Thesis Title	A Study on the Diuretic Effects of *Pluchea indica* in Man
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ABSTRACT

A single dose of *Pluchea indica* (PI; 3.6 gm of herbal powder packed in 12 capsules) as prepared in the form of freeze dry aqueous extract by the method developed by the Government Pharmaceutical Organization, Ministry of Public Health, was tested for its diuretic effect in 15 healthy adult Thai male volunteers and 30 randomly selected patients with renal calculi in one or both sides of the kidneys in a cross-over experimental design with a washout period of 24 hours. Hydrochlorothiazide (HCT, 50 mg, PO) was also used as a positive control and for comparison.

When the urine output from each of these 15 healthy volunteers and 30 patients receiving PI or HCT was analyzed statistically by using paired t-test, a significant difference in the 6-hr urine output was found only with HCT but not with PI when compared to that of the control. The 22-hr urine output caused by HCT was significantly higher than that of the control in both volunteers and patients, whereas PI produced a marginally significant urine output in only the healthy volunteers but not the patients.

A reproducibility study on the 22-hr urine output was conducted in 5 healthy volunteers, and it was found that the average intraindividual variation of the urine output of the volunteers given water or PI was 20%. This was equivalent to the diuretic index of 1.2, which was then used as a cut-off point to classify all 45 subjects as "responders" and "nonresponders". With this criterion, it was found that 8 subjects or 53% of the healthy volunteers and 7

subjects or 23% of the patients were responders to the diuretic action of PI. Similarly, 87% of the volunteers and 67% of the patients were found to be responders to the diuretic action of HCT.

When the data from both the volunteers and patients were pooled and stratified according to age, it was clear that the subjects in the age group of 31-40 years were most responsive to the diuretic action of PI. Declining renal functions with advancing age and renal stones as well as psychological stress inherent in the patients may be the responsible factors explaining this difference.

There was a great variation in the onset of the diuretic effect of PI. It was rapid in some and relatively slow in the others. This variation may be due to pharmacokinetic factors including different bioavailability as well as varying rate of metabolism of the active compounds or environmental factors such as room temperature or emotional stress. All subjects that were responsive to the diuretic action of PI were also responsive to that of HCT, but many who were responsive to HCT did not show any response to PI. Except in only 1 subject, the diuretic index of PI in all responders was lower than that of HCT, thus suggesting that PI possess a weaker diuretic action than HCT. As for their acute effects (6-hr urine output), both PI and HCT caused significant losses of sodium and chloride in the urine when compared to that of the control while only PI conserved potassium. However, both PI and HCT produced significant losses of all 3 urinary electrolytes in the 22-hr urine.

Based on the known mechanism of action of each prototype diuretic on the pattern of urinary electrolyte excretions, it is tempting to speculate that PI might exert its acute effect similar to that of the potassium-sparing diuretics such as spironolactone. This speculation is reasonable, since PI contains many active compounds in the class of the so-called "saponins" such as stigmasteryl glucoside whose chemical structure resembles spironolactone. However, the prolonged effect (22-hr urine output) of PI was similar to that of HCT, since both of them caused losses of all 3 major electrolytes.

Adverse drug reactions such as headache, dry mouth and throat, sedation and heartburn were observed in 6 out of 45 subjects (13%) receiving PI, but all of them were either transient or mild and did not seem to have any clinical significance. However, it is still uncertain whether these side effects are due directly to PI per se or to other pre-existing conditions of the subjects.