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# Antihypertensive Effects of *Centella asiatica* Extract

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**Abstract.** This study assessed effects of *Centella asiatica* extract on blood pressure and heart rate (HR) of N-nitro-L-arginine methyl ester (L-NAME) induced hypertensive rats. Male Wistar rats were anesthetized with sodium pentobarbital (50 mg/kg, i.p.) and their left carotid arteries were cannulated for invasive blood pressure measurement. Mean arterial blood pressure (MABP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR were recorded continuously throughout the experiment using PowerLab system. Thirty minutes after administration of L-NAME (40 mg/kg, i.p.), rats were intragastrically administered with DDD water (20 ml/kg), quercetin (5 mg/20 ml/kg), propylene glycol (20 ml/kg), or *Centella asiatica* extract (4, 8, 16, or 32 g/20 ml/kg), n=8 each. All recordings were further continued for 90 minutes. L-NAME significantly increased MABP, SBP and DBP. *Centella asiatica* extract (16 g/20 ml/kg) and quercetin significantly lowered the elevated MABP, SBP, and DBP in L-NAME induced hypertensive rats. *Centella asiatica* extract and quercetin did not cause any change in HR of rats receiving L-NAME. The present study demonstrated blood pressure lowering effect of *Centella asiatica* extract in L-NAME induced hypertensive rats. These findings provide scientific support for tradition use of this plant to modify the actions of human cardiovascular system.

**Keywords:** Hypertension, blood pressure, *Centella asiatica*, quercetin, rat

## 1. Introduction

Hypertension is a major risk factor for chronic renal failure, cardiovascular disease and stroke, thus prevention of hypertension is important in reducing the risk of these debilitating ailments [1]. Identification of antihypertensive foods is currently interested because they are expected to prevent hypertension with lower side-effects than antihypertensive drugs [2]. Many researchers are actively looking for antihypertensive compounds derived from various natural products for the use in functional foods. Several studies have shown that food ingredients rich in flavonoids and other polyphenols can lower blood pressure [3]-[6].

*Centella asiatica* (L.) Urban, known as *Asian pennywort*, *guta kola* (Indian) and *bua-bok* (Thai), is a small creeping herb that has long been used in traditional medicine and various purposes. It is a tropical medicinal plant with a long history of therapeutic used for many conditions such as dermal disorder, vascular diseases, microangiopathy, and inflammatory [7]-[9].

*Centella asiatica* extract exerted potent antioxidative activity as indicated by various assay system [10]. *Centella asiatica* contains high total phenolic content which contributed by the flavonoids such as quercetin, kaempherol, catechin, rutin, apigenin and naringin [11] and is said to have a direct effect in lowering blood pressure and is often referred to as a rejuvenating medicament in Ayurvedic Pharmacopoeia [12], [13]. Therefore, this study aimed to determine acute effects of *Centella asiatica* extract on blood pressure and heart rate of anaesthetized hypertensive rats. A flavonoid quercetin found in *Centella asiatica* was used as positive control in this study since it has been shown to promote relaxation of cardiovascular smooth muscle (antihypertensive effects) [14].

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## 2. Materials and Methods

### 2.1. Plant Material

*Centella asiatica* plant was obtained from local market in Nakhon Ratchasima province during June-August 2010. A voucher specimen number of *Centella asiatica* is BFK184894 from BGO Plant Database, The Botanical Garden Organization, Ministry of Environment and Natural Resources, Thailand.

Edible parts of *Centella asiatica* were washed with copious amounts of water and allowed to air dry at room temperature for 2 to 3 h. The plant was then cut into small thin pieces and dried at room temperature for 2 to 4 days. The dried thin pieces of plant were powdered using an electric mill with a 1 mm mesh. The dried powder was extracted by maceration method with 80% aqueous ethanol (100 g dried powder/500 ml of 80% aqueous ethanolic solution) for 7 days in the dark at room temperature. The obtained suspension was filtered through No.1 Whatman filter paper. The filtrate was collected, concentrated using a rotary evaporator and then converted into crude extract by freeze dryer. The obtained crude extract was stored at -20 ℃ until further used. On the day of each experiment, *Centella asiatica* extract was freshly prepared by dissolving in double deionized distilled (DDD) water at the desired concentration.

### 2.2. Animals

Male Wistar rats (200-250 g) were obtained from Institutional Animal Care, Suranaree University of Technology (SUT). They were maintained under standard laboratory conditions (12:12 h dark-light cycle, ambient temperature 20 ± 1 ℃) with free access to food and water. This study was conducted under permit of the SUT Animal Care and Use Committee.

### 2.3. L-NAME Induced Hypertension

Hypertension was induced experimentally in rats by N-nitro-L-arginine methyl ester (L-NAME), a nitric oxide synthase inhibitor (40 mg/ml/kg, i.p.) [15]. L-NAME was prepared everyday by dissolving in isotonic saline (0.9% NaCl).

### 2.4. Experimental Procedure

The rats were anaesthetized with sodium pentobarbital (50 mg/kg, i.p.) [16]. The trachea was exposed and cannulated to facilitate spontaneous respiration [17] and the left carotid artery was cannulated. For intragastric administration of the drugs, the stomach was intubated. The blood pressure was recorded directly through carotid artery cannulation by a pressure transducer coupled to PowerLab system with Chart program (ADInstruments) [18] and the Chart recorder was calibrated in mmHg to measure the blood pressure. After a 30 min period of equilibration, mean arterial blood pressure (MABP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were recorded 5 min before the rats (n=56) were intraperitoneally injected with L-NAME (40 mg/ml/kg, [15]). Thirty minutes later, *Centella asiatica* extract at the doses of 4, 8, 16, and 32 g/20 ml/kg, DDD water (20 ml/kg), quercetin (5 mg/20 ml/kg) [19] and propylene glycol (20 ml/kg) were intragastrically injected, n=8 each. The blood pressure and heart rate were then recorded for a further 90 min. At the end of experiment, rats were terminated with an overdose of sodium pentobarbital.

### 2.5. Statistics

All data were expressed as means ± SEM. Statistical analysis was peformed by two-way repeated measured ANOVA followed by Fisher LSD method using the software SigmaStat (version 3.5, Systat Software Inc., USA.). *P*-values less than 0.05 ($P<0.05$) were considered statistically significant.

## 3. Results

### 3.1. Effects on Arterial BP and HR of Anaesthetized Hypertensive Rats

In pentobarbital-anaesthetized rats, L-NAME significantly increased MABP, SBP and DBP, but not HR (Fig. 1). A single intragastric administration of *Centella asiatica* extract (4, 8 and 32 g/20 ml/kg) did not

cause changes in MABP, SBP and DBP (Fig. 1-3) of pentobarbital-anaesthetized L-NAME induced hypertensive rats. At 90 min after administration, *Centella asiatica* extract (16 g/20 ml/kg) significantly decreased the elevated MABP and DBP compared to control (DDD water) as shown in Fig. 1 and 3. During the period of 75-90 min, *Centella asiatica* extract (16 g/20 ml/kg) significant decreased the elevated SBP compared to control (DDD water) as shown in Fig. 2. From 10 min until 90 min after admistration of guercetin (5 mg/20 ml/kg) caused significantly decreased in the elevated MABP when compared to control (propylene glycol) as shown in Fig. 1. During the period of 45-90 min after administration, quercetin significantly decreased the elevated SBP and DBP (Fig. 2 and 3). All doses of *Centella asiatica* extract and quercetin had no effect on HR (All doses of *Centella asiatica* extract and quercetin had no effect on HR of anaesthetized hypertensive rats (data not shown).

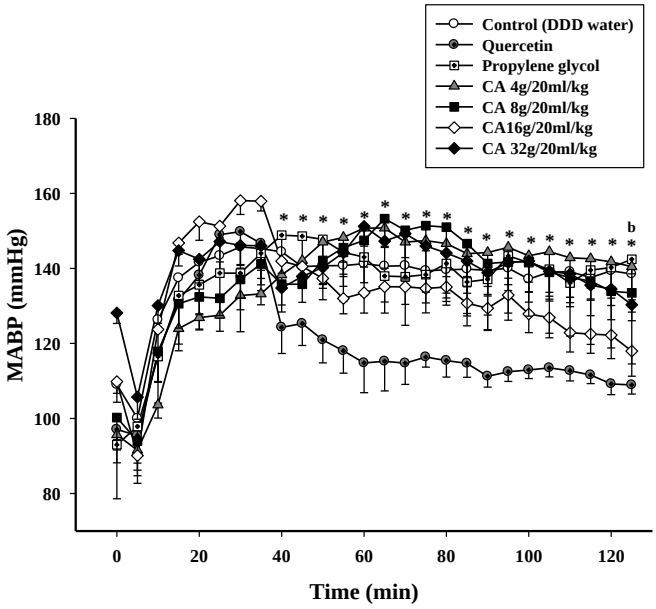


Fig. 1: Effects of the *Centella asiatica* extract (CA) on MABP of anaesthetized hypertensive rats. b denotes significant difference ($P$< 0.05) between CA at concentrations of 16 g/20 ml/kg compared to control (DDD water). * denotes significant difference ($P$<0.05) between quercetin compared to control (propylene glycol).

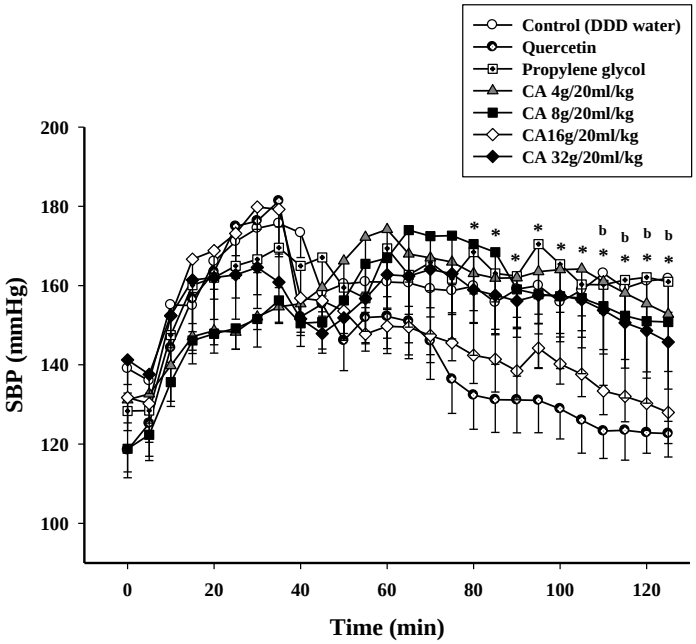


Fig. 2: Effects of the *Centella asiatica* extract (CA) on SBP of anaesthetized hypertensive rats. b denotes significant difference ($P$< 0.05) between CA at concentrations of 16 g/20 ml/kg compared to control (DDD water). * denotes significant difference ($P$<0.05) between quercetin compared to control (propylene glycol).

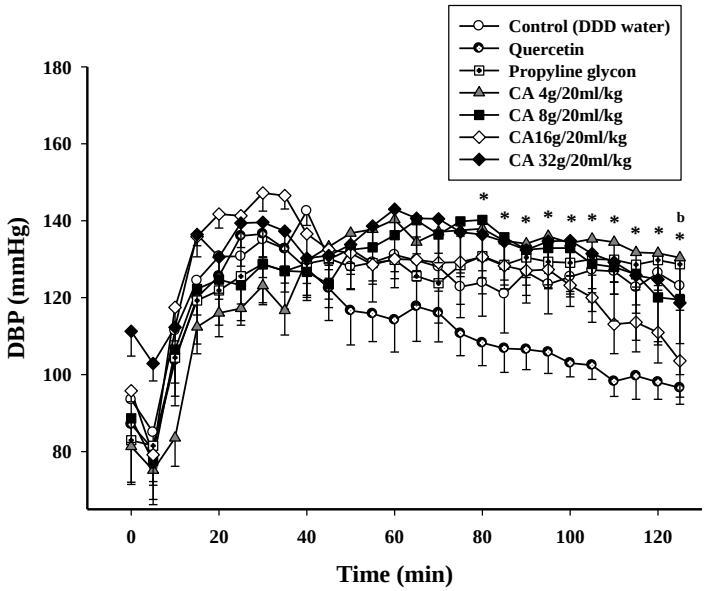


Fig. 3: Effects of the *Centella asiatica* extract (CA) on DBP of anaesthetized hypertensive rats. b denotes significant difference ($P< 0.05$) between CA at concentrations of 16 g/20 ml/kg compared to control (DDD water). * denotes significant difference ($P<0.05$) between quercetin compared to control (propylene glycol).

## 4. Discussion and Conclusion

The present results demonstrated antihypertensive effect of *Centella asiatica* extract at the concentration of 16 g/20 ml/kg (i.g.) and it flavonoid quercetin at the concentration of 5 mg/20 ml/kg (i.g.) in L-NAME induced hypertensive rats. Significant decreases in the elevated MBP, SBP and DBP in L-NAME induced-hypertensive rats were found after administration of *Centella asiatica* extract. These findings could be implied that *Cenella asiatica* extract possessed hypotensive effects on L-NAME induced-hypertensive rats. The findings of the current study are consistent with those of Muangnongwa (2004) [20] who found that fresh juice of *Centella asiatica* (32 g/kg, p.o.) could decrease SBP in deoxycorticosterone acetate (DOCA)-salt induced hypertensive rats, but had no effect in normotensive rats.

Quercetin, a flavonoid found in *Centella asiatica*, was found to possess hypotensive effects in L-NAME induced hypertensive rats. Quercetin significantly decreased the elevated MBP, SBP and DBP in L-NAME induced-hypertensive rats. These findings are an important extension of previous studies showing that quercetin can lower blood pressure in hypertensive animals [21]-[25]. *Centella asiatica* extract and quercetin administration did not caused alterations in heart rate in L-NAME induced hypertensive rats.

In conclusion, *Centella asiatica* extract supplement resulted in antihypertensive effects in hypertensive rats. Quercetin may be in part responsible for the antihypertensive effect of *Centella asiatica* extract. More detailed studies are required to evaluate the hypotensive and hypertensive effects of purified flavonoids from *Centella asiatica.*

## 5. Acknowledgements

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