paracetamol. Empirically, the Indonesian people are using the leaves of silk cotton tree (*Gossypium arboreum* L., Malvaceae) and cotton tree (*Ceiba pentandra* Gaertn., Malvaceae) as an antipyretic. The *G. arboreum* leaves contain polysaccharides, lipids, caffeic acid derivatives, saponins, polyphenolic compounds, flavonoids, iridoid glycosides, terpenoids, alkaloids and some organic acids. Empirically, the *G. arboreum* leaves are used to treatment the skin wounds, respiratory organs, digestive organs, cancer prevention, pain relief, infection, enteritis, fever, and cough. The *G. arboreum* leaves extract have activity of antibacterial, antioxidant, and fibroblast growth stimulation (Annan and Houghton, 2008).

The *C. pentandra* contain polyphenolic compounds, saponins, bitter resins, carbohydrates, and flavonoids in the leaves and the fixed oil in the seeds. The *C. pentandra* leaves are used to treatment of scabies, fever, eye fatigue, asthma, expectorant, inflammation (Heyne, 1987, Perry, 1980), gonorrhea, mouthwash, scars relief (Lanting and Palaypayon, 2002), and antigastritis (Wasito, 2009). The infusion of the *C. pentandra* leaves is used to treatment of cough, intestinal and mucous membranes inflammation, and urethritis. There is no scientific evidence on the antipyretic activity of the ethanolic extract of leaves of *G. arboreum* and *C. pentandra*. Hence, the antipyretic dose for these extracts refer to *G. arboreum* extract as an anti-inflammatory, i.e. 400 mg/kg rat (Osuntoki and Olagundoye, 2007) and *C. pentandra* extract as antigastritis, i.e. 270 mg/kg rat (Wasito, 2009). The aim of this present study was to compare the antipyretic activity on ethanolic extract of leaves of *G. arboreum* and *C. pentandra.*

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MATERIALS AND METHODS

Materials

The *G. arboreum* and *C. pentandra* leaves were collected from Manoko, West Java, Indonesia. Swiss mice (18-25 g) was obtained from Center for Biological Sciences, Institute of Technology Bandung, Indonesia. Paracetamol with pharmaceutical grade. All chemicals with analytical grade (Merck) are ferric chloride, hydrochloric acid, sodium hydroxide, sodium acetate, n-hexane, methanol, chloroform, sulfuric acid, glacial acetic acid, ethanol, ether, Mayer, Dragendorff, and Bouchardat reagent.

Samples Preparation

Simplicia were extracted in a reflux apparatus with 70% ethanol at 40 ºC by continuous heat extraction for 12 hours. Each 4 hours, the solvent changed with the fresh one. All extract were collected and vapored with rotary rotavapor at temperature not exceeding 50 ºC. For experimental purpose the ethanolic extract was prepared in distilled water containing 2% v/v Tween 80 (as a suspending agent). Phytochemical screening was conducted to simplicia and extract with Fransworth method (Fransworth, 1996).

Antipyretic Activity Assay

Antipyretic activity was determined by modified method previously described by Al-Ghamdi (Al-Ghamdi, 2001). The mice were fasted overnight but were provided with water *ad libitum* before the experiments. The mice were divided into eight groups of five animals each. Basal rectal temperatures was measured by introducing a 3 cm digital thermometer (Model MT-101, N and B Medical). The mice were administered 20% yeast suspension with subcutaneous treatment and 4 h later, rectal temperatures of the hyperpyrexic mice were measured.

The leaves extracts of *G. arboreum* (280, 560, and 1120 mg/kg) and *C. pentandra* (189, 378, and 756 mg/kg), saline, and paracetamol (50 mg/kg) were orally administered to the animals. The rectal temperatures were measured every 1 h upto 4 h. The last temperature were compared with pre-treatment temperature (temperature taken at 4 h post yeast suspension injection).

Statistical analysis

Results are presented as the mean + standard error of the mean (SEM). Data comparisons between treatment groups were done by oneway ANOVA followed by Tukey-Kramer post hoc test. Values were considered statistically significant at $p < 0.05$.

RESULTS AND DISSCUSSION

Sample Preparation

G. arboreum and *C. pentandra* are ethnoremedies. The Indonesian people are prepared these remedies by boiling the simplicia, so reflux was chosen as extraction method. Reflux was conducted by three times of the solvent replacement to maximize the extraction of secondary metabolites from the simplicia. Phytochemical screening was conducted to determine the group of secondary metabolites in the simplicia and extract. The results showed that extract has same constituents as simplicia (Table 1). It's mean that reflux can extract all secondary metabolites in simplicia and heating process doesn't damage the secondary metabolites. *C. pentadra* have no alkaloids and quinones compared to *G. arboreum* (Table 1). These results are consistent with previous studies (Annan and Houghton, 2008, Heyne, 1987).

The yield of *G. arboreum* (7.15%) is smaller than *C. pentadra* (10.78%) with ratio of 1: 1.51. This indicates that the secondary metabolites in *C. pentadra* are more soluble in ethanol than the *G. arboreum*.

Table 1: Phytochemical Screening Result.

Sample	Secondary metabolite	Simplicia	Extract
G. arboreum	Flavonoids	+	+
	Polyphenolics	+	+
	Tannins	+	+
	Alkaloids	+	+
	Saponins	+	+
	Quinones	+	+
	Steroids /triterpenoids	+	+
C. pentandra	Flavonoids	+	+
	Polyphenolics	+	+
	Tannins	+	+
	Alkaloids	-	-
	Saponins	+	+
	Quinones	-	-
	Steroids /triterpenoids	+	+

Note: +: detected, -: undetected

Antipyretic Activity Assay

The yeast was used to initiate the pyrexia. The yeast-induced pyrexia is due to the PGE2 production which set the thermoregulatory center at a higher temperature (Alzubier and Okechukwu, 2011). The hypothalamus PGE2 was produced by COX 2 is principle downstream mediator of fever (Cheng *et al*., 2005). Yeast can produced an increase in the mice body temperature from normal (35.93 ± 0.22 °C) to 36.72 ± 0.32 °C after 4 h of yeast injection. Paracetamol is potent antipyretic and analgesic activities with minimal antiinflammatory activity. It may selectively inhibit specific COX isoform in the CNS to inhibit PGE2 synthesis to achieve its antipyretic effect, but does not influence body temperature when it is elevated by other factors such as exercise or increase in ambient temperature (Goodman and Gilman, 2001). The possible mechanism for the antipyretic activity of ethanolic extract is due to the inhibition of PGE2 synthesis (Dinarello and Porat, 2008, Igbe *et al*., 2009). Paracetamol as standard drug, was reduced the body temperature, from 36,84 + 0.30 °C to 35,38 + 0.23 °C after 4 h of drug treatment. The leaves extract of *G. arboreum* and *C. pentandra* possessed antipyretic activity to yeast-induced pyrexia in mice, but their activities are lower than paracetamol (Table 2). The antipyretic doses for *C. pentadra* and *G. arboreum* was calculated from previous study. The anti-inflammatory dose of *G. arboreum* extract (400 mg/kg rat) (Osuntoki and Olagundoye, 2007) was bigger than the antigastritis dose of *C. pentadra* (270 mg/kg rat) (Wasito, 2009) with ratio of 1: 1:48.

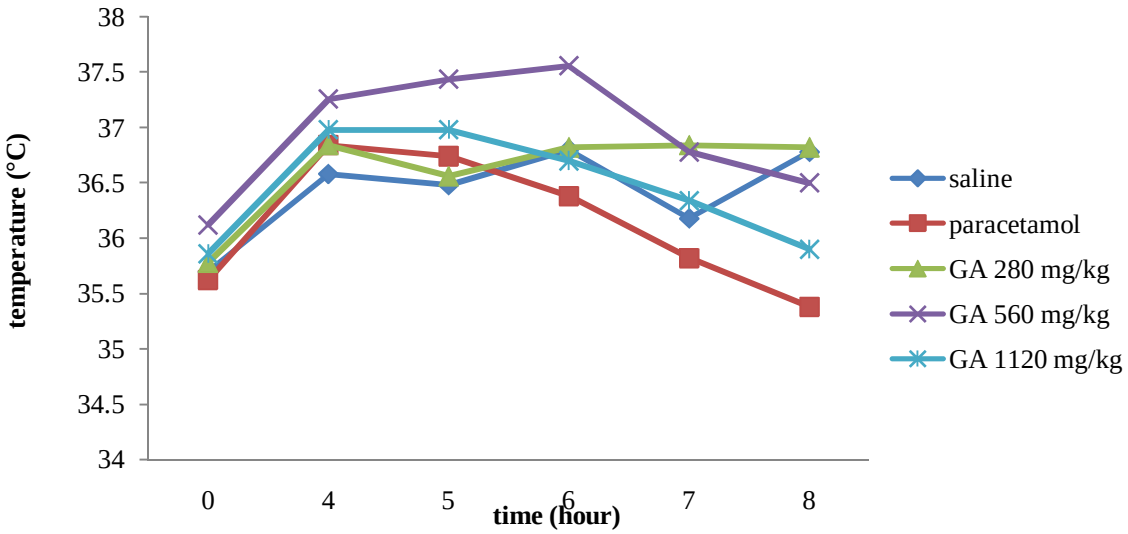

Fig. 1: Antipyretic activity of *G. Arboreum.*

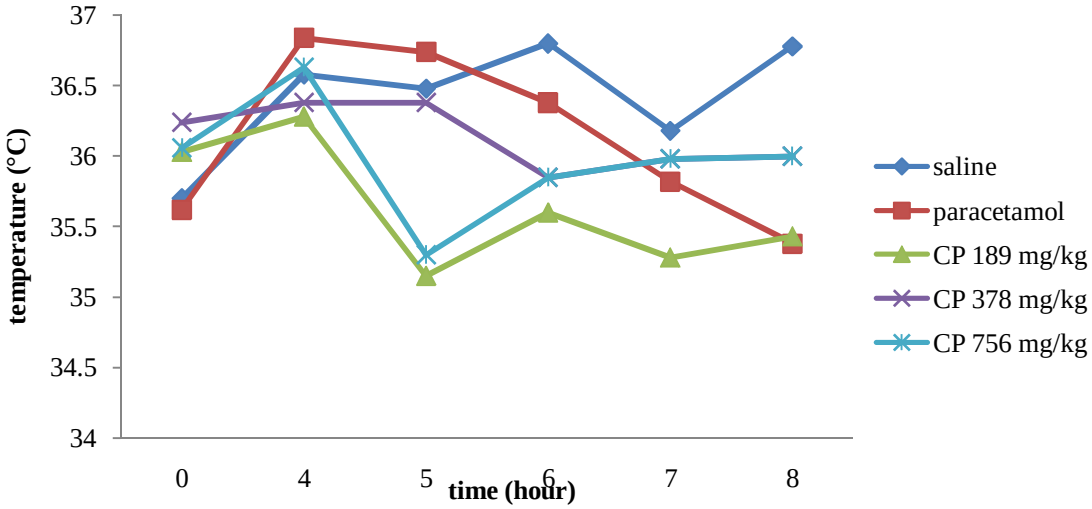

Fig. 2: Antipyretic activity of C. pentandra

Table 2: Result of Antipyretic Activity Assay

Group	Weight (g)	T basal (°C)	T after induction (°C)	T after treatment (°C)				Δt (°C)
				T1	T2	T3	T4	
GA 280 mg/kg	19,40±0.76	35,78±0.42	36,84±0.32	36,56±0.70	36,82±0.25	36,84±0.37	36,82±0.35	-0,02±0.24
GA 560 mg/kg	19,20±0.83	36,12±0.37	37,26±0.38	37,44±0.29	37,56±0.33	36,78±0.33	36,50±0.46	-0,76±0.29
GA 1120 mg/kg	22.00±0.43	35,86±0.33	36,98±0.15	36,98±0.15	36,70±0.27	36,34±0.62	35,90±0.22	-1,08±0.19
CP 189 mg/kg	20,50±0.83	36,03±0.49	36,28±0.32	35,15±0.31	35,60±0.78	35,28±0.17	35,43±0.57	-0,85±0.58
CP 378 mg/kg	20,27±0.56	36,24±0.53	36,38±0.46	36,38±0.46	35,85±0.40	35,98±0.66	36,00±0.55	-0,43±0.84
CP 756 mg/kg	20,04±0.85	36,06±0.56	36,63±0.89	35,30±0.79	35,85±0.26	35,98±0.66	36,00±0.75	-0,63±0.79
Saline	24,60±0.91	35,70±0.27	36,58±0.28	36,48±0.23	36,80±0.42	36,18±0.36	36,78±0.33	1.08±0.40
Paracetamol	19,60±0.82	35,62±0.18	36,84±0.30	36,74±0.23	36,38±0.28	35,82±0.25	35,38±0.23	-1,46±0.30

This causes the dose differences of *C. pentadra* and *G. arboreum* extracts. The antipyretic activity of the *G. arboreum* extract was dose-dependent, higher dose will produce higher activity (Fig. 1), but not applicable to the *C. pentandra* extract. This present study indicate that the *C. pentandra* extract possesses significant antipyretic activity compared to the *G. arboreum* (Fig. 2) on yeast-induced pyrexia in mice. The effective dose of *C. pentadra* (189 mg / kg) lower than G. arboreum (1120 mg / kg) with ratio of 1: 5.93. This may caused by the secondary metabolites content which had antipyretic activity is higher in *C. pentadra* compared to *G. arboreum*. We suggested that the contribution of alkaloids and quinones as antipyretic activity is small. This is because although *G. arboreum* have alkaloids and quinones content, but its antipyretic activity is smaller than *C. pentadra*. This results is consistent with previous studies which states that tannins, triterpenoids, and coumarin glycosides (Buppachart *et al*., 2008), steroids and flavonoid (Buppachart *et al*., 2008, Reshmi *et al*., 2010, El-Hamss *et al*., 2003, Parganiha *et al*., 2011, Sunila and

Kuttan, 2004) may be responsible for antipyretic activity in plants. The antipyretic activity of *G. arboreum* and *C. pentandra* may be due to flavonoids, polyphenolics, tannins, steroids, and triterpenoids (Table 1). This study also correlates with the study of Zakaria *et al* (2007) which stated that flavonoids and saponins are suggested work synergistically to exert the pharmacological activity (Zakaria *et al*., 2007). Flavonoids and saponins may be involved in inhibition of PGE2 synthesis. Flavanoids have antipyretic activity by suppressing TNF-α (Adesokan *et al*., 2008) and its related compounds (polyphenolics) also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever and pain (Taiwe *et al*., 2011).

Statistical analysis

The statistical analysis showed that the observation time after treatment and the extract dose provide a stastically significant on the body temperature reduction after yeast induction ($p < 0.05$).

CONCLUSION

The leaves extract of *G. arboreum* and *C. pentandra* have antipyretic activity. The antipyretic activity of the leaves extract of *C. pentandra* better than *G. arboreum*.

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