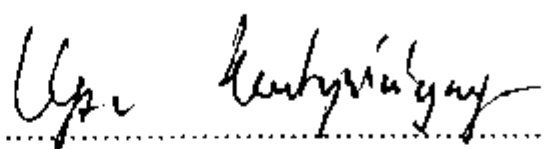
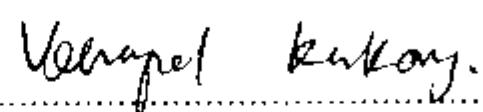


THESIS TITLE : ANTIHYPERTENSIVE EFFECT OF COMPOUNDS FROM *Centella asiatica* (L.) Urban. IN EXPERIMENTALLY INDUCED HYPERTENSIVE RATS

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ABSTRACT

Bua-Bok (*Centella asiatica* (L.) Urban.), a well-known Thai vegetable and medicinal herb, has long been used to relieve many kinds of illness, such as wound healing, peptic ulcer, varicose vein and venous hypertension, etc. The present study demonstrates the antihypertensive effect of the extracts from Bua-Bok in Goldblatt 2 kidney-1 clip (2K-1C) and N^G-nitro-L-arginine methyl ester (L-NAME)-induced hypertensive rats. The whole herb was dried and extracted either with 95% ethanol (called crude ethanol) or sequentially extracted by polarity with N-hexane, dichloromethane and 95% ethanol. In 2K-1C renovascular hypertension, male Sprague-Dawley rats were induced to hypertensive state by placing the 0.2 mm. of internal diameter silver clip onto the left renal artery while the two kidneys were intact. Systolic blood pressure (SP) measured by tail cuff method was more than 180 mmHg within 4 weeks after renal artery clipping. The other model of hypertension, male Sprague-Dawley rats was given 40 mg / kg BW / day L-NAME, a nitric oxide synthase inhibitor, in drinking water for 3 weeks. It was shown that L-NAME produced a progressive increase in SP which was above 180 mmHg after 2 weeks of treatment. Experiments were commenced after the fourth week in renovascular hypertension model and after the second week in L-NAME hypertension model.

Renal hypertensive rats were studied in two sets of experiments. In the first set, 2K-1C hypertensive rats were divided into 3 groups. Group 1 (n=6), served as control group, was fed orally with 1% tragacanth solution. Group 2 (n=5) and 3 (n=6) were fed daily with herb extract from crude

ethanol at dosage of 1 and 2 g / kg BW / day respectively, for 7 days. In the second set, 2K-1C hypertensive rats were assigned to 4 groups. Control group (n = 6) was fed with 1% tragacanth solution. Group 2-4 were fed once a day with the extract of herb from hexane (n=6), dichloromethane (n=5), and 95% ethanol (n=6) at dosage of 1 g / kg BW / day respectively, for 7 days. Heart rate, SP, body weight, water intake and urine output, urine osmolality, urinary electrolytes (Na^+ , K^+ and Cl^-) and vanillylmandelic acid (VMA) excretions were monitored throughout the experiments whereas mean arterial blood pressure (MAP) and hindlimb blood flow (HBF) were measured on the last day of the experiments. Results showed that the percent changes in SP in hexane, dichloromethane and high dose of crude ethanol treated rats were significantly decreased ($p < 0.05$). SP of treated rats decreased by $23.7 \pm 4.0\%$ in hexane group, $19.2 \pm 2.6\%$ in dichloromethane group and $23.2 \pm 4.0\%$ in high dose-crude ethanol group. The MAP measured directly from femoral artery was significantly reduced in hexane, dichloromethane, and high dose-crude ethanol groups ($p < 0.05$). Hindlimb vascular resistance (HVR) were found to be reduced in all treated groups, nevertheless hindlimb blood flow (HBF) was increased. While blood pressure was significantly decreased in some treatment groups, heart rate was unchanged when compared to the respective control and before treatments. Herb extract from hexane fraction was selected for screening the antihypertensive activity in L-NAME-induced hypertension model. Hexane fraction (1 g / kg BW / day, for 7 days; N=7) slightly attenuated the rise in systolic blood pressure when compared with the control group (N=6). Interestingly, the herb extract from hexane fraction significantly produced a fall in MAP, a rise in HBF and a decrease in HVR in L-NAME hypertensive rats ($p < 0.05$). For the rest of parameter measurements, volume of water intake and urine output, urine osmolality and urinary Na^+ , K^+ , Cl^- & VMA excretions within 24 hours in all experimental groups of both hypertensive animal models were not significantly different. Body weight, kidney and liver function tests by BUN, creatinine, AST and ALT measurements indicated that the herb extracts is inherent with low toxicity after repeated dose administration. In conclusion, these results suggest that the antihypertensive effect of compounds from *Centella asiatica* (L.) Urban. could not be due to the negative chronotropic effect, diuretic action or inhibition of sympathetic discharge. However, mechanism that might be contributable to the hypotensive properties of these herb extracts is the vasodilator effect which may lead to a reduction in peripheral vascular resistance.