ORIGINAL ARTICLE

Acute and subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch. in rats

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Abstract

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The water extract from root of *Imperata cylindrica* (Linn.) Raeusch. was studied for acute and subchronic toxicities. The extract at a single dose of 5,000 mg/kg was administered orally to female and male rats (5 male, 5 female). After 14 days, signs and behavioral changes, mortality, gross and histopathological changes of internal organs were examined. The extract did not produce signs of toxicity. For the subchronic toxicity test, the extract at doses of 300, 600 and 1,200 mg/kg body weight was orally administered to rats daily for 90 days (10 male, 10 female). The observation of signs, behavior and health status showed no

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abnormality in the test groups as compared with the controls. At the end of the study, necropsy and histopathology examination were performed in all animals in the control group, the test groups and the satellite group in which the extract was discontinued for another 28 days. Body and organ weights, hematological and blood clinical chemistry were also examined. The results suggest that the water extract of *Imperata cylindrica* (Linn.) Raeusch does not cause acute and subchronic toxicities in rats.

Key words : acute toxicity, subchronic toxicity, *Imperata cylindrica* (Linn.) Raeusch

บทคัดย่อ

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การศึกษาความเป็นพิษเฉียบพลันและกึ่งเรื้อรังของสารสกัดน้ำจากรากหญ้าคาในหนูขาว

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การศึกษาความเป็นพิษเฉียบพลันและพิษกึ่งเรื้อรังของสารสกัดน้ำจากรากหญ้าคา (*Imperata cylindrica* (Linn.) Raeusch) พบว่า การป้อนสารสกัดครั้งเดียวทางปากขนาด 5,000 มก./กก.น้ำหนักตัว (เพศผู้ 5 ตัว เพศเมีย 5 ตัว) ไม่ก่อให้เกิดอาการแสดงความเป็นพิษ การเปลี่ยนแปลงพฤติกรรม การตายและความเปลี่ยนแปลงของลักษณะทางกายวิภาคและจุลพยาธิวิทยาของอวัยวะภายใน ผลการศึกษาความเป็นพิษกึ่งเรื้อรังโดยการป้อนสารสกัดทางปากแก่หนูขาวทั้งเพศผู้และเพศเมียทุกวันในขนาด 300 600 และ 1,200 มก./กก.น้ำหนักตัวเป็นเวลา 90 วัน (เพศผู้ 10 ตัว เพศเมีย 10 ตัว) ไม่พบความผิดปกติทางอาการ พฤติกรรม และสุขภาพของหนูขาวกลุ่มที่ได้รับสารสารสกัดเมื่อเทียบกับกลุ่มควบคุม ผลการชั่งน้ำหนักตัวสุดท้าย การผ่าพิสูจน์ซากสัตว์ทดลอง การชั่งน้ำหนักอวัยวะ การตรวจค่าโลหิตวิทยา ค่าเคมีคลินิกของเลือดและการตรวจจุลพยาธิวิทยาของหนูกลุ่มทดสอบ กลุ่มควบคุม และกลุ่มติดตามผลซึ่งหยุดยา 28 วัน พบว่าปกติ ดังนั้นการศึกษานี้สามารถสรุปได้ว่าสารสกัดน้ำจากรากหญ้าคาไม่ก่อพิษเฉียบพลันและพิษกึ่งเรื้อรังในหนูขาว

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Imperata cylindrica (Linn.) Raeusch, the noxious rhizomatous grass in Gramineae family, with Thai name of Yakha, is widely distributed in the tropics and subtropical regions. It has been ranked as one of the 10 worst weeds in the world. It is also found in some parts of the temperate regions in Asia as well as Australia and South Africa (Garritty *et al*., 1997; Holm *et al*., 1977; Kumar *et al*., 1998; Terry *et al*., 1997). The rhizomes of *I. cylindrica* have been described as diuretic, anti-inflammatory or antipyretic agent in Korean traditional herbal medicine (Park, 2004). It was reported by Sripanidkulchai *et al*. (2001), that the water extract from *I. cylindrica* rhizomes apparently inhibits the urination in rats. On the contrary, Kanchanapee (1966, 1967) showed an antidiuretic effect of *I. cylindrica*. Thus, a more critical review of *I. cylindrica* is required before continuing to prescribe it as a diuretic drug and it needs further investigation to determine the effectiveness of *I. cylindrica* in the treatment of dysuria.

Several studies have documented several compounds isolated from the rhizomes of *I. cylindrica* such as arundoin, cylindrin, fernenol, cylindol, cylindrene, graminones and imperanene (Matsunaga *et al*., 1994a, 1994b, 1994c, 1995). Cylindol A possesses 5-lipoxygenase inhibitory activity, whereas graminone B inhibits the contraction of the rabbit aorta (Matsunaga *et al*., 1994a, 1994c). Cylindrene shows an inhibitory activity on contractions of vascular smooth muscle

(Matsunaga *et al*., 1994b). In addition, the platelet aggregation inhibitory activity of imperanene has been reported (Matsunaga *et al*., 1995). The methanolic (MeOH) extract of the rhizomes of *I. cylindrica* is constituted of four compounds, 5-hydroxy-2-(2-phenylethyl) chromone (1), 5-hydroxy-2-[2-(2-hydroxyphenyl) ethyl] chromone (2), flidersiachromone (3), and 5-hydroxy-2-styrylchromone (4). The first and the second compound have neuroprotective activity against glutamate-induced neurotoxicity in primary cultures of rat cortical cells at a concentration of 10.0 μM (Yoon *et al*., 2006).

Harbored inside the normal stem of healthy *I. cylindrica*, an endophyte, *Chaetomium globosum* IFB-E019, can produce cytotoxic cytochalasan-based alkaloid named chaetoglobosin U. This substance exhibits cytotoxic activity against the human nasopharyngeal epidermoid tumor KB cell line with an IC_{50} valve of 16.0 μM (Ding *et al*., 2006). However, no study on the systemic toxicity of *I. cylindrica* has been reported. The purpose of this study was to evaluate the safety of water extract of I. cylindrica in rats by determining both oral acute and subchronic toxicities.

Materials and methods

Plant material

The roots of *I. cylindrica* were collected from Songkhla, Thailand. The voucher specimen (SBK 0011) was kept and identified by the National Park, Wildlife and Plant Conservation Department, Ministry of Natural Resources and Environment, Bangkok, Thailand.

Preparation of plant extract

Root powder of *I. cylindrica*, 500 grams was wrapped in a calico bag and put into a stainless boiler. Ten liters of water were added, then boiled for 3-4 hours and collected the filtrate. The residue was extracted again. The combined filtrates were evaporated to dryness in a rotary evaporator.

Laboratory animals

Male and female Sprague-Dawley rats, weighing 130-190 g were obtained from the National Laboratory Animal Center, Nakorn Pathom, Thailand. They were all clinically healthy and maintained in environmentally controlled conditions at 24±1°C under a 12-hour-dark-light cycle, and given a standard diet and water ad libitum, throughout the experimental period. All of the experimental protocols in animals were ethically approved by The Animal Ethics Committee of Faculty of Medicine, Thammasat University.

Acute toxicity study

Acute toxicity test was performed according to the World Health Organization (WHO) guideline (WHO, 2000) and the Organization of Economic Co-operation and Development (OECD) guideline for testing of chemicals (OECD, 2001). The extract was prepared at the concentration of 2,500 mg/ml in distilled water. Five animals per sex were administered a single oral dose of 5,000 mg/kg body weight while distilled water was given to the other group of rats as a control. All rats were observed at the first, second, fourth and sixth hours and thereafter once daily over 14 days for clinical signs of toxicity such as respiratory pattern, color of body surfaces, frequency and nature of movement, marked involuntary contraction or seizures of contraction of voluntary muscle, and loss of reflex etc. After the experimental period, all animals were sacrificed and their internal organs including heart, lungs, livers, kidneys, spleen, adrenals, sex organs and brain were weighted and taken for gross pathological examination.

Subchronic toxicity study

The method was performed following the protocol described by the WHO guideline (WHO, 2000) and the OECD guideline for testing of chemicals (OECD, 1981). Male and female rats were randomly divided into four groups of ten. The extract was prepared at concentrations of 300, 600 and 1,200 mg/ml in distilled water. The extract was orally administered to treated groups at doses of 300, 600 and 1,200 mg/kg/day, while distilled water was given to the control group. An additional

group was devised as the satellite group in order to observe the reverse sign of any toxicity. The satellite group was orally treated with the extract at a daily dose of 1,200 mg/kg/day for 90 days, and no further treatment for the following 28 days before termination of the study.

At the end of the study, all rats were fasted overnight and anesthetized with ether for blood collection. Blood was collected from the common carotid artery into a heparinized tube for hematological studies (complete blood count, red blood cell count, platelet count and red cell indices). The serum was separated for determining the concentrations of glucose, blood urea nitrogen (BUN), creatinine, total protein, albumin, total bilirubin, direct bilirubin, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT) and alkaline phosphatase (ALP).

After the blood collection, internal organs including heart, lungs, thymus, liver, kidneys, spleen, adrenals, small intestine, stomach and duodenum, muscle with sciatic nerve, thoracic spines, brain, eyes, sex organs, uterus and epididymis were examined for gross pathology. All tissues were fixed in 10% buffered formalin solution. After routine processing, the paraffin sections of each tissue were cut at 5 μm thickness and stained with haematoxylin and eosin for histopathological examination.

Statistical Analysis

Results were expressed as mean ± standard error of mean (S.E.M.). Statistical significance was determined by one-way analysis of variance (ANOVA) and post hoc least-significant difference (LSD) test. The data obtained from acute toxicity studies was analyzed using Student's paired t-test. P values less than 0.05 were considered significant.

Results and discussion

The percentage of yield of water extract was 50.86. In the acute toxicity study, rats fed with the water extract of *I. cylindrica* at the dose of 5,000 mg/kg did not show any signs of toxicity in the entire period of 14 days of observation. There were no significant differences in body weight gain or internal organ weight when compared with the control group as showed in Tables 1 and 2, respectively. Moreover, gross and pathological examinations of the internal organs revealed no pathological abnormality. These results suggest that the water extract from root of *I. cylindrica* is not toxic after an acute exposure to the dose of 5,000 mg/kg..

For the subchronic toxicity study, the body weight and body weight gain of both male and female treated groups are shown in Table 3. The body weight of both female and male rats treated with the extract at all three doses (300, 600, and 1,200 mg/kg/day) showed a significant decrease on day 90^{th} as compared with that of the control groups. In the satellite groups, the body weight gain of the male rats on day 90^{th} was significantly less than that of the control group, but the weight gain was still normal in the female rats. These results suggest that the extract from *I. cylindrica* affected the body weight gain. However, all of the animals were healthy as shown by the normal appearance of respiratory pattern, color of body surfaces, frequency and nature of movement, marked involuntary contraction or seizures of contraction of voluntary muscle, and loss of reflex etc. As shown in Table 4, the internal organ weights were not significantly changed in female treated groups except for heart and kidneys as compared with those of the control, whereas male treated groups had significant decreases in heart and spleen weights. In the satellite male group, only the heart weight was significantly decreased. Nonetheless, all of the increases or decreases were slight changes and the differences could have been due to the variation in size of internal organs of the animals (Carol, 1995). Moreover, there were no signs of behavior changes in any treated groups. Following necropsy and pathological examination, no abnormal change in the internal organs of any rats was observed. To determine intravascular effect and bone marrow activity in rats treated with the extract, hematological parameters of female and male rats were examined as presented in Tables 5

Table 1. Body weights of rats in the acute toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Body weight (g)			
	Day 0	**Day 7th**	**Day 14th**	**Weight gain on day 14th**
Female				
Control	130.80±10.67	158.00±6.32	172.00±9.34	41.20±1.62
I. cylindrical 5,000 mg/kg	125.20±4.32	160.00±6.75	174.80±6.53	49.60±3.87
Male				
Control	142.00±4.43	190.00±7.56	228.00±10.53	86.00±6.60
L. cylindrical 5,000 mg/kg	138.40±2.79	184.40±3.12	220.00±4.00	81.60±2.86

Values are expressed as mean ± S.E.M., n = 5.
There were no significant differences at p<0.05.

Table 2. Organ weights of rats in the acute toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Organ weight (g)	
	Control	***I. cylindrica* 5,000 mg/kg**
Female		
Lung	1.06±0.06	1.16±0.06
Heart	0.76±0.04	0.89±0.07
Liver	7.63±0.39	6.31±0.3
Spleen	0.50±0.02	0.57±0.04
Adrenal	0.04±0.00	0.03±0.00
Kidney	0.79±0.03	0.78±0.02
Ovary	0.06±0.00	0.07±0.00
Male		
Lung	1.14±0.05	1.17±0.06
Heart	0.99±0.04	0.90±0.04
Liver	8.38±0.88	7.04±0.18
Spleen	0.77±0.06	0.73±0.02
Adrenal	0.04±0.00	0.03±0.00
Kidney	1.03±0.04	0.98±0.02
Testis	1.80±0.07	1.28±0.02

Values are expressed as mean ± S.E.M., n = 5.
There were no significant differences at p<0.05.

and 6, respectively. The results showed no change in hematological parameters in the female rats treated with the extract. In contrast, red blood cells, hemoglobin concentration and hematocrit in male rats treated with 300 and 600 mg/kg/day were significantly lower than those of the control values. Administration of 1,200 mg/kg/day led to a significant increase in mean corpuscular hemoglobin (MCH) when compared to that of the control group. In the satellite group, mean corpuscular volume, MCH and mean corpuscular hemoglobin concentration were significantly increased, but red

Table 3. Body weights of rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Body weight (g)			
	Day 0	**Day 90th**	**Day 118th**	**Weight gain on day 90th**
Female				
Control	146.40±3.63	275.50±4.17	-	129.10±5.89
I. cylindrica 300 mg/kg	147.20±2.58	259.00±4.41*	-	111.80±3.45*
I. cylindrica 600 mg/kg	140.90±3.10	256.40±4.71*	-	115.50±2.38
I. cylindrica [a] 1,200 mg/kg	143.20±3.79	256.20±5.58*	-	113.00±5.73*
I. cylindrica [b] 1,200 mg/kg	138.20±2.72	264.20±5.18	277.60±6.59	126.00±5.24
Male				
Control	175.40±5.93	431.20±17.66	-	255.80±19.44
I. cylindrica 300 mg/kg	174.40±3.81	378.80±8.41*	-	204.40±10.29*
I. cylindrica 600 mg/kg	177.40±2.13	360.80±7.47*	-	183.40±6.81*
I. cylindrica [a] 1,200 mg/kg	185.60±5.10	391.20±12.16*	-	205.60±16.29*
I. cylindrica [b] 1,200 mg/kg	189.00±7.74	386.80±10.70*	415.40±9.55	197.80±15.56*

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, p<0.05.**

Table 4. Organ weights of rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	***I. cylindrica***			
		300 mg/kg	**600 mg/kg**	**1,200 mg/kg [a]**	**1,200 mg/kg [b]**
Female					
Lung	1.29±0.03	1.34±0.04	1.20±0.03	1.17±0.04	1.24±0.06
Heart	1.06±0.03	0.99±0.02	0.97±0.02*	0.92±0.02*	1.07±0.04
Liver	5.76±0.16	6.21±0.38	5.47±0.18	5.48±0.11	6.13±0.31
Spleen	0.68±0.02	0.67±0.01	0.68±0.02	0.62±0.02	0.74±0.04
Adrenal	0.05±0.00	0.04±0.00	0.05±0.00	0.04±0.00	0.04±0.00
Kidney	1.00±0.03	0.89±0.02*	0.85±0.01*	0.82±0.01*	0.84±0.01*
Ovary	0.11±0.00	0.10±0.00	0.10±0.00	0.08±0.00*	0.07±0.00*
Male					
Lung	1.74±0.10	1.57±0.06	1.50±0.05*	1.74±0.09	1.61±0.03
Heart	1.53±0.04	1.29±0.02*	1.21±0.02*	1.31±0.03*	1.38±0.04*
Liver	10.64±0.40	10.02±0.17	9.72±0.60	9.82±0.46	9.76±0.23
Spleen	0.95±0.03	0.81±0.02*	0.75±0.02*	0.84±0.02*	0.89±0.03
Adrenal	0.04±0.00	0.04±0.00	0.04±0.00	0.04±0.00	0.05±0.00
Kidney	1.34±0.02	1.23±0.01	1.12±0.03	1.22±0.02	1.23±0.01
Testis	1.96±0.02	1.90±0.03	1.88±0.03	1.93±0.02	1.92±0.03

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, p<0.05.**

Table 5. Hematological values of female rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	*I. cylindrica*			
		300 mg/kg	600 mg/kg	1,200 mg/kg [a]	1,200 mg/kg [b]
Red blood cells (x10^6/µl)	6.75±0.08	6.73±0.08	6.69±0.10	6.60±0.10	6.67±0.15
Hemoglobin (g/dl)	14.72±0.14	14.49±0.19	14.53±0.18	14.42±0.13	14.31±0.29
Hematocrit (%)	40.44±0.50	40.10±0.65	41.00±0.81	39.30±0.39	40.50±0.68
Mean corpuscular volume (fl)	59.81±0.38	59.64±0.43	60.96±0.53	59.3 0±0.44	60.42±0.58
Mean corpuscular hemoglobin (pg)	21.81±0.32	21.61±0.09	21.71±0.22	21.86±0.21	21.47±0.26
Mean corpuscular hemoglobin concentration (g/dl)	36.46±0.46	36.24±0.24	35.64±0.40	36.89±0.16	35.52±0.41
Platelet (x10^5/µl)	7.45±0.14	7.85±0.18	7.40±0.29	7.61±0.27	7.97±0.11

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.

Table 6. Hematological values of male rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	*I. cylindrica*			
		300 mg/kg	600 mg/kg	1,200 mg/kg [a]	1,200 mg/kg [b]
Red blood cells (x10^6/µl)	7.99±0.17	7.34±0.09*	7.59±0.14*	7.67±0.06	7.45±0.06*
Hemoglobin (g/dl)	15.56±0.26	14.39±0.16*	14.59±0.22*	15.29±0.24	15.44±0.12
Hematocrit (%)	46.40±1.01	43.00±0.61*	44.10±0.78*	44.60±0.30	44.80±0.80
Mean corpuscular volume (fl)	57.32±0.33	58.48±0.33	57.72±0.22	58.02±0.27	59.74±0.70*
Mean corpuscular hemoglobin (pg)	19.06±0.42	19.61±0.07	19.22±0.18	19.93±0.37*	20.70±0.11*
Mean corpuscular hemoglobin concentration (g/dl)	33.25±0.63	33.53±0.20	33.32±0.20	34.33±0.54	34.68±0.39*
Platelet (x10^5/µl)	7.99±0.09	7.95±0.09	7.86±0.11	8.23±0.16	8.34±0.24

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, p<0.05.**

blood cells decreased. The differential white blood cell count values of female and male treated rats are shown in Table 7. In the female treated groups, there were no significant changes in any values at any of the three given doses compared with their control values. Yet, a significant decrease in neutrophil and a significant increase in lymphocyte and eosinophil were observed in the female satellite group. In male rats treated with 1,200 mg/kg/day, neutrophil, lymphocyte and eosinophil were significantly different from the control values. However, such changes of these values were minor, and most importantly the alteration of hematological and white blood cell count values were insignificant and remained within the normal range (Feldman *et al*., 2000; Inala *et al*., 2002). In addition, the normal blood smear was detected.

Clinical blood chemistry examination was

Table 7. Differential white blood cell count values of rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	*I. cylindrica*			
		300 mg/kg	600 mg/kg	1,200 mg/kg [a]	1,200 mg/kg [b]
Female					
White blood cells (x10^3/µl)	3.10±0.27	2.91±0.18	2.91±0.24	2.54±0.28	3.21±0.23
Neutrophil (%)	19.44±1.85	15.60±1.44	17.10±1.21	15.80±1.60	11.10±1.62*
Lymphocyte (%)	73.56±2.04	78.10±1.72	74.80±1.52	78.50±1.66	80.10±1.79*
Monocyte (%)	6.22±0.49	5.00±0.49	6.00±0.29	5.00±0.33	6.40±0.73
Eosinophil (%)	0.78±0.36	1.30±0.30	1.10±0.23	1.00±0.29	2.40±0.37*
Basophil (%)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Male					
White blood cells (x10^3/µl)	3.84±0.15	3.76±0.15	3.46±0.28	3.73±0.23	4.08±0.14
Neutrophil (%)-	14.90±1.52	17.20±2.85	15.50±2.10	24.90±2.42*	19.70±1.17
Lymphocyte (%)	77.90±1.26	75.10±3.34	76.60±2.20	68.80±2.40*	73.90±1.68
Monocyte (%)	5.10±0.91	5.90±1.11	5.80±0.69	5.90±1.10	5.30±0.68
Eosinophil (%)	2.30±0.51	1.80±0.32	2.10±0.80	0.70±0.49*	1.10±0.31
Basophil (%)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, $p<0.05$.**

performed in order to evaluate any toxic effects on liver and kidney. The results are summarized in Tables 8 and 9. A significant decrease only in BUN in female rats treated with the extract at the dose of 300 mg/kg/day was observed. Treatment with 600 mg extract/kg/day caused significant decreases in BUN, creatinine, and total bilirubin as compared with the controls. In the satellite female group, BUN, creatinine and alkaline phosphatase (ALP) were significantly decreased from their control values; on the contrary, a significant increase in total protein concentration was found. In male rats treated with 300 mg/kg/day showed a significant decrease in BUN, while SGPT was found to be significantly increased relative to the control group. Giving the extract at the dose of 600 mg/kg/day caused a significant increase in total protein concentration, while SGOT was significantly decreased at the dose of 1,200 mg/kg/day. In the satellite group, creatinine and total protein were significantly increased relative to its control value. However, the levels of these clinical blood chemical parameters were minor changes and still within the normal range (Angkhasirisap *et al*., 2002; Barry, 1995; Caisey and King, 1980; Sacher and McPherson, 1991a, 1991b). Because these clinical blood chemical parameters are the index of kidney and liver function, it suggests that the extract does not induce toxicity to the kidneys and liver. These observations were further confirmed by the histological assessment of the organs shown in Figures 1-4. The results showed that the extract of *I. cylindrica* did not produce a significant damage in the internal organs such as liver and kidney. In conclusion, the extract from the root of *I. cylindrica* at the oral doses treated did not cause either acute or subchronic toxicities in rats.

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Table 8. Clinical blood chemistry values of female rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	*I. cylindrica*			
		300 mg/kg	600 mg/kg	1,200 mg/kg [a]	1,200 mg/kg [b]
Glucose (mg/dl)	104.30±2.52	100.30±3.79	101.90±4.36	100.90±2.97	109.20±2.13
BUN (mg/dl)	22.70±1.23	19.90±0.48*	20.00±0.68*	20.90±0.98	19.00±0.73*
Creatinine (mg/dl)	0.41±0.02	0.40±0.01	0.35±0.01*	0.38±0.01	0.35±0.01*
Total protein (g/dl)	5.06±0.08	5.10±0.07	5.15±0.09	5.13±0.06	5.46±0.13*
Albumin (g/dl)	3.57±0.05	3.62±0.05	3.55±0.04	3.58±0.06	3.66±0.04
Total bilirubin (mg/dl)	0.16±0.01	0.15±0.01	0.12±0.01*	0.15±0.01	0.17±0.01
Direct bilirubin (mg/dl)	0.00±0.00	0.00±0.00	0.00±0.00	0.01±0.01	0.00±0.00
SGOT (U/l)	103.80±2.55	98.00±4.61	110.60±10.61	91.90±3.93	98.20±6.74
SGPT (U/l)	30.33±1.50	26.90±1.11	29.70±4.18	27.20±2.48	31.30±3.16
ALP (U/l)	42.00±2.52	40.00±1.79	40.40±2.68	39.90±1.79	31.40±2.63*

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, p<0.05.**

Table 9. Clinical blood chemistry values of male rats in the subchronic toxicity study of the water extract from root of *Imperata cylindrica* (Linn.) Raeusch.

	Control	*I. cylindrica*			
		300 mg/kg	600 mg/kg	1,200 mg/kg [a]	1,200 mg/kg [b]
Glucose (mg/dl)	126.00±4.42	130.80±5.95	120.20±5.95	129.80±4.87	134.30±3.97
BUN (mg/dl)	21.00±0.91	18.70±0.47*	19.30±0.85	22.60±0.58	20.10±0.64
Creatinine (mg/dl)	0.30±0.02	0.29±0.01	0.27±0.01	0.29±0.01	0.37±0.01*
Total protein (g/dl)	5.06±0.08	5.10±0.07	5.15±0.09	5.13±0.11	5.46±0.13*
Albumin (g/dl)	3.57±0.05	3.62±0.05	3.55±0.04	3.58±0.06	3.66±0.04
Total bilirubin (mg/dl)	0.16±0.01	0.15±0.01	0.12±0.01*	0.15±0.00	0.17±0.01
Direct bilirubin (mg/dl)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
SGOT (U/l)	112.20±4.90	126.60±8.58	97.60±2.40	89.50±3.91*	112.80±7.09
SGPT (U/l)	39.80±4.21	53.10±5.52*	37.70±1.84	34.90±1.88	38.30±2.76
ALP (U/l)	68.20±6.09	83.70±4.54	82.50±7.76	67.50±4.56	66.40±8.85

Values are expressed as mean ± S.E.M., n = 10
a: A group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days.
b: A satellite group was treated with the water extract from root of *I. cylindrica* at 1,200 mg/kg/day for 90 days followed by no treatment for 28 days.
*** Significantly different from control, p<0.05.**

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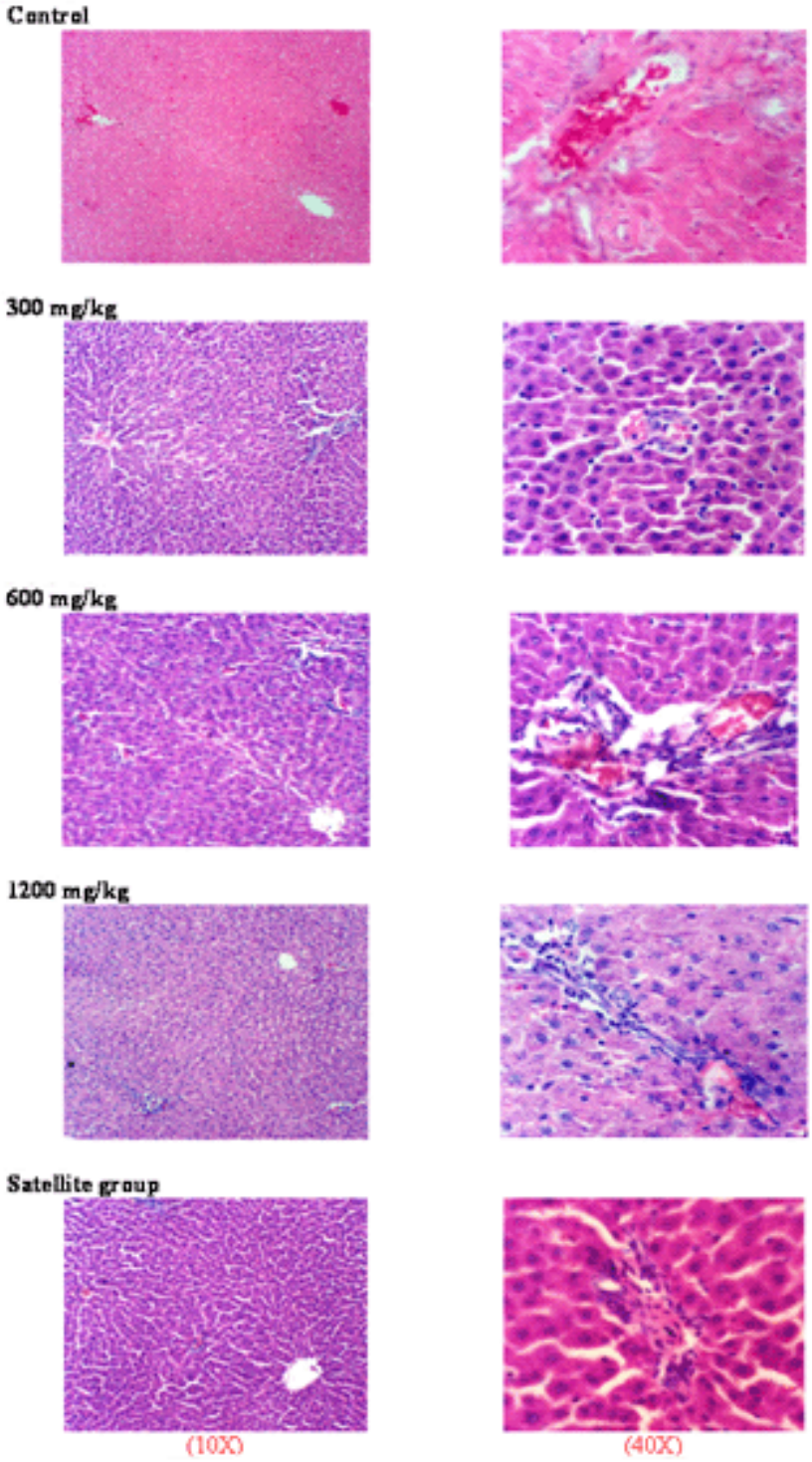

Figure 1. The histology of male liver from the control and treated groups (the 10x and 40x magnifications). No significant damage was detected in any treatment group.
[Color figure can be viewed in the electronic version]

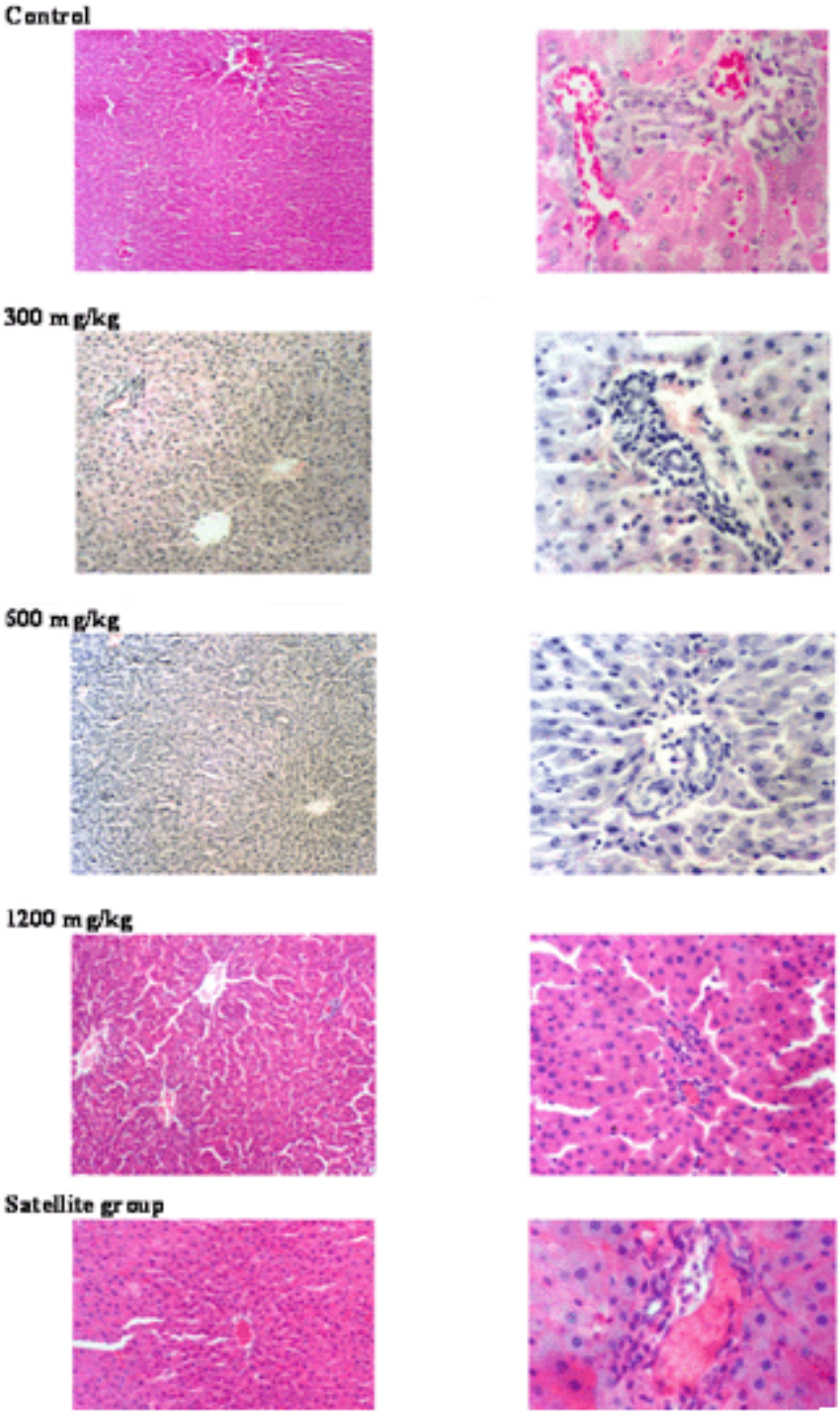

Figure 2. The histology of female liver from the control and treated groups (the 10x and 40x magnifications). No significant damage was detected in any treatment group.

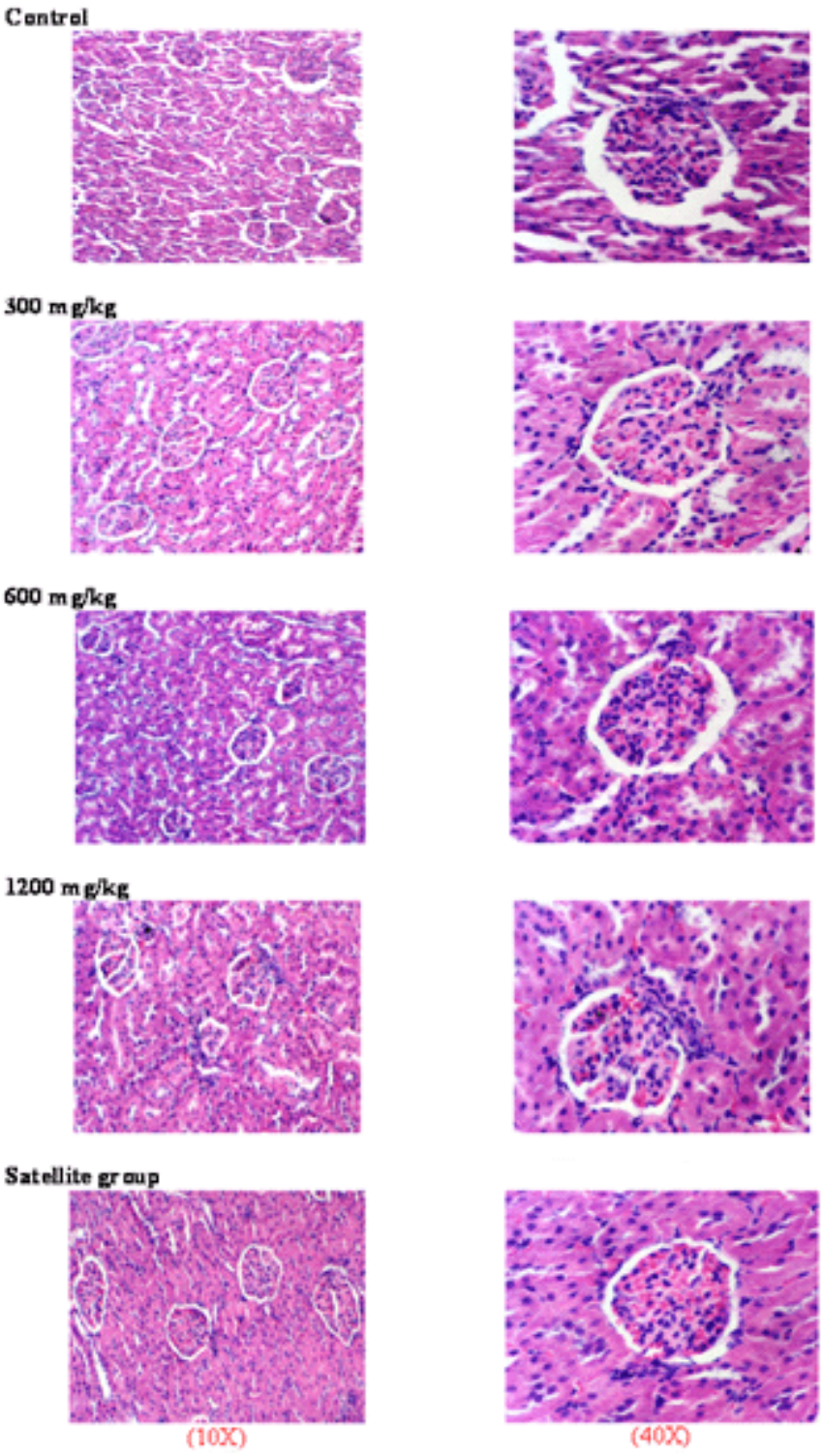

Figure 3. The histology of male kidney from the control and treated groups (the 10x and 40x magnifications). No significant damage was detected in any treatment group.

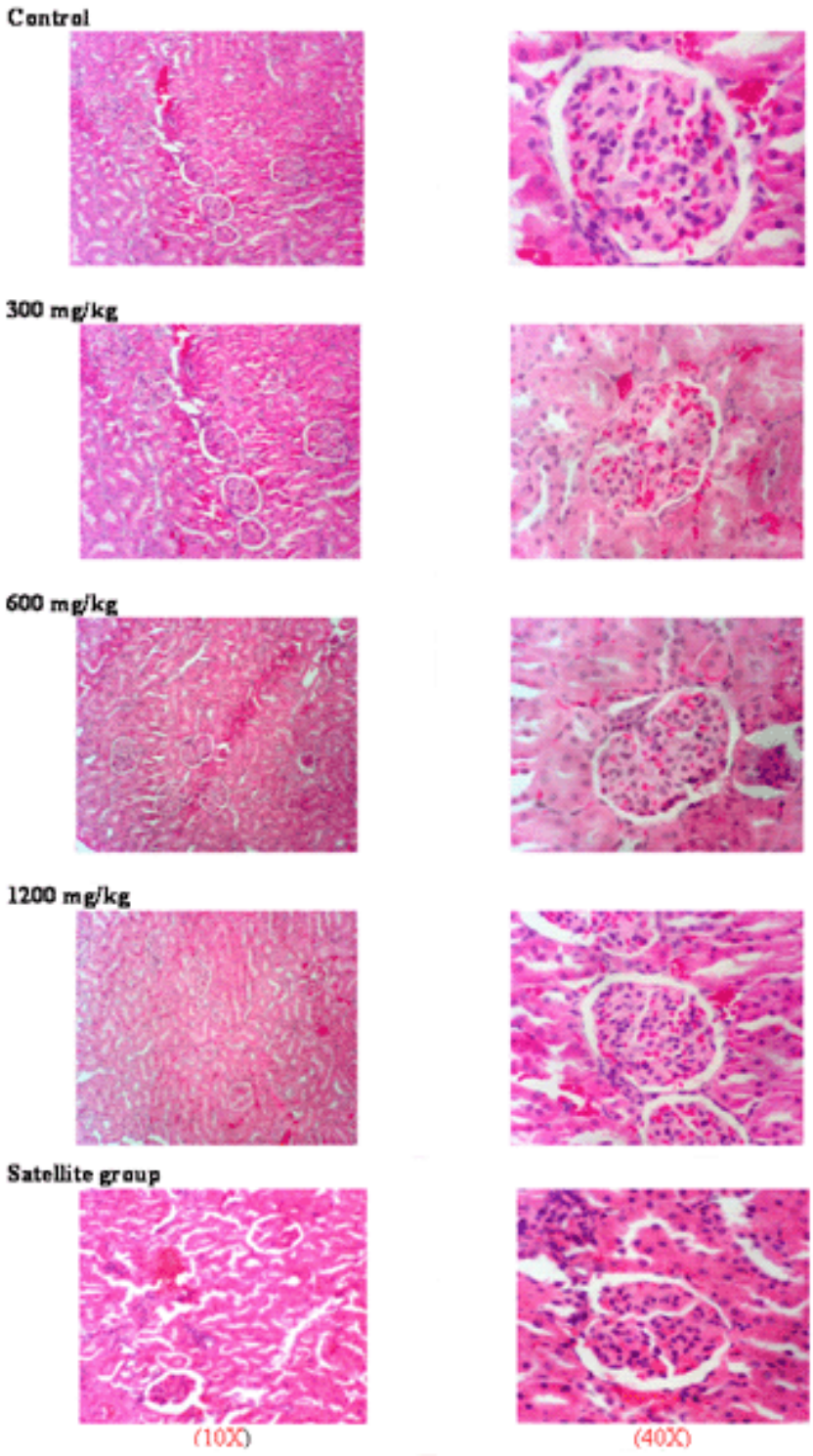

Figure 4. The histology of female kidney from the control and treated groups (the 10x and 40x magnifications). No significant damage was detected in any treatment group.

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