Acute and Sub-Chronic Toxicity of Tri-Sa-Maw Recipe in Rats

Urarat Nanna MS*,
Kanjana Jaijoy PhD**, Nirush Lertprasertsuke PhD***,
Noppamas Soonthornchareonnon PhD****, Seewaboon Sireeratawong PhD*,*****

** Division of Pharmacology, Department of Preclinical Science, Faculty of Medicine, Thammasat University, Rungsit Campus, Pathumthani, Thailand*
*** McCormick Faculty of Nursing, Payap University, Chiang Mai, Thailand*
**** Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*
***** Department of Pharmacognosy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand*
****** Department of Pharmacology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*

Background: *Tri-sa-maw recipe is a botanical preparation comprised of equal proportions of the three herbal fruits, namely Terminalia chebula Retz., Terminalia sp. and Terminalia bellirica Roxb. This recipe is used for antipyretic, expectorant, periodic maintenance, and relieving stomach tight.*
Objective: *To evaluate the acute and sub-chronic toxicities of Tri-sa-maw recipe extract in rats.*
Material and Method: *In the present study of acute toxicity, a single oral dose 5,000 mg/kg of Tri-sa-maw recipe extract was administered to rats. Sub-chronic toxicity was studied by the daily oral administration of the extract at the doses of 600, 1,200 and 2,400 mg/kg body weight for consecutive 90 days.*
Results: *Tri-sa-maw recipe extract at the dose of 5,000 mg/kg showed no signs of differences as compared to the control rat. No abnormalities were found in the sub-chronic toxicity study; none of the parameters for body and organ weights, hematology, blood chemistry, necropsy, and histopathology showed any differences between the control and all treatment groups.*
Conclusion: *Tri-sa-maw recipe extract did not significantly cause acute toxicity or sub-chronic toxicity in rats.*

Keywords: *Tri-sa-maw recipe, Acute toxicity, Sub-chronic toxicity*

J Med Assoc Thai 2015; 98 (Suppl. 2): S8-S15
Full text. e-Journal: *http://www.jmatonline.com*

Tri-sa-maw recipe is a botanical preparation comprised of equal proportions of the three herbal fruits, including *Terminalia chebula* Retz., *Terminalia sp.* and *Terminalia bellirica* Roxb. This recipe has long been used for reducing fever, expectorant, periodic maintenance, and relieving stomach tightness. The toxicity evaluation of *T. chebula* and *T. bellirica* has been reported in previous studies. The water extract of *T. chebula*[1] and *T. bellerica*[2] given orally to female and male rats did not produce acute nor chronic toxicities. Nonetheless, toxicity effects of a Tri-sa-maw recipe have never been determined. The aim of the present study is therefore to assess the adverse effects related to different doses in order to find the acceptably safe levels of the Tri-sa-maw recipe in rats by determining both oral acute and sub-chronic toxicities.

Correspondence to:
Nanna U, Division of Pharmacology, Department of Preclinical Science, Faculty of Medicine, Thammasat University, Rungsit Campus, Pathumthani 12120, Thailand.
Phone: +66-2-9269710, Fax: +66-2-9269711
E-mail: assist.prof.ae@gmail.com

Material and Method

Plant materials

The fruits of *T. chebula*, *T. bellerica* and *Terminalia sp.* were identified by Associate Professor Dr. Noppamas Soonthornchareonnon, Department of Pharmacognosy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand. The voucher specimen has been kept at the Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.

Extraction method

Each plant material was dried in hot air oven at 50°C, ground into a fine powder and sifted through a sieve (No. 100). The Tri-sa-maw recipe was prepared by the Thai-China Flavours and Fragrnces Industry Co., Ltd. The quality control of raw materials and the water extract of the Tri-sa-maw recipe was followed by

Thai Herbal Pharmacopoeia including organoleptic examination, % loss on drying, extractive values, total ash and acid insoluble ash[3]. The chemical constituents in raw materials and the extract were also studied using thin layer chromatography (TLC) following the method of Farnswort[4].

Experimental animals

Male and female Sprague Dawley rats, weighing within 220-270 g were obtained from the National Laboratory Animal Center, Mahidol University, Nakorn Pathom, Thailand. Animals were housed under standard environmental conditions of 24±1°C, under a 12 h dark-light cycle, and were allowed free access to drinking water and standard pellet diet. The Animal Ethics Committee of Faculty of Medicine, Thammasat University, Pathumthani, Thailand, approved all experimental protocols (009/2555).

Acute toxicity[5,6]

Ten rats per sex were administrated a single oral dose of 5,000 mg/kg body weight while the control group received water vehicle. The animals were observed for any signs of toxicity, body weight, and mortality over 14 days. On the 15th day, all rats fasted overnight, and then sacrificed (pentobarbital sodium, 50 mg/kg, ip) for necropsy examination. The internal organs (brain, heart, lung, liver, spleen, pancreas, adrenal, kidney, ovary, uterus, testis, epididymis) were excised and weighed. The gross pathological observations of the tissues were performed.

Sub-chronic toxicity[5,7]

Rats were divided into 5 groups of 20 animals (10 male and 10 female). Tri-sa-maw recipe at the doses of 600, 1,200 and 2,400 mg/kg were administered orally for consecutive 90 days, while the control groups received distilled water. Signs of toxicity, mortality and body weight changes were monitored daily. At the end of the experiment, all animals were kept fasted for 16-18 h and then anesthetized with pentobarbital sodium (50 mg/kg, ip). Blood samples were collected from the common carotid artery for hematological examination and clinical blood chemistry. The internal organs (heart, lung, thymus, liver, kidney, spleen, adrenal, small intestine, stomach and duodenum, muscle with sciatic nerve, thoracic spines, brain, eyes, ovary, uterus, testis and epididymis) were weighed and observed for gross lesions. All tissues were preserved in 10% neutral buffered formaldehyde solution for histopathological examination.

Statistical analysis

The results were expressed as mean ± standard error of mean (SEM). The statistical significance was determined by one-way analysis of variance (ANOVA) and Dunnett's test. The *p*-values less than 0.05 were considered significant.

Results and Discussion

In the present study of acute toxicity, both female and male rats received the Tri-sa-maw recipe extract 5,000 mg/kg did not show any toxic signs and symptoms during the experimentation period. The body weight and internal organ weight of the treated rats were relatively similar to that of the control group (Table 1-3). The internal organs (brain, lung, heart, liver, spleen, pancreas, adrenal gland, kidney, and sex organ) of all groups of rats had no difference in gross and weight examinations. This suggests that the Tri-sa-maw recipe

Table 1. Effect of Tri-sa-maw recipe of body weights of rats in acute toxicity study

	Body weight (g)			
	Day 0	Day 7th	Day 14th on 14th day	Weight gain
Female				
Control	230.50±3.37	250.50±4.11	267.50±3.25	37.00±3.67
Tri-sa-maw recipe 5,000 mg/kg	229.00±5.04	248.50±3.73	264.50±3.53	35.50±4.18
Male				
Control	229.00±3.05	262.50±4.03	302.00±5.88	73.00±4.48
Tri-sa-maw recipe 5,000 mg/kg	222.50±4.24	252.00±5.49	297.50±4.17	72.00±2.81

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

extract is not toxic after an acute exposure in rats.

In the sub-chronic toxicity, Tri-sa-maw recipe extract (600, 1,200 and 2,400 mg/kg) did not cause any change neither in general behavior nor in health condition during the experimentation period. Furthermore, no morbidity or disease was observed during the entire experimentation period. At day 90th, the body weights of the female rats were not different in all test groups (Table 4). However, we detected a significant decrease in body weight of male rats receiving extract at 2,400 mg/kg (Table 5). However, the effect on body weight may have resulted from physiological changes such as less food intake, and metabolism. The internal organs of the treated and the control rats were not different in both gross and microscopic examination (Table 6, 7). Kidney weight of the satellite female group and lung weight of 2,400 mg/kg male treatment group showed significant differences when compared with those of the control group.

The hematological values reflect any toxic effects on function of bone marrow. White blood cell count was used to evaluate the immune system. The hematological values (Table 8, 9) and differential white blood cell counts (Table 10, 11) of female and male treatment rats were not significantly different from those of the control.

The clinical blood chemistry values were used to evaluate any toxic effects on liver, kidney and pancreas, as shown in Table 12, 13. The significant differences among the satellite female groups were evident in the parameters of glucose, blood urea nitrogen (BUN), total protein and total bilirubin. In the treated male rats, the values of creatinine, total protein, albumin and serum glutamic-oxaloacetic transaminase

Table 2. Effect of Tri-sa-maw recipe extract on internal organ weights (gram) of female rats in acute toxicity study

	Control	Tri-sa-maw recipe 5,000 mg/kg
Brain	1.81±0.03	1.80±0.03
Lung	1.43±0.03	1.42±0.03
Heart	0.86±0.03	0.81±0.01
Liver	7.63±0.19	7.25±0.17
Pancreas	0.91±0.03	0.86±0.03
Spleen	0.68±0.03	0.63±0.01
Adrenal	0.04±0.00	0.04±0.00
Kidney	0.88±0.01	0.90±0.02
Ovary	0.09±0.00	0.06±0.00
Uterus	0.63±0.09	0.52±0.06

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 3. Effect of Tri-sa-maw recipe extract on internal organ weights (gram) of male rats in acute toxicity study

	Control	Tri-sa-maw recipe 5,000 mg/kg
Brain	1.78±0.04	1.73±0.04
Lung	1.34±0.07	1.39±0.02
Heart	0.84±0.03	0.91±0.03
Liver	8.88±0.39	9.43±0.52
Pancreas	0.81±0.06	0.84±0.03
Spleen	0.71±0.04	0.63±0.03
Adrenal	0.03±0.00	0.03±0.00
Kidney	1.03±0.02	1.05±0.02
Testis	1.68±0.02	1.73±0.03
Epididymis	0.44±0.01	0.44±0.01

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 4. Effect of Tri-sa-maw recipe on body weights of female rats in sub-chronic toxicity study

	Body weight (g)					Weight gain on day 90 (g)
	Day 0	Day 30	Day 60	Day 90	Day 118	
Control	253.50±3.17	292.50±3.44	305.50±3.83	322.50±4.10	-	69.00±3.23
Tri-sa-maw recipe						
600 mg/kg	258.50±2.89	295.00±3.33	302.50±3.67	319.50±3.11	-	61.00±3.32
1,200 mg/kg	256.00±2.96	287.50±5.59	306.00±5.04	320.00±3.87	-	64.00±1.94
2,400 mg/kg	258.00±3.67	287.50±5.93	305.00±6.06	320.00±6.50	-	62.00±5.07
Satellite	257.50±4.79	293.00±5.17	304.50±4.50	323.50±5.48	328.50±6.24	66.00±4.82

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 5. Effect of Tri-sa-maw recipe on body weights of male rats in sub-chronic toxicity study

	Body weight (g)					Weight gain on day 90 (g)
	Day 0	Day 30	Day 60	Day 90	Day 118	
Control	266.00±3.56	396.50±10.03	452.50±11.58	486.50±11.40	-	220.50±10.07
Tri-sa-maw recipe						
600 mg/kg	266.50±2.36	378.50±5.78	436.50±5.73	465.00±7.71	-	198.50±6.24
1,200 mg/kg	270.00±2.36	397.00±4.55	447.50±4.61	477.50±4.67	-	207.50±4.61
2,400 mg/kg	269.00±2.56	374.50±3.37*	423.50±4.35*	449.50±6.60*	-	180.50±5.89*
Satellite	264.50±2.63	382.00±4.48	447.50±6.02	483.00±5.73	499.50±6.17	218.50±3.88

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 6. Effect of Tri-sa-maw recipe on internal organ weights (gram) of female rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Brain	1.92±0.02	1.88±0.02	1.93±0.05	1.89±0.02	1.93±0.03
Lung	1.46±0.08	1.44±0.09	1.49±0.07	1.39±0.04	1.30±0.04
Heart	1.21±0.05	1.13±0.03	1.14±0.03	1.16±0.03	1.10±0.04
Liver	8.61±0.16	8.97±0.21	9.01±0.26	8.46±0.24	8.28±0.43
Spleen	0.70±0.02	0.75±0.03	0.77±0.03	0.70±0.03	0.64±0.02
Pancreas	0.67±0.02	0.68±0.04	0.70±0.02	0.73±0.04	0.80±0.07
Adrenal	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00
Kidney	1.04±0.01	1.06±0.02	1.08±0.02	1.05±0.03	0.90±0.02*
Ovary	0.06±0.00	0.07±0.00	0.06±0.00	0.06±0.00	0.06±0.00
Uterus	0.57±0.04	0.68±0.15	0.59±0.05	0.64±0.08	0.68±0.07

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 7. Effect of Tri-sa-maw recipe on internal organ weights (gram) of male rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Brain	2.02±0.01	1.99±0.02	2.01±0.02	2.00±0.02	2.01±0.02
Lung	1.52±0.06	1.55±0.04	1.60±0.04	1.99±0.23*	1.61±0.04
Heart	1.57±0.05	1.55±0.04	1.63±0.03	1.56±0.05	1.47±0.04
Liver	13.39±0.54	13.23±0.41	13.21±0.26	12.12±0.31	12.69±0.50
Spleen	0.88± 0.02	0.88±0.03	0.93±0.03	0.93±0.03	0.91±0.03
Pancreas	0.76±0.03	0.86±0.06	0.81±0.04	0.84±0.07	0.92±0.12
Adrenal	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00
Kidney	1.54±0.04	1.46±0.03	1.56±0.03	1.39±0.03	1.47±0.03
Testis	2.01±0.02	2.01±0.02	2.01±0.02	1.99±0.02	2.02±0.02
Epididymis	0.75±0.02	0.73±0.01	0.75±0.01	0.76±0.02	0.79±0.01

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 8. Effect of Tri-sa-maw recipe on hematological values of female rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Red blood cell ($x10^6$/µl)	7.23±0.09	7.13±0.07	7.24±0.12	7.14±0.06	6.81±0.12
Hemoglobin (g/dl)	14.45±0.12	14.16±0.12	14.24±0.20	14.10±0.17	13.81±0.19
Hematocrit (%)	41.40±0.40	40.50±0.45	41.20±0.65	40.80±0.33	39.70±0.65
Mean corpuscular volume (fl)	57.27±0.44	56.81±0.18	56.90±0.27	56.91±0.26	58.37±0.44
Mean corpuscular hemoglobin (pg)	20.01±0.17	19.86±0.08	19.67±0.09	19.86±0.10	20.30±0.14
Mean corpuscular hemoglobin concentration (g/dl)	34.91±0.18	34.95±0.16	34.58±0.17	34.65±0.08	34.76±0.19
Platelet ($x10^5$/µl)	6.41±0.16	6.55±0.16	6.09±0.33	5.62±0.45	6.61±0.18

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 9. Effect of Tri-sa-maw recipe on hematological values of male rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Red blood cell ($x10^6$/µl)	7.79±0.13	7.58±0.10	7.59±0.07	7.61±0.08	7.72±0.12
Hemoglobin (g/dl)	15.13±0.20	14.84±0.14	14.74±0.14	14.77±0.17	15.03±0.13
Hematocrit (%)	43.00±0.71	41.90±0.55	41.70±0.45	41.70±0.30	43.10±0.46
Mean corpuscular volume (fl)	54.98±0.24	55.17±0.19	55.90±1.05	55.49±0.42	55.74±0.42
Mean corpuscular hemoglobin (pg)	19.44±0.17	19.59±0.12	19.43±0.11	19.42±0.16	19.49±0.22
Mean corpuscular hemoglobin concentration (g/dl)	35.35±0.27	35.50±0.20	35.24±0.19	35.00±0.33	35.00±0.22
Platelet ($x10^5$/µ)	6.78±0.44	7.59±0.25	7.15±0.19	7.00±0.35	7.72±0.72

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 10. Effect of Tri-sa-maw recipe on differential white blood cell count values of female rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
White blood cell ($x10^3$/µl)	2.46±0.11	2.97±0.21	2.97±0.27	2.33±0.18	3.18±0.41
Neutrophil ($x10^3$/µl)	0.46±0.06	0.46±0.06	0.46±0.05	0.32±0.03	0.61±0.15
Lymphocyte ($x10^3$/µl)	1.83±0.09	2.26±0.15	2.26±0.22	1.81±0.14	2.34±0.21
Monocyte ($x10^3$/µl)	0.11±0.01	0.18±0.03	0.20±0.03	0.16±0.03	0.16±0.04
Eosinophil ($x10^3$/µl)	0.06±0.01	0.06±0.01	0.06±0.01	0.05±0.01	0.07±0.02
Basophil ($x10^3$/µl)	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 ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 11. Effect of Tri-sa-maw recipe on differential white blood cell count values of male rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
White blood cell ($x10^3$/µl)	4.59±0.29	4.65±0.23	4.33±0.41	4.68±0.31	4.13±0.23
Neutrophil ($x10^3$/µl)	0.83±0.09	0.86±0.06	0.73±0.11	0.85±0.06	0.76±0.15
Lymphocyte ($x10^3$/µl)	3.37±0.24	3.31±0.18	3.30±0.28	3.41±0.29	3.09±0.15
Monocyte ($x10^3$/µl)	0.35±0.08	0.39±0.05	0.24±0.05	0.33±0.07	0.21±0.03
Eosinophil ($x10^3$/µl)	0.09±0.01	0.09±0.01	0.06±0.01	0.09±0.01	0.06±0.01
Basophil ($x10^3$/µl)	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 ± SEM, n = 10
* Significantly different from control, $p<0.05$

(SGOT) were significantly different from those of the control. However, these values were not lower or higher than one-fold when compared with those of the control group, and these significant values remained within

Table 12. Effect of Tri-sa-maw recipe on clinical blood chemistry values of female rats in sub-chronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Glucose (mg/dl)	138.00±4.28	127.60±4.13	131.80±4.77	128.10±3.23	169.60±11.0*
BUN (mg/dl)	24.32±1.32	19.89±1.00*	21.55±0.84	21.35±0.73	20.37±0.52*
Creatinine (mg/dl)	0.72±0.03	0.66±0.03	0.70±0.03	0.67±0.03	0.73±0.02
Total protein (g/dl)	6.88±0.13	6.65±0.15	6.76±0.18	6.45±0.20	7.68±0.16*
Albumin (g/dl)	3.39±0.05	3.29±0.04	3.38±0.06	3.27±0.07	3.24±0.04
Total bilirubin (mg/dl)	0.13±0.02	0.15±0.02	0.14±0.02	0.13±0.02	0.28±0.02*
Direct bilirubin (mg/dl)	0.07±0.00	0.08±0.00	0.07±0.00	0.07±0.00	0.08±0.00
SGOT (U/l)	126.80±4.60	149.50±28.04	136.80±9.79	119.40±12.45	114.70±7.81
SGPT (U/l)	39.40±2.70	61.30±21.37	42.80±3.98	39.60±1.69	45.30±4.52
Alkaline phosphatase (U/l)	49.90±3.15	49.30±2.20	46.60±1.80	46.40±2.09	46.50±3.15

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

Table 13. Effect of Tri-sa-maw recipe on clinical blood chemistry values of male rats in subchronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1,200	2,400	Satellite
Glucose (mg/dl)	136.00±2.98	139.10±5.88	134.00±5.07	127.70±5.32	150.60±3.72
BUN (mg/dl)	16.61±0.40	34.69±16.93	17.69±0.57	18.26±0.72	16.44±0.32
Creatinine (mg/dl)	0.55±0.03	0.52±0.02	0.53±0.01	0.52±0.02	0.45±0.01*
Total protein (g/dl)	7.07±0.08	6.94±0.10	6.95±0.10	6.99±0.16	6.03±0.05*
Albumin (g/dl)	3.27±0.03	3.19±0.03	3.30±0.03	3.16±0.03*	3.16±0.02*
Total bilirubin (mg/dl)	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00
Direct bilirubin (mg/dl)	0.06±0.00	0.06±0.00	0.06±0.00	0.06±0.00	0.06±0.00
SGOT (U/l)	129.00±5.20	125.00±4.91	137.70±6.38	123.20±4.89	84.70±7.36*
SGPT (U/l)	39.10±1.48	38.50±1.48	45.90±3.56	43.30±3.67	45.00±5.93
Alkaline phosphatase (U/l)	60.90±2.00	58.40±2.58	55.30±1.93	67.90±9.20	51.80±1.35

Values are expressed as mean ± SEM, n = 10
* Significantly different from control, $p<0.05$

the normal range[8].

Necropsy and histopathological examinations were performed further to confirm whether or not the internal organs or tissues had been damaged[9]. The results showed neither macroscopic nor microscopic changes in the internal organs or tissues in any of the treatment rats, indicating that this test substance has no toxic effect.

In conclusion, Tri-sa-maw recipe extract did not produce both acute and sub-chronic oral toxicities in either female or male rats. These data confirm that this Tri-sa-maw recipe is safe for experimental animals. Further study regarding toxicology of this extract should be carried out in non-rodent or humans in order to increase the confidence in their safety for the development of pharmaceutical products in the future.

Acknowledgement

The authors wish to extend their grateful thanks to Thammasat University for providing the funds required for the present study.

Potential conflicts of interest

None.

References

1. Panunto W, Jaijoy K, Soonthornchareonnon N, Lertprasertsuke N, Sireeratawong S. Acute and chronic toxicity studies of the water extract from dried fruits of *Terminalia chebula* Rezt. in rats. Int J Appl Res Nat Prod 2010; 3: 36-43.
2. Sireeratawong S, Jaijoy K, Panunto W, Nanna U, Lertprasertsuke N, Soonthornchareonnon N. Acute and chronic toxicity studies of the water extract from dried fruits of *Terminalia bellerica* (Gaertn.) Roxb. In Spargue-Dawley rats. Afr J Tradit Complement Altern Med 2012; 10: 223-31.
3. Department of Medical Sciences, Ministry of Public Health. (2000). Thai Herbal Pharmacopoeia Volume II. Nonthaburi, Thailand.
4. Farnsworth NR. Biological and phytochemical screening of plants. J Pharm Sci 1966; 55: 225-76.
5. World Health Organization (WHO). General guidelines for methodologies on research and evaluation of traditional medicine. Geneva: WHO; 2000.
6. Organization of Economic Co-operation and Development (OECD). Test guideline 420. Acute oral toxicity-fixed dose method. OECD Guideline for testing of chemicals. Paris: OECD; 2001.
7. Organization of Economic Co-operation and Development (OECD). Test guideline 408. Repeated dose 90-day oral toxicity study in rodents. OECD Guidelines for the testing of chemicals. Paris: OECD; 1998.
8. Angkhasirisap W, Inala P, Sirimontaporn A, Inpunkaew R, Rungrojejinda K, Kengkoom K, et al. Blood chemistry profiles of outbred Sprague-Dawley rat in The Facility of National Laboratory Animal Centre; 28th Congress on Science and Technology of Thailand. The Science Society of Thailand under the Patronage of His Majesty the King, Bangkok, Thailand; 2002.
9. Wilson NH, Hardisty JF, Hayes JR. Short-term, subchronic, and chronic toxicology studies. In: Hayes AW, editor. Principle and method of toxicity. 4th ed. Philadelphia: Taylor & Francis; 2001: 917-55.

ความเป็นพิษเฉียบพลันและพิษกึ่งเรื้อรังของตำรับยาตรีสมอในหนูแรท

อุรารัตน์ แน่นหนา, กาญจนา ใจจ้อย, นิรัชร์ เลิศประเสริฐสุข, นพมาศ สุนทรเจริญนนท์, สืวบูรณ์ สิริรัฐวงศ์

ภูมิหลัง: *ตำรับยาตรีสมอเป็นการเตรียมทางพฤกษศาสตร์ที่ประกอบด้วยสัดส่วนที่เท่ากันของผลสมุนไพร 3 ชนิดคือ สมอไทย (Terminalia chebula Retz.) สมอเทศ (Terminalia sp.) และสมอพิเภก (Terminalia bellirica Roxb.) ตำรับยานี้ใช้ลดไข้ ขับเสมหะ บำรุงร่างกายและบรรเทาอาการปวดแน่นท้อง*

วัตถุประสงค์: *เพื่อประเมินความเป็นพิษเฉียบพลันและพิษกึ่งเรื้อรังของสารสกัดตำรับยาตรีสมอในหนูแรท*

วัสดุและวิธีการ: *ในการศึกษาความเป็นพิษเฉียบพลัน สารสกัดตำรับยาตรีสมอขนาด 5,000 มิลลิกรัม/กิโลกรัม จะถูกนำมาป้อนให้หนูแรทครั้งเดียว ความเป็นพิษกึ่งเรื้อรังจะศึกษาโดยป้อนสารสกัดในขนาด 600, 1,200 และ 2,400 มิลลิกรัม/กิโลกรัมน้ำหนักตัวทุกวันเป็นเวลา 90 วัน*

ผลการศึกษา: *สารสกัดตำรับยาตรีสมอขนาด 5,000 มิลลิกรัม/กิโลกรัมไม่แสดงอาการผิดปกติเมื่อเทียบกับหนูแรท กลุ่มควบคุม ไม่พบความผิดปกติใด ๆ ในการศึกษาความเป็นพิษกึ่งเรื้อรัง ไม่ว่าจะเป็นน้ำหนักตัว น้ำหนักอวัยวะ ค่าโลหิตวิทยา ค่าเคมีคลินิกในเลือด การตรวจชิ้นเนื้อและจุลพยาธิวิทยา ซึ่งพบว่าไม่มีความแตกต่างระหว่างกลุ่มควบคุมกับกลุ่มที่ได้รับสารสกัด*

สรุป: *สารสกัดตำรับยาตรีสมอไม่ทำให้เกิดความเป็นพิษเฉียบพลันและพิษกึ่งเรื้อรังในหนูแรท*