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Crude water extracts of Cymbopogon citratus (C. citratus) 1.25, 2.5, 5 and 10 g/kg-bw. was given orally via oro-gastric tubes in dogs anesthetized with sodium pentobarbital. Renal functions were elucidated every 30 min in the 4 hours following administration. The results found insignificant changes of circulatory hemodynamics and renal functions in 1.25, 2.5 and 5 g/kg-bw. dogs. Dogs receiving 10 g/kg-bw C. citratus showed significant decreases in heart rate during the first 1.5 - 2.5 hours. Urine volume, glomerular filtration rate and renal plasma flow decreased, while hematocrit increased significantly with slight change of the filtration fraction. Significant decreases in the plasma clearance of osmolality, accompanied with small decreases in free water clearance were demonstrated. Urinary excretion of sodium, potassium and chloride fell significantly with a decrease in fractional excretion. The results could be concluded that oral administration of crude water extracts of C. citratus do not have diuretic effects. The increases in urine flow may be due to the drinking of large amounts of water. Furthermore, higher doses may have some toxic effects. However, the mechanism is still unclear and needs to be investigated.

Key words : *Lemongrass, Cymbopogon citratus, Renal functions, Dogs.*

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พร้อมสุข ชุตาภา, บังอร ชมเดช. ผลของน้ำสกัดตะไคร้ต่อการทำหน้าที่ของไตสุนัข. จุฬาลงกรณ์เวชสาร 2538 มิถุนายน; 39(6): 425-435

ให้น้ำสกัดตะไคร้ขนาด 1.25, 2.5, 5 และ 10 กรัมต่อน้ำหนักตัว 1 กิโลกรัม ทางปากโดยผ่านท่อเข้าสู่กระเพาะอาหารแก่สุนัขที่สลบด้วยโซเดียมเพนโตบาร์บิตาล ตรวจวัดการทำหน้าที่ของไตทุกครึ่งชั่วโมงจนครบ 4 ชั่วโมงหลังให้น้ำสกัดตะไคร้ ผลการทดลองพบว่าน้ำสกัดตะไคร้ขนาด 1.25, 2.5 และ 5 กรัมต่อน้ำหนักตัว 1 กิโลกรัมไม่เปลี่ยนแปลงพลวัตของเลือดและการทำหน้าที่ของไต สุนัขกลุ่มที่ได้รับน้ำสกัดตะไคร้ขนาด 10 กรัมต่อน้ำหนักตัว 1 กิโลกรัมนั้นพบว่าอัตราการบีบตัวของหัวใจลดลงอย่างมีนัยสำคัญทางสถิติในช่วงเวลา 1.5-2.5 ชั่วโมง การขับถ่ายปัสสาวะ อัตราการกรอง และปริมาตรพลาสมาผ่านไตลดลงขณะที่ปริมาตรเซลล์เม็ดเลือดเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ พร้อมกับสัดส่วนของอัตราการกรองต่อพลาสมาเปลี่ยนแปลงเพียงเล็กน้อย การกำจัดออสโมลาลิตี้ออกทางปัสสาวะของไตลดลงร่วมไปกับกำจัดน้ำอิสระออกได้เพียงเล็กน้อย อัตราการขับถ่ายโซเดียม โปแตสเซียม และคลอไรด์ทางปัสสาวะลดลงอย่างมีนัยสำคัญทางสถิติพร้อมกับสัดส่วนของการขับออกต่ออัตราการกรองลดลง ผลของการศึกษาครั้งนี้พอจะสรุปได้ว่าการดื่มน้ำสกัดตะไคร้ไม่เพิ่มอัตราการขับปัสสาวะ ความเชื่อเดิมที่ว่าน้ำต้มตะไคร้มีฤทธิ์ในการขับปัสสาวะน่าจะเกิดจากการดื่มน้ำปริมาณมากนั่นเอง ยิ่งกว่านั้นยังพบว่าน้ำสกัดตะไคร้ที่ขนาดสูงเกินไปอาจจะเป็นพิษต่อร่างกายได้ อย่างไรก็ตามกลไกที่แน่นอนยังคงต้องทำการศึกษาต่อไปอีก

Cymbopogon citratus (lemongrass) is widely employed as a folk medicinal plant for the treatment of several diseases and symptoms. A herbal tea or decoction prepared from the dried leaves is called 'abafado' in Brazil. It is frequently used as a sedative and hypnotic, analgesic, antiemetic, antispasmodic and for other stomach disorders.[1,2] In Nigeria it is used as an antipyretic and antispasmodic.[3]

In Angola and India it is considered to be an antitussive, antiemetic, antiseptic and anti-rheumatic agents.[4] In Indonesia it is employed to help digestion and as a diuretic.[5] In ancient Thai medicinal treatments, it has been used as carminative, diuretic, antihypertensive, antianorexic, antispasmodic and analgesic agents, and it has been used for urinary tract problems.

Locksley et al. (1982) also reported that hot water extracts of dried leaves and stems of lemongrass has been used as an effective renal antispasmodic and diuretic in Egypt.[6] However, its action on renal functions has never previously been studied. Our research aimed to study the effects of crude water extracts on renal functions in order to confirm the diuretic effect which was previously conceptualized in many countries, including Thailand. Lemongrass is easily obtained and is very cheap in Thailand. This plant may be used as a medicine in the future.

Materials and methods

Preparation of crude extract of C. citratus

100 grams of lower lemongrass leaves of which had been dried in an oven at 60-70° C for 24-36 hours then boiled in distilled water for 5 minutes and then readjusted to a volume of 100 ml after filtration through muslin, The decoctions came to 100g/dl.

Animals and treatment

Twenty adult male mongrel dogs weighing 12-18 kg were maintained with free access to water and food. Each had been kept for at least 7 days prior to the experiment. They were fasted for 12 hours preceeding each operation. Each animal was anesthetized by intravenous injection of 25 mg/kg of sodium pentobarbital. A tracheostomy was performed and the animals were allowed to ventilate spontaneously in room air. Both femoral veins were catheterized, one for infusion of inulin and the other for infusion of normal saline and supplemental doses of sodium pentobarbital.

A catheter was inserted into the right femoral artery and connected to a pressure transducer for recording the systemic arterial blood pressure and heart rate on a Harvard universal oscillograph. The left kidney was exposed retroperitoneal through a flank incision and the left ureter was cannulated. The left renal artery was encircled with an electromagnetic flow probe and connected to electromagnetic blood flowmeter for recording the renal blood flow.

During the surgical and experimental procedures, isotonic saline was infused continuously at a rate 1.0-1.5 ml/min in order to maintain the extracellular fluid volume. A priming dose of 50 mg/kg inulin was administered, followed by sustaining infusion sufficient to maintain the plasma inulin concentration at approximately 20 mg/dl. A period of 50 min was allowed to elapse for stabilization of the general condition and plasma inulin concentration. Blood and urine samples were obtained for two control periods of 30 minutes. Arterial blood was drawn at the midpoint of each urine collection period.

C. citratus in 10 ml doses of 1.25, 2.5, 5 or 10g/kg was intragastrically administered as a single dose in each group of 5 dogs. The concentrations of sodium and potassium, chloride and inulin were determined by use of a flame photometer (KLiNa Flame Operating-Bechman Instrument, Instrument Lab. model 343), chloride analyzer (Bechman Instrument), and Jaffy reaction,(7) respectively. Plasma osmolality was measured by freezing point depression technique. Hematocrit was also determined from each blood sample.

At the end of experiment the left kidney was excised, stripped of surrounding fat and tissue, blotted dry and weighed so that the kidney functions could be expressed as per gram kidney weight. The results are shown as mean ± SEM between before and after feeding. The statistical significance was assessed by using the Student's paired t-test with a p value less than .05.

Results

Effect of C. citratus on mean arterial pressure, heart rate and hematocrit.

Figure1 demonstrated that during experimental period, there were slightly changes in mean arterial pressure (MAP), heart rate (HR) and hematocrit (Hct) in small doses until 5 g/kg. In 10 g/kg dogs, the increase of MAP and the decrease of HR were significant during 1-2.5 hrs as compared to the control value. Although the Hct was significantly increased throughout the experimental period as shown in figure 1 and table 1.

Effect of C. citratus on urine flow rate, renal plasma flow, glomerular filtration rate and filtration fraction.

As shown in figure 2 and table 1, the urine flow rate (V) was significantly decreased in 10 g/

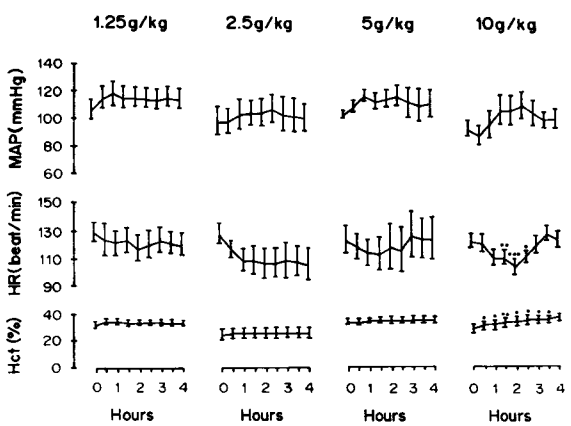

Figure 1. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of mean arterial pressure (MAP), heart rate (HR) and hematocrit (Hct).
*p < .05, **p <.01, ***p <.005

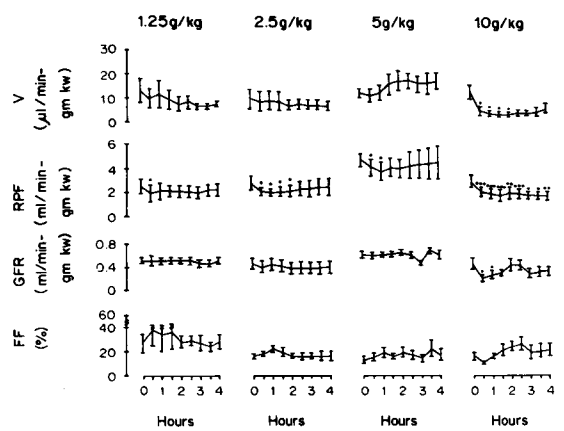

Figure 2. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of urine flow rate (V), renal plasma flow (RPF), glomerular filtration rate (GFR) and filtration fraction (FF).
*p < .05, **p <.01, ***p <.005

Table 1. The significant changes in mean ± SEM of renal and circulatory hemodynamics following C. citratus administration.

Parameters	Doses	Hours								
	g/kg	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
HR	10	122.20	120.00	110.80	109.60**	103.4***	110.40*	119.00	127.20	123.00
beat/min		±5.51	±6.54	±6.09	±5.84	±6.98	±3.71	±5.81	±5.57	±5.97
Hct	10	29.40	31.20*	32.60*	33.40**	34.20*	35.00*	34.80*	34.80*	37.00
%		±1.99	±1.88	±1.97	±1.86	±1.93	±2.30	±2.29	±2.11	±2.42
V	10	12.48	4.59*	3.46*	3.26*	3.34*	3.73	3.46	3.95	5.75
µl/min-g kw		±3.19	±1.86	±1.38	±1.01	±0.89	±0.99	±0.94	±1.08	±1.80
	1.25	2.47	2.08*	2.17	2.14	2.11	2.12	2.08	2.20	2.21
		±0.67	±0.72	±0.60	±0.58	±0.51	±0.48	±0.53	±0.49	±0.50
RPF	2.5	2.86	2.12*	1.99*	2.09*	2.15*	2.33	2.33	2.52	2.50
ml/min-g kw		±0.58	±0.38	±0.31	±0.41	±0.49	±0.58	±0.68	±0.71	±0.76
	5	4.74	4.09*	3.86*	4.10	4.04	4.29	4.39	4.44	4.57
		±0.57	±0.68	±0.79	±0.83	±0.86	±1.18	±1.26	±1.32	±1.40
	10	2.99	2.13***	1.87***	1.83***	1.98**	1.94***	1.86*	1.86*	1.85**
		±0.48	±0.43	±0.41	±0.48	±0.52	±0.45	±0.35	±0.36	±0.41
GFR	10	0.47	0.22*	0.29*	0.31	0.42	0.42	0.30	0.33	0.35
ml/min-g kw		±0.11	±0.04	±0.07	±0.03	±0.09	±0.08	±0.07	±0.08	±0.08

* P<.05, **p<.01, ***p<.005

kg dogs at the period of 2 hrs. The decrease of renal plasma flow (RPF) was seen significantly in 1.25 g/kg dogs at the period of 30 min. However, this decrease of RPF was stayed for 2 hrs in 2.5 g/kg dogs. In addition, the results were shown that RPF of the 5 g/kg dogs was significantly decreased during the first hour as compared to the control value.

At the highest dose (10 g/kg), the RPF was decreased significantly throughout the experimental period. Besides, during the first hour, the glomerular filtration rate (GFR) was decreased significantly without significant change in filtration fraction (FF) throughout the experimental period as demonstrated in figure 2.

Effect of C. citratus on plasma concentration, excretion rate and fractional excretion of sodium.

The results shown in figure 3 and table 2 indicated that plasma concentration of sodium (P_{Na}) was not altered after administration of C. citratus, while there were significant decreases of excretion rate ($U_{Na}V$) and fractional excretion (FE_{Na}) except dogs that received 2.5 g/kg of C. citratus. The reduction of $U_{Na}V$ in 1.25 g/kg dogs was observed during 1.5 hrs. However, at 5 g/kg, $U_{Na}V$ and FE_{Na} were significantly decreased observed only at one hour period after the C. citratus administration. The results monitored from 10 g/kg indicated that $U_{Na}V$ was significantly decreased during the period of 0.5-3.5 hrs. In addition, FE_{Na} was significantly decreased during the period of 1.0-2.5 hrs as shown in table 2.

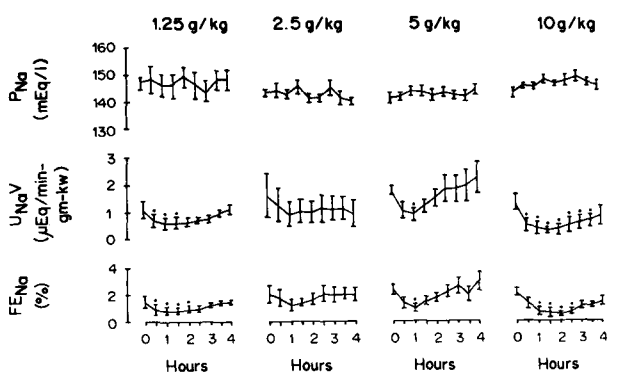

Figure 3. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of plasma concentration of sodium (P_{Na}),excretion rate of sodium ($U_{Na}V$) and fractional excretion of sodium (FE_{Na}).
*p < .05, **p <.01, ***p <.005

Effect of C. citratus on plasma concentration, excretion rate and fractional excretion of potassium.

The results shown in figure 4 and table 2 indicated that the plasma concentration of potassium (P_K) was significantly increased during 1-2.5 hrs, while the excretion rate of potassium (U_KV) was significantly decreased during the period of 0.5-1.5 hrs after the administration of 10 g/kg C. citratus without significantly changes of fractional excretion of potassium (FE_K).

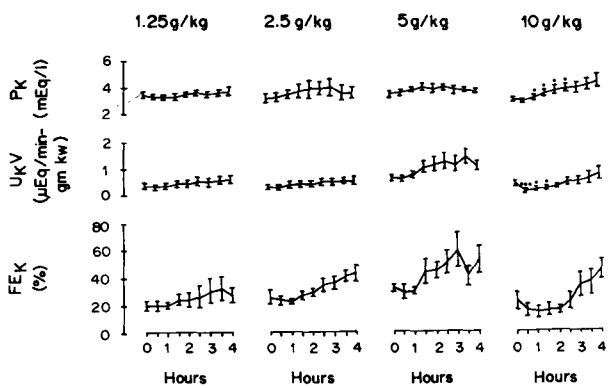

Figure 4. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of plasma concentration of potassium (P_K),excretion rate of potassium (U_KV) and fractional excretion of potassium (FE_K).
*p < .05, **p <.01, ***p <.005

Effect of C.citratus on plasma concentration, excretion rate and fractional excretion of chloride.

There were slightly changes in plasma concentration of chloride (P_{Cl}) as demonstrated in figure 5. The significant decrease in excretion rate ($U_{Cl}V$) during 1 to 3 hrs after the administration of 10 g/kg was observed. However, the reduction of fractional excretion (FE_{Cl}) was only observed at 2 hrs as shown in figure 5 and table 2.

Table 2. The significant changes in mean ± SEM of electrolytes and osmolality following C. citratus administration.

Parameters	Doses	Hours								
	g/kg	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
	1.25	1.13	0.68*	0.61*	0.59*	0.61	0.71	0.75	0.95	1.09
		±0.27	±0.21	±0.19	±0.16	±0.09	±0.09	±0.12	±0.14	
$U_{Na}V$	5	1.75	0.99	0.87*	1.15	1.47	1.83	1.82	1.93	2.22
μEq/min-g kw		±0.16	±0.28	±0.24	±0.23	±0.29	±0.50	±0.52	±0.60	±0.61
	10	1.33	0.47*	0.35*	0.27*	0.33*	0.47*	0.57*	0.62*	0.81
		±0.35	±0.26	±0.24	±0.16	±0.21	±0.24	±0.27	±0.25	±0.38
	1.25	1.51	0.91*	0.79*	0.81*	0.85*	0.96	1.20	1.39	1.39
		±0.38	±0.39	±0.27	±0.24	±0.23	±0.17	±0.14	±0.15	±0.12
FE_{Na}	5	2.33	1.28	0.95*	1.46	1.66	2.12	2.56	1.87	2.85
%		±0.41	±0.38	±0.22	±0.37	±0.30	±0.46	±0.62	±0.48	±0.75
	10	1.99	1.21	0.61*	0.56*	0.40*	0.66*	1.07	1.09	1.37
		±0.28	±0.46	±0.27	±0.30	±0.16	±0.22	±0.33	±0.24	±0.35
P_K	10	3.02	2.99	3.24*	3.49*	3.68*	3.85*	3.94	4.14	4.42
μEq/L		±0.16	±0.18	±0.19	±0.22	±0.28	±0.34	±0.37	±0.42	±0.56
$U_K V$	10	0.41	0.15***	0.20*	0.21*	0.29	0.45	0.50	0.63	0.77
μEq/min-g kw		±0.58	±0.03	±0.07	±0.06	±0.08	±0.11	±0.15	±0.21	±0.24
$U_{Cl}V$	10	1.18	0.39	0.25*	0.19*	0.17	0.25*	0.24*	0.38	0.60
μEq/min-g kw		±0.33	±0.25	±0.18	±0.12	±0.11	±0.17	±0.13	±0.17	±0.29
FE_{Cl}	10	2.31	1.24	0.52	0.51	0.26*	0.39	0.53	0.77	1.30
%		±0.62	±0.59	±0.25	±0.29	±0.11	±0.19	±0.21	±0.28	±0.50
C_{Osm}	10	14.96	5.15**	5.75*	5.26*	6.59*	7.95*	7.82*	9.05	12.32
μl/min-g kw		±3.24	±2.31	±2.55	±1.55	±2.28	±2.43	±2.45	±2.72	±3.85

*p<.05, **p<.01, ***<.005

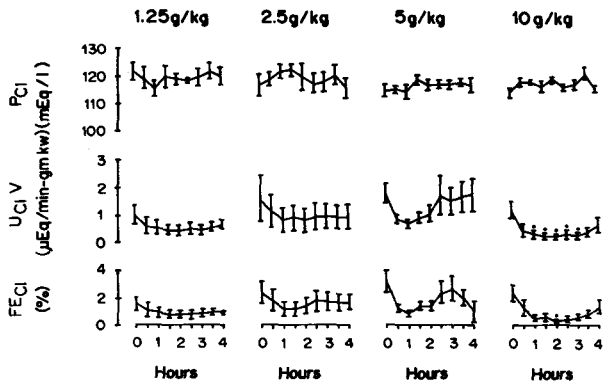

Figure 5. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of plasma concentration of chloride (P_{Cl}),excretion rate of chloride ($U_{Cl}V$) and fractional excretion of chloride. (FECl)
*p < .05, **p <.01, ***p <.005

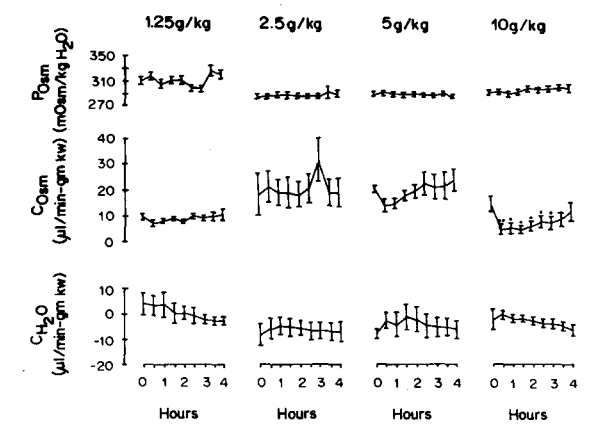

Figure 6. Effect of C. citratus 1.25,2.5,5 and 10 g/kg on mean ± SEM of plasma osmolality (P_{Osm}), clearance of osmolality (C_{Osm}) and free water clearance (C_{H2O}).
*p < .05, **p <.01, ***p <.005

Effect of C. Citratus on plasma osmolality, plasma clearance of osmolality and free water clearance.

Plasma osmolality (P_{Osm}), plasma clearance of osmolality (C_{Osm}) and free water clearance (C_{H2O}) were altered insignificantly in dogs received 1.25, 2.5 and 5 g/kg as indicated in figure 6. In 10 g/kg, the C_{Osm} was decreased significantly during the period of 0.5-3 hrs without significant changes in C_{H2O} as shown in figure 6 and table 2.

Discussion

Preliminary studies demonstrated that a 0.3 g/kg decoction of C. citratus showed hypotensive effects when given intravenously to rats, while 5 g/kg decoction showed diuretic effects when given orally.[8] Conversely, our investigations found that 1.25 and 2.5 g/kg of decoction had no effects on arterial blood pressure whereas 10 g/kg showed slight increases at the period of1.5-2.5 hrs after feeding and this was accompanied with a significant decrease in HR (figure 1 and table 1).

The increment of vascular resistance may be responsible for the increase in arterial blood pressure that in turn elicited reflex decreases in heart rate and cardiac output via the arterial baroreceptor.[9] In addition, the augmentation of arterial blood pressure is probably due to an increase in blood viscosity which was shown by the hematocrit. The increase in hematocrit was probably caused by an increase in circulating red cell mass induced by splenic contraction as described by Bell et al., (1981).[10] However, this may be unlikely because in the third hour of highest concentration of decoction the MAP returned to its baseline value whereas the Hct continued to increase (figure 1 and table 1).

GFR and RPF were decreased after intragastric administration of 10 g/kg decoction (figure 2 and table 1). These changes may be due to the action of some substances in C. citratus on

vascular smooth muscle. The increase in vascular resistance accompanied with hematocrit becomes important in the distal glomerular capillaries and efferent arterioles. In efferent arteriole, Hct was even higher than in the afferent arterioles due to glomerular filtration. Thus, the decrease in GFR was less than RPF resulting increases in FF (figure 2 and table 1).

In addition, the alternation of resistance in renal vessels that decrease GFR and RPF may be caused by the secretion of renin from JG-cells resulting in vasoconstriction. Nevertheless, Linas et al.(1980) reported that pentobarbital anesthesia decreased RBF, increased systemic and renal vascular resistances and contributed to the failure to excrete a normal saline load.[11]

The urine flow rate and osmolar clearance were significantly decreased when the dogs were given the crude extract from C. citratus at 10 g/kg oral doses (figures 2 and 6, tables 1 and 2). These changes may result from the decrease in RPF and GFR. Since vasopressin causes increases of water reabsorption in distal and collecting tubules, the decrease in the urine flow rate and negative free water clearance which was exhibited probably due to the same reason. It has been demonstrated by Robertson (1977) and Goetz et al. (1988) that vomit is a potent stimulus for vasopressin secretion.[9,12] In the present study, two dogs at the highest dose vomited after receiving the decoction. Therefore, this may suggest that dogs have some increases in circulating vasopressin levels.

The decreases in the urinary excretion rates of sodium, potassium and chloride in 10 g/kg dogs as demonstrated in figures 3, 4, 5 and table 2 may be due to a vasoconstrictive action of some substances in lemongrass causing a substantial decreases in GFR that in turn is responsible for the reduced electrolyte excretion. The significant increases in plasma potassium (P_K) may result from permeability changes in the membrane of erythrocytes or damage of the Na^+, K^+-pump at this membrane. It would cause leakage of K^+ efflux to blood circulation. However, the hemolysis may not support the change of P_K in this experiment because there was no evidence of hemolysis in the plasma samples.

The increment of P_K is probably due to pseudohyperkalemia while the elevated potassium concentration occurs in vitro not in vivo.[13,14] In addition, Ifudu et al. (1992) described that a circulating uremic toxin which inhibits cell membrane ouabain sensitive Na^+, K^+-ATPase has been implicated as the cause of lowered intracellular potassium.[15] They suggested that if this inhibition is present in vitro, it might lead to increased leakage of potassium from cells in serum samples with resultant exaggeration of pseudohyperkalemia in the uremic patients.

The loss of potassium from the leukocytes may increase extracellular potassium concentrations. In undialysed patients with advanced renal failure, leukocyte sodium and water contents were significantly greater than normal, while leukocyte potassium content was reduced.[16] These changes may occur because when potassium is lost from the cells, its replacement by sodium might increase the total osmotically active cation and hence cell water. The alternation may cause the increased plasma potassium and the reduction of sodium excretion in the urine for stability of plasma sodium.

This study could be summarized that the effects of intragastric administration of crude water decoction from C. citratus at concen-

trations of less than 5 g/kg on hemodynamics and renal functions were not different from the baseline control at the starting time. Therefore, these results did not agree with original concept that the drinking of this decoction cause increases in urine flow as a diuretic. Thus, the increases in urine flow in that concept may be due to drinking a large amount of water. Besides, at highest concentrations, the decreasing of urine flow rate and urinary excretion of electrolytes and this may be due to hemoconcentrations to trigger the kidney to reabsorb water and electrolyte. However, the direct mechanism is still unclear and it needs to be searched for and investigated.

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